

Twin Birth: Double Trouble or Double Joy?



Badreldeen Ahmed FRCOG MD (Newcastle – UK)





three chorionic



three amniotic

TRIPLETS



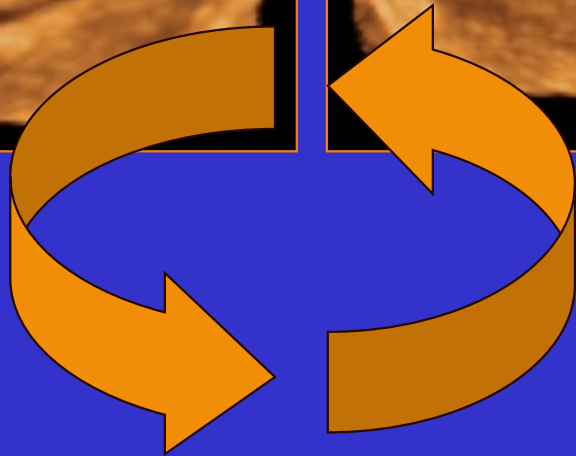
TRIPLETS



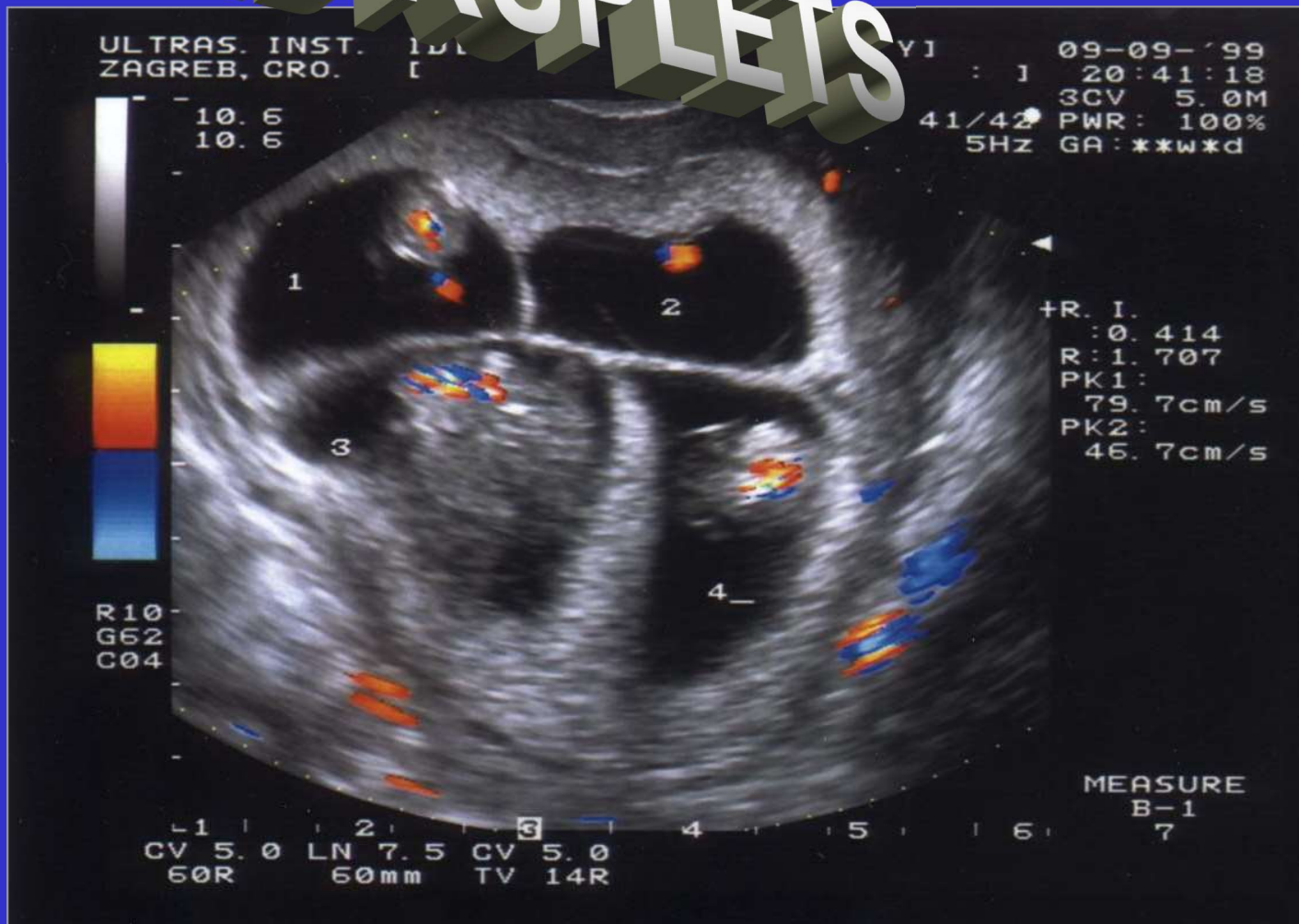
FRONT



BACK

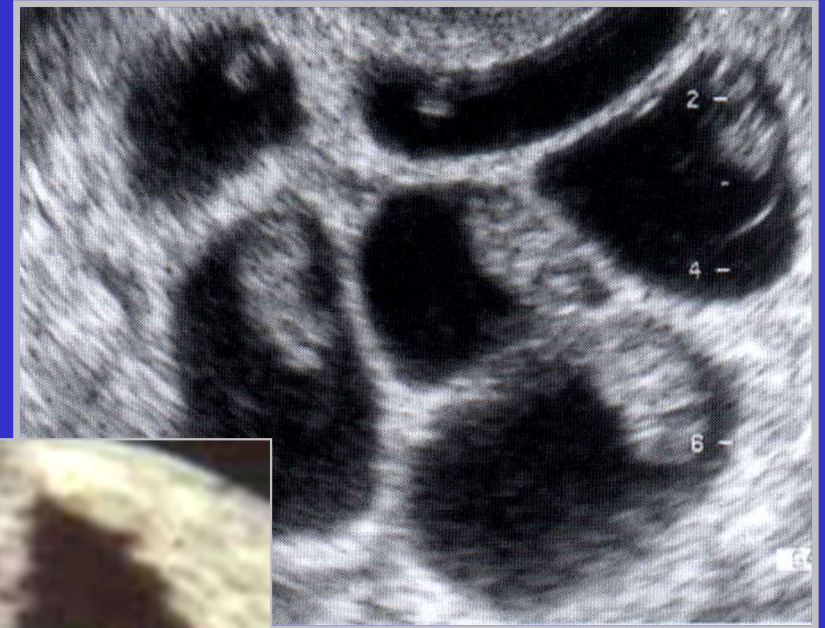


QUADRUPLETS



HIGH-ORDER MULTIPLE PREGNANCY

Pregnancy with three or more fetuses



Maternal age & multiple pregnancy

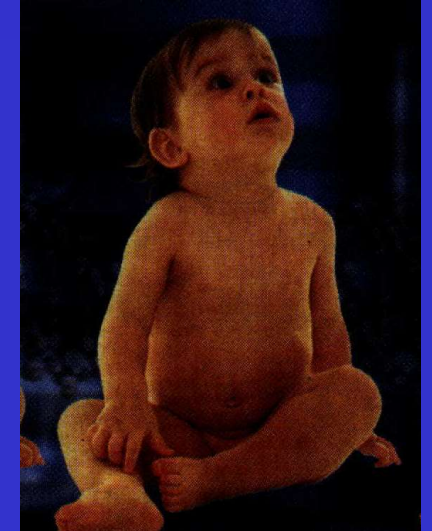
AGE	MP
< 30	44 %
30-34	40 %
35-39	25 %
> 40	<10 %



The Croatian Soc Human Reprod & MAR, 2000.



ASSISTED REPRODUCTION TECHNIQUES



**“ACCEPTABLE”
RATE OF
MULTIPLE
PREGNANCY**

**“SATISFACTORY”
PREGNANCY
RATE**

MULTIPLE PREGNANCY RATE

32 %



TWINS 30 %

TRIPLETS 5 %

HIGHER MULTIPLES 0.6 %

1th World Congress

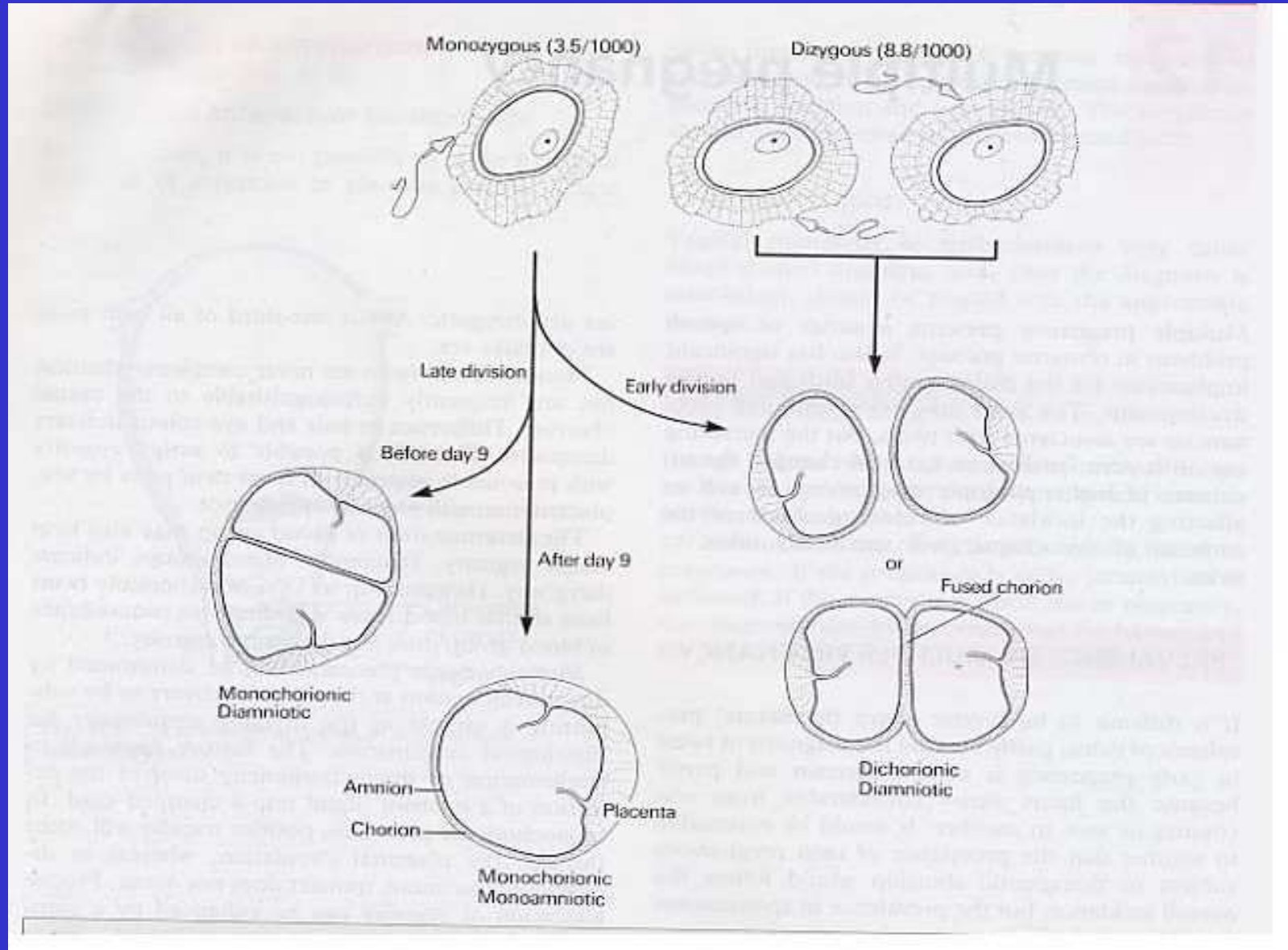
Twins Pregnancy – a Global Perspective

Venice – April 16 – 18, 2009

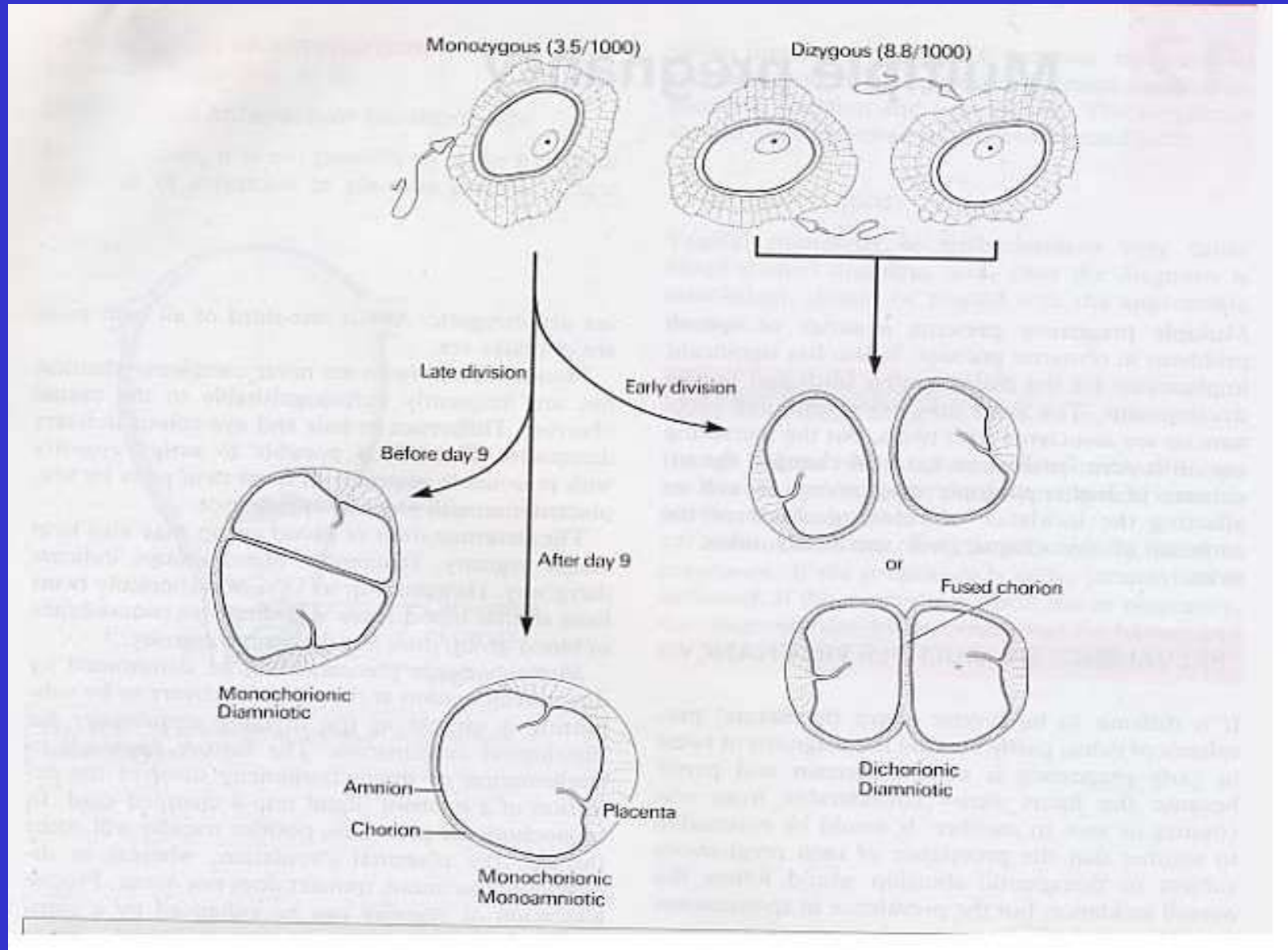
Transfer of Embryos: number?

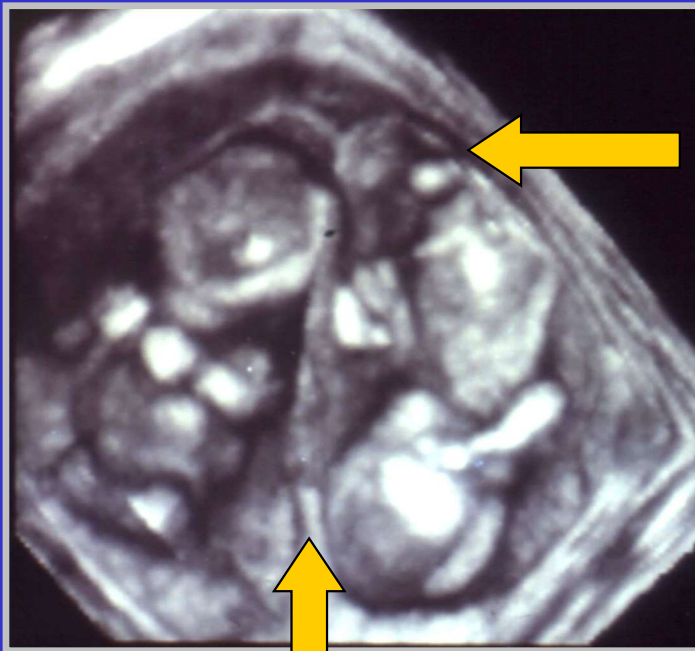
**PGD does it improve the delivery rate in
Women age 35 years and above**

Chorionicity Versus Zygosity

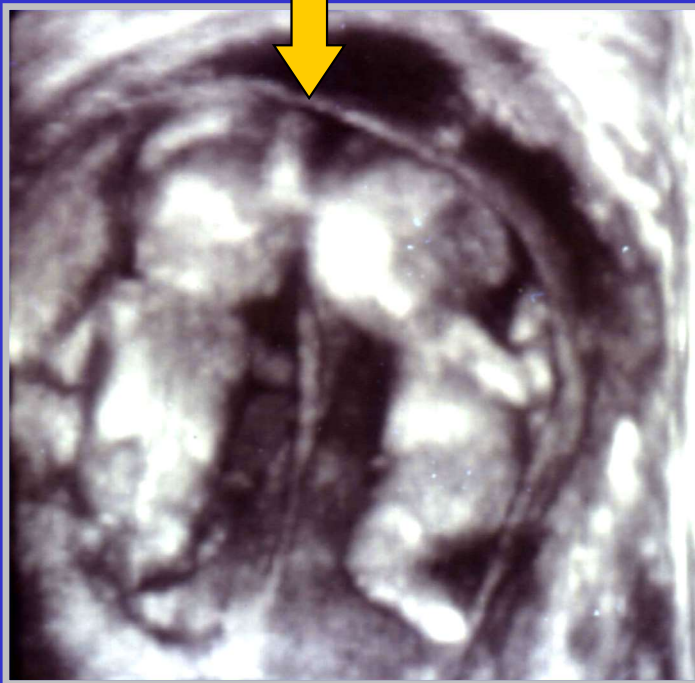


Chorionicity Versus Zygosity

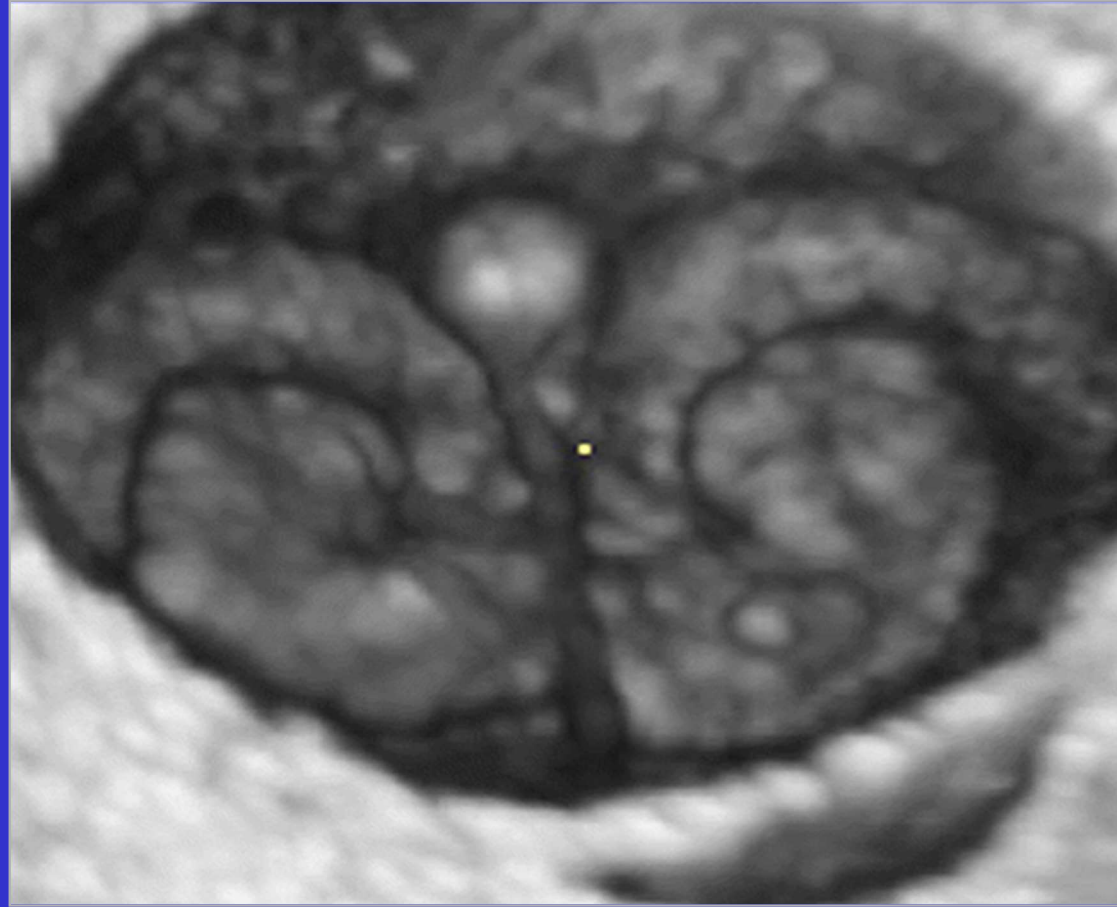




membranes' folding

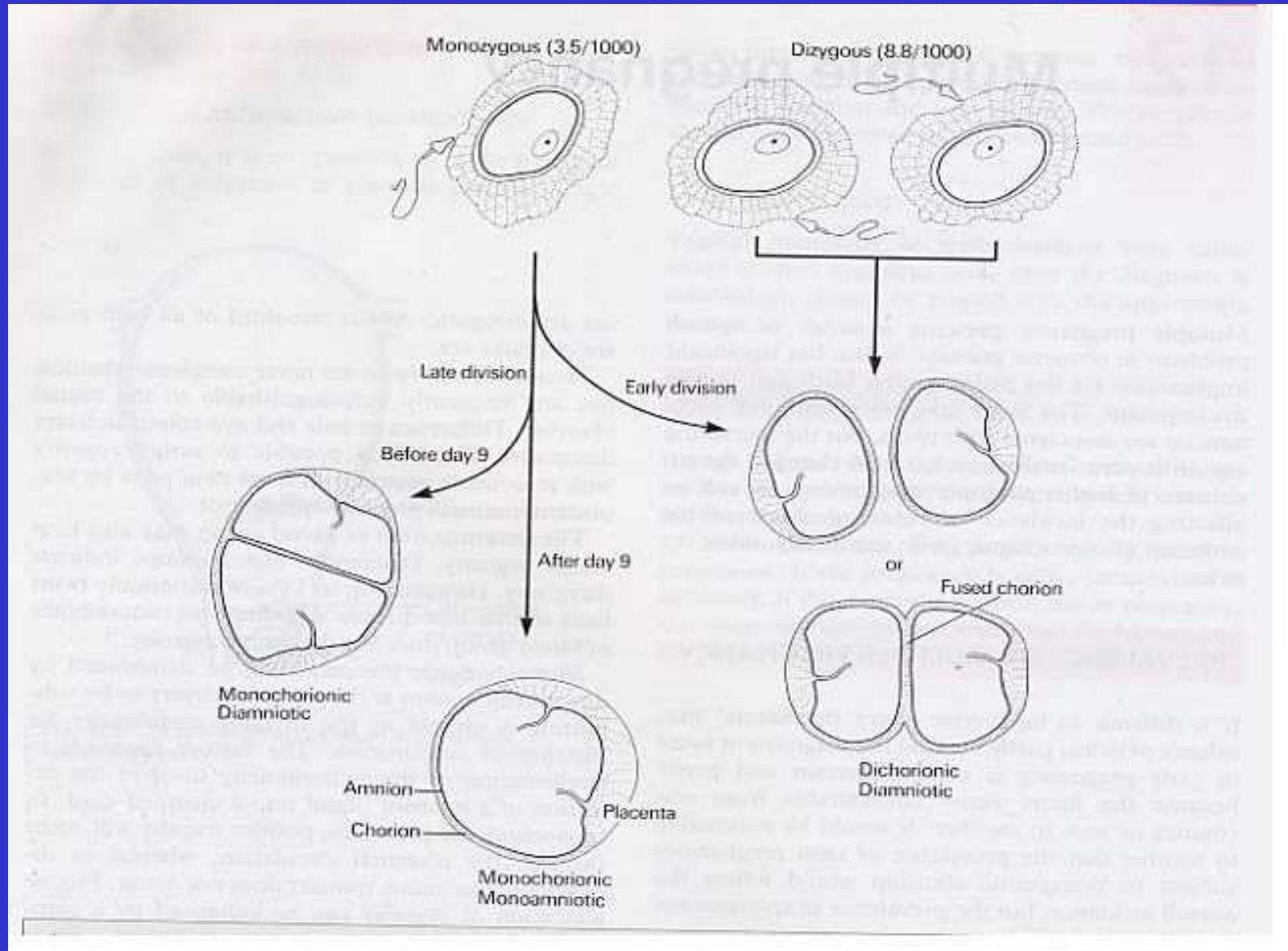


**DIAMNIOTIC
DICHORIONIC
TWINS**



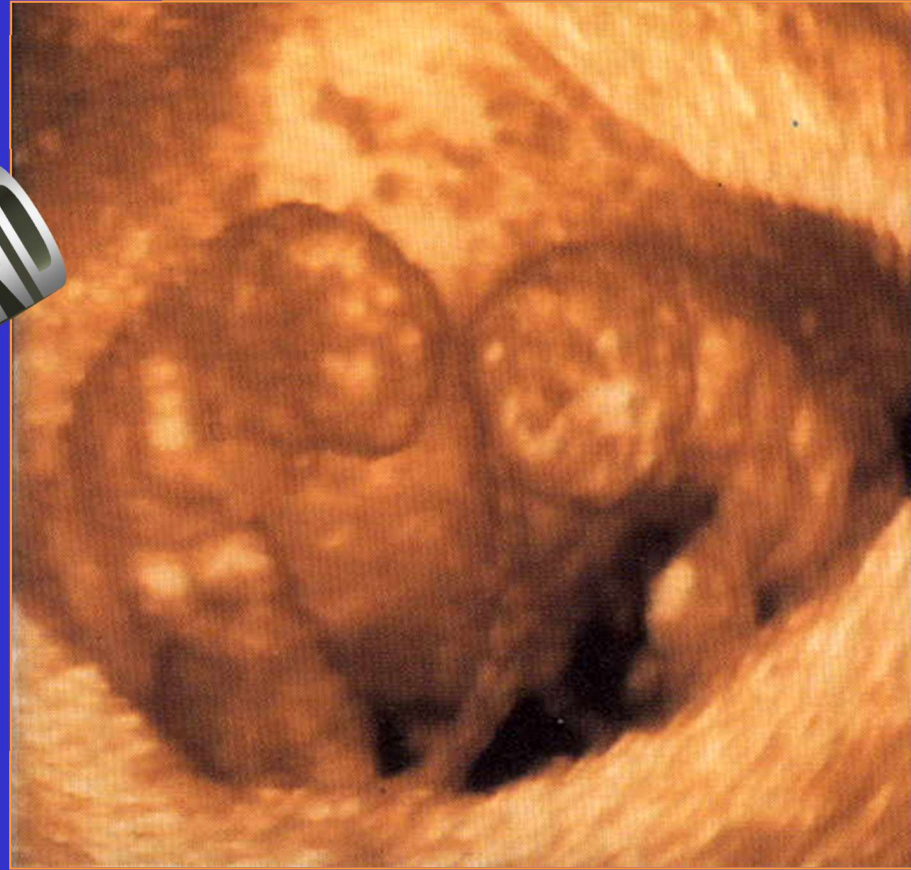
MULTIPLE PREGNANCY

Chorionicity Versus Zygosity



MONOCHORIONIC MONOAMNIOTIC TWINS

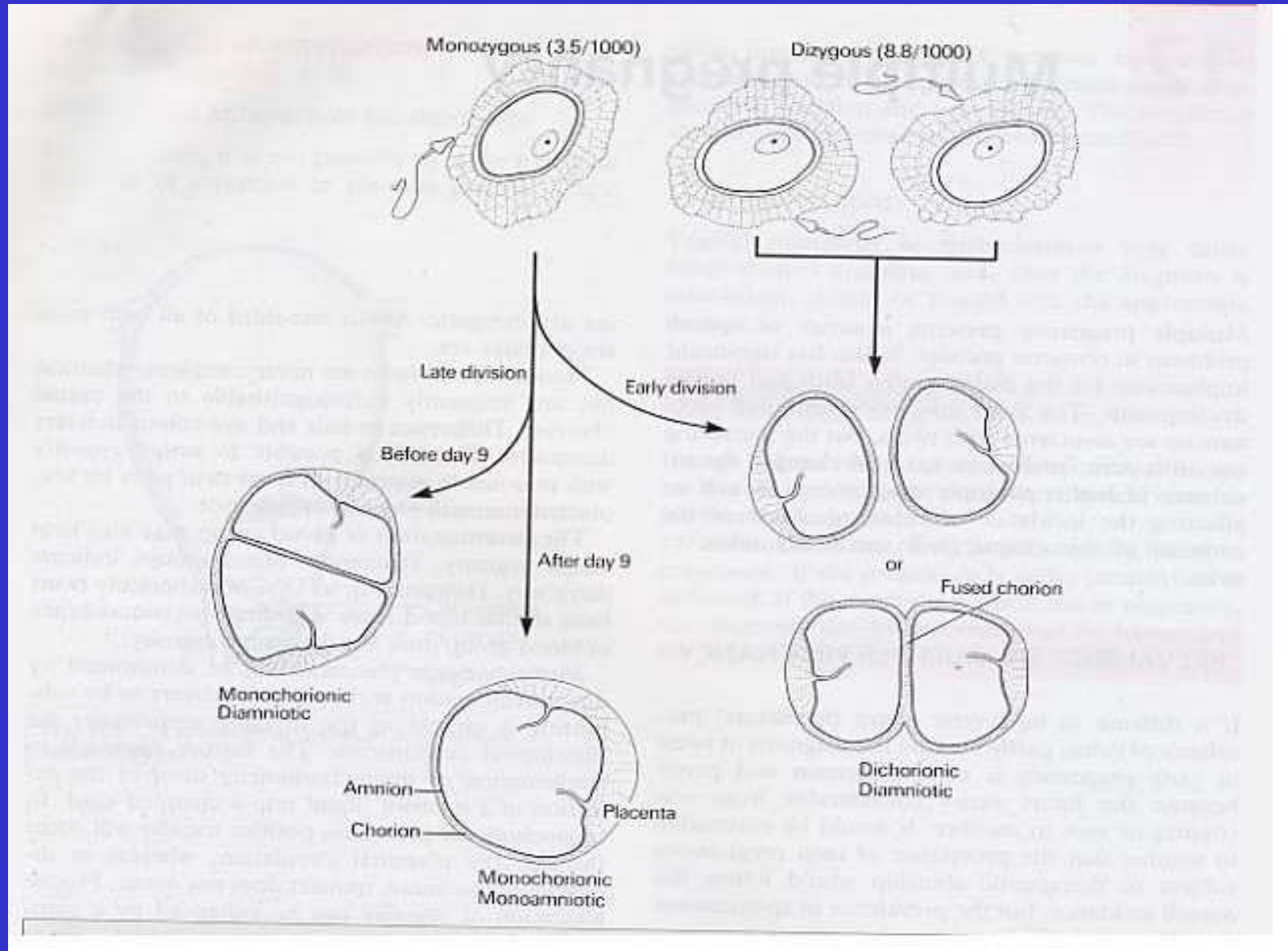
3-D ULTRASOUND



MONOAMNIOTIC MONOCHORIONIC TWINS



Chorionicity Versus Zygosity



TWINNING = SHARING



The same organs

Chorionicity Versus Zygosity

Dichorionicity



T sign in MC twins



Lamba sign in DC twins



Ultrasound Screening at 10-14 wks

Prevalence 2% (467 / 24,959)

MISCARRIAGE	DC	MC
12-24 wks	1.8%	12.2%

PERINATAL DEATH	DC	MC
>24 wks	1.6%	2.8%

GROWTH RETARDATION	DC	MC
Total fetuses	12%	21%

PRETERM DELIVERY	DC	MC
Gestation <32 wks	5.5%	9.2%

MC

X6

X2

X2

X2

Twin Pregnancy



Monochorionic 20%



Dichorionic 20%

Multiple pregnancies are:

The risk of producing a child with cerebral palsy is:

8 times greater in twins

47 times greater in triplets

compared to singletons

Substitutions



- (1) Thickness of the dividing membrane
- (2) Counting the number of the layers in the dividing Membrane

Diagnosis:

As good as histopathology

The base and thickness

Errors in placental pathology

MC/MA TWINS

**NORMAL
TWIN**



TWINNING = SHARING

MONOCHORIONIC

Splitting of One Egg

Sharing of the same Circulation

TWINNING = SHARING

Congenital Malformation

**Three fold increase in the incidence of
congenital malformation in MC compared to Dichorionic**

TWINNING = SHARING



II. The same uterine milieu

TWINNING = SHARING

Congenital Malformation

Splitting of One Egg

Sharing of the same Circulation

Anencephalus

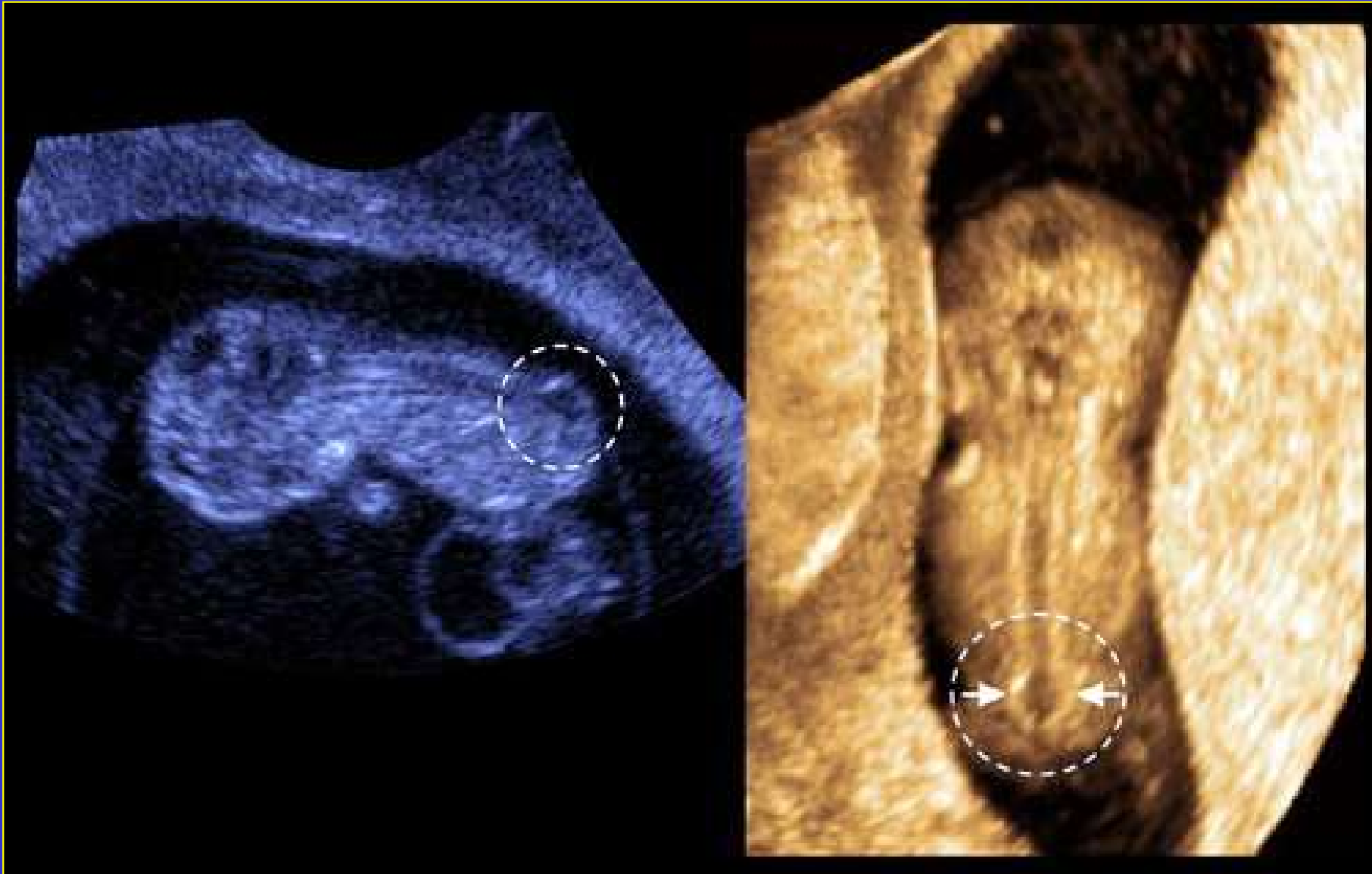
AREA CEREBROVASCULOSA



OMPHALOCELE

Spina bifida

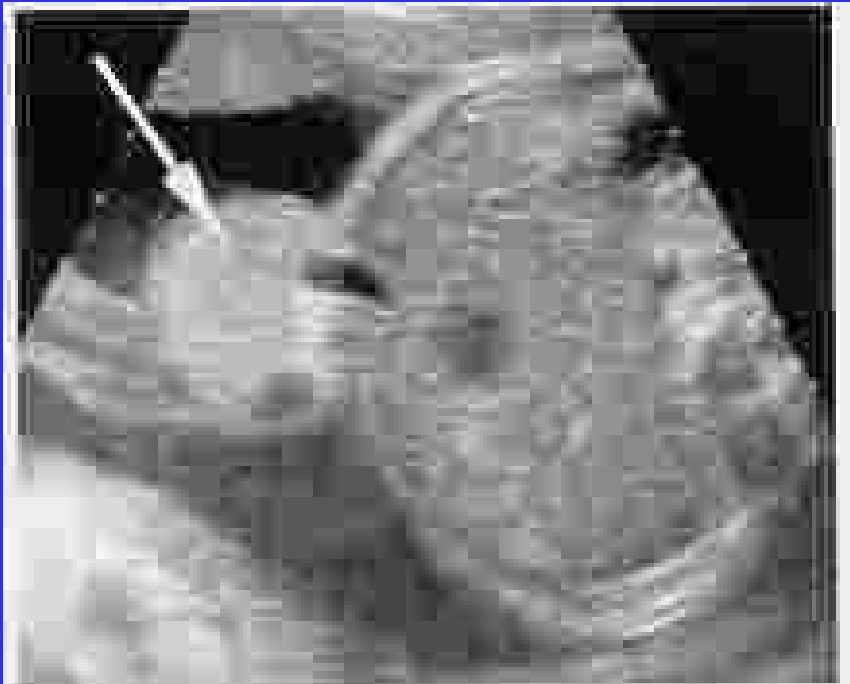
9 weeks



Gastroschisis



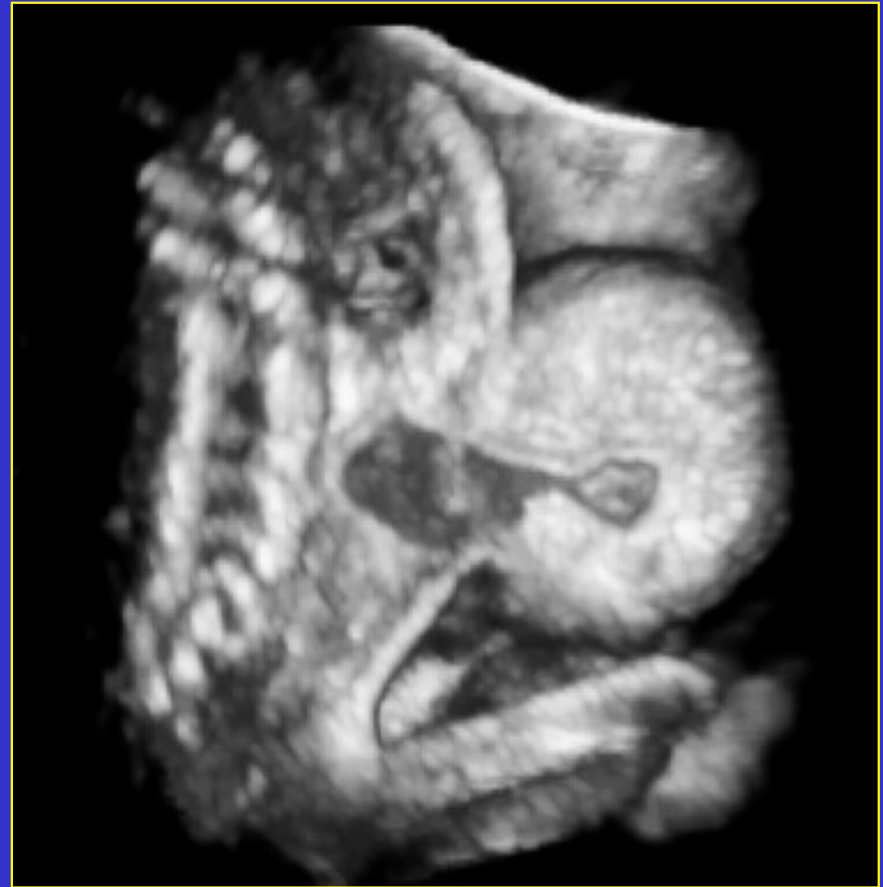
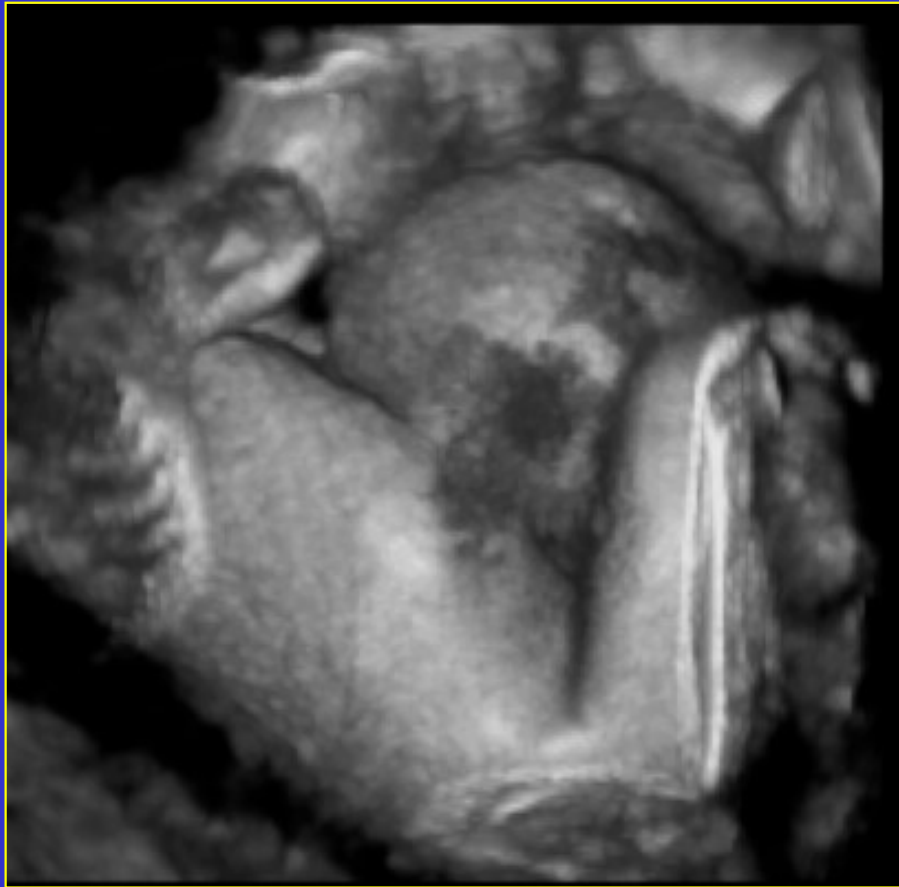
Exomphalos



3D



OMPHALOCOELE



Surface mode “electronic dissection”

TWINNING = SHARING

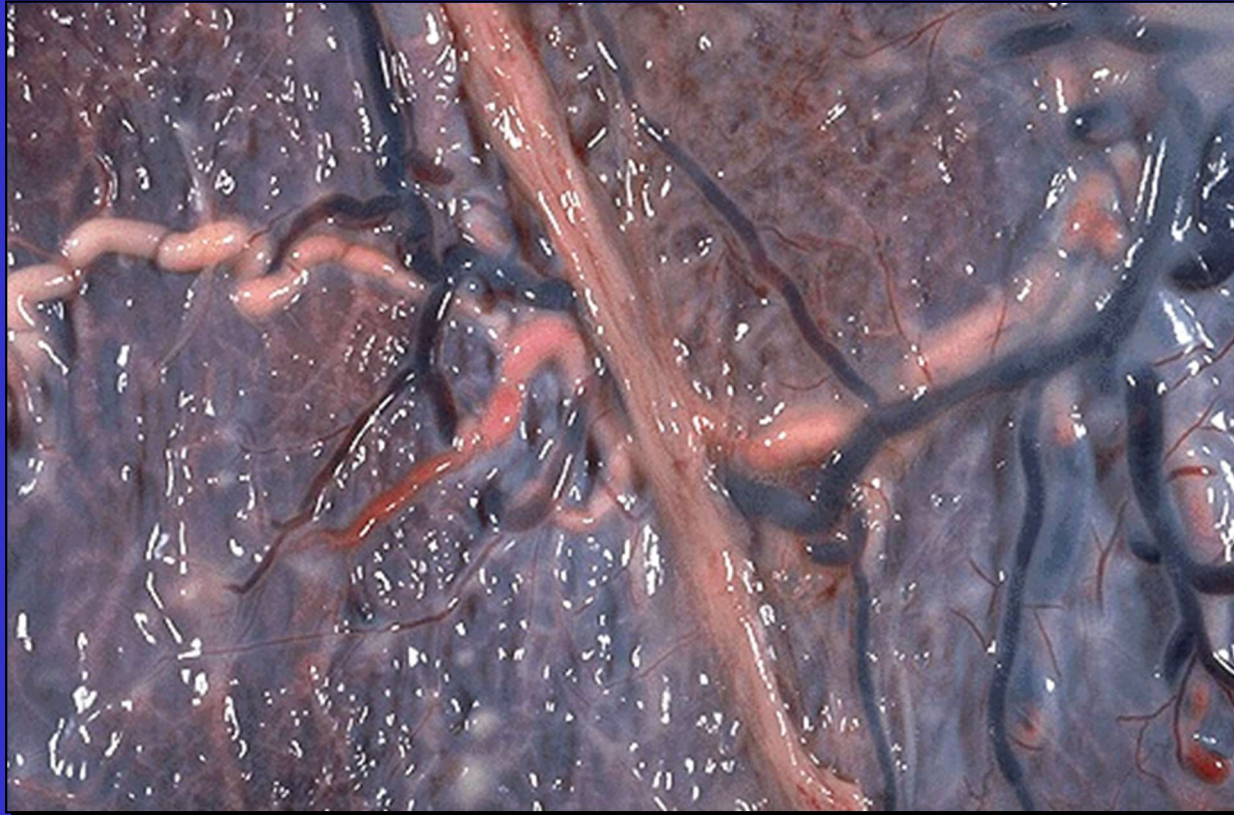
Congenital Malformation

Splitting of One Egg

Sharing of the same Circulation

The same circulation

A



A

A

V

⇒ **Difference in blood pressure** ⇒ **Ischemic Vascular sequences**

This can affect any system BUT more spectacular in Brain and Gastrointestinal system:

Report from a conference:

1th World Congress

Twins Pregnancy – a Global Perspective

Venice – April 16 – 18, 2009

Aberrant growth



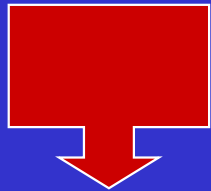
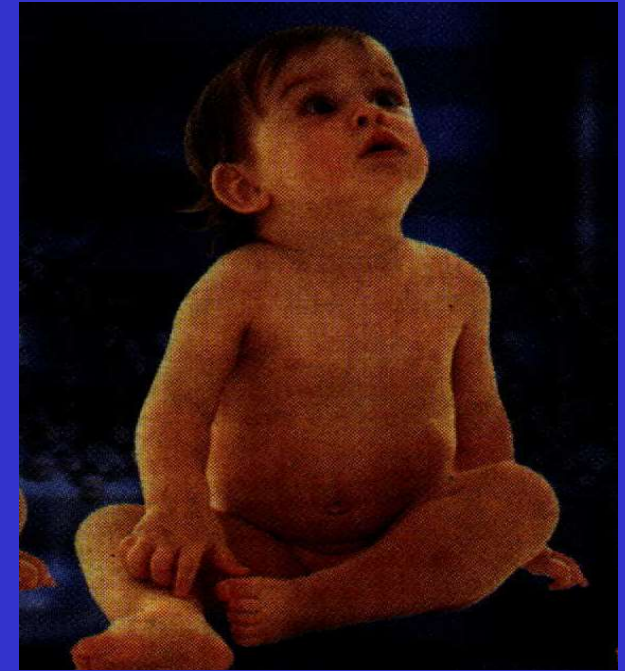
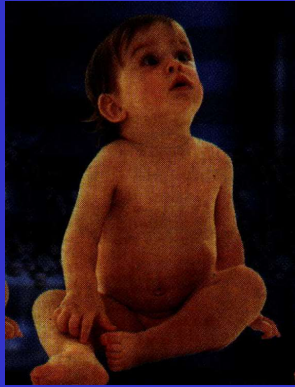
Twin-Twin Transfusion Syndrome



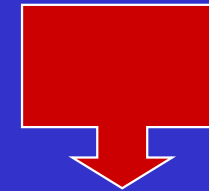
10-15% of all MC twins

Most can be diagnosed at 18-24 wk

If not treated, mortality >80%

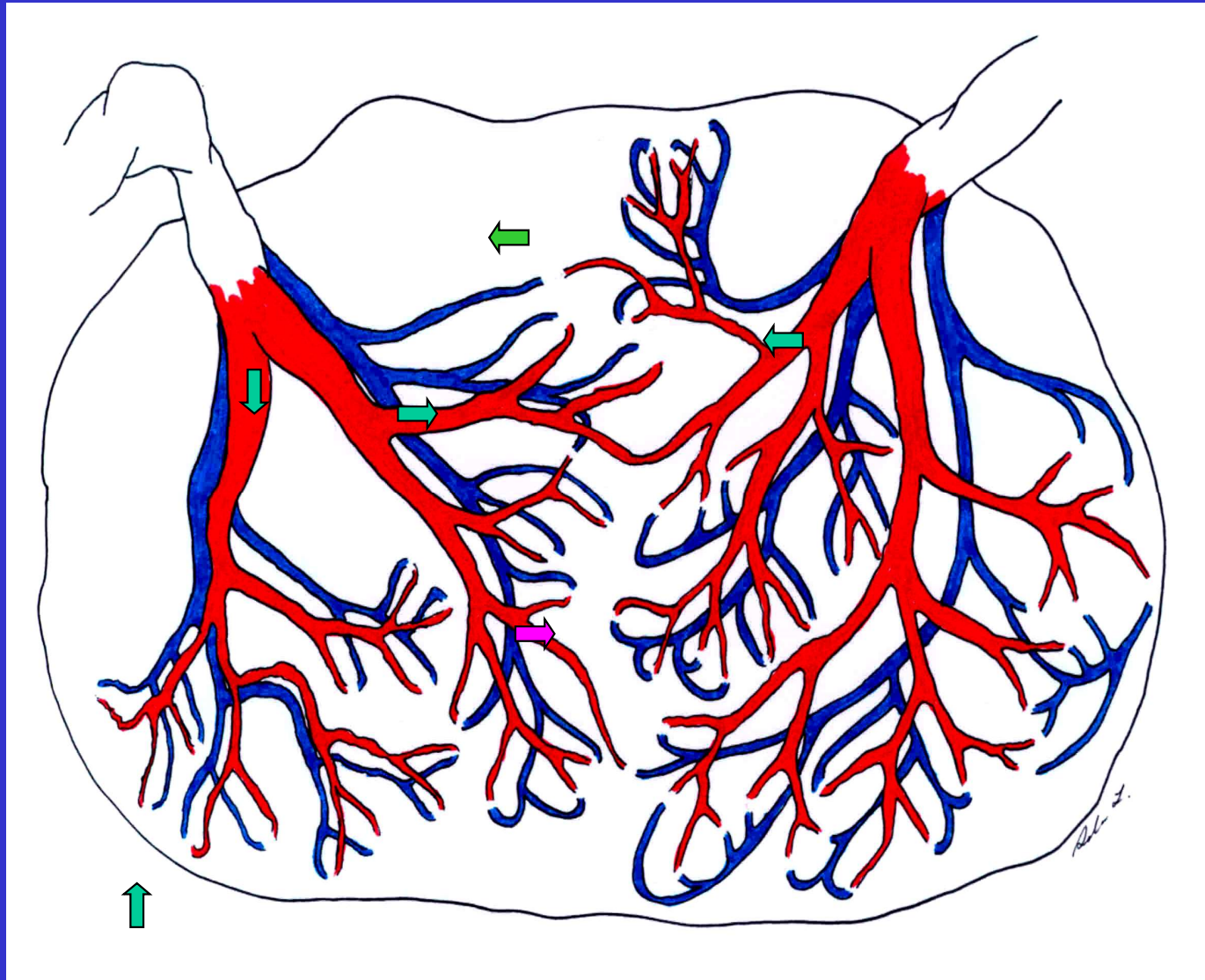


Donor: (Anemia)
Activation of Renin Angiotensin system
Oligouria.



Recipient: (Polycythemia)
Release of
Atrial Natriuretic Hormone
Polyuria

Pathophysiology (MC twin)



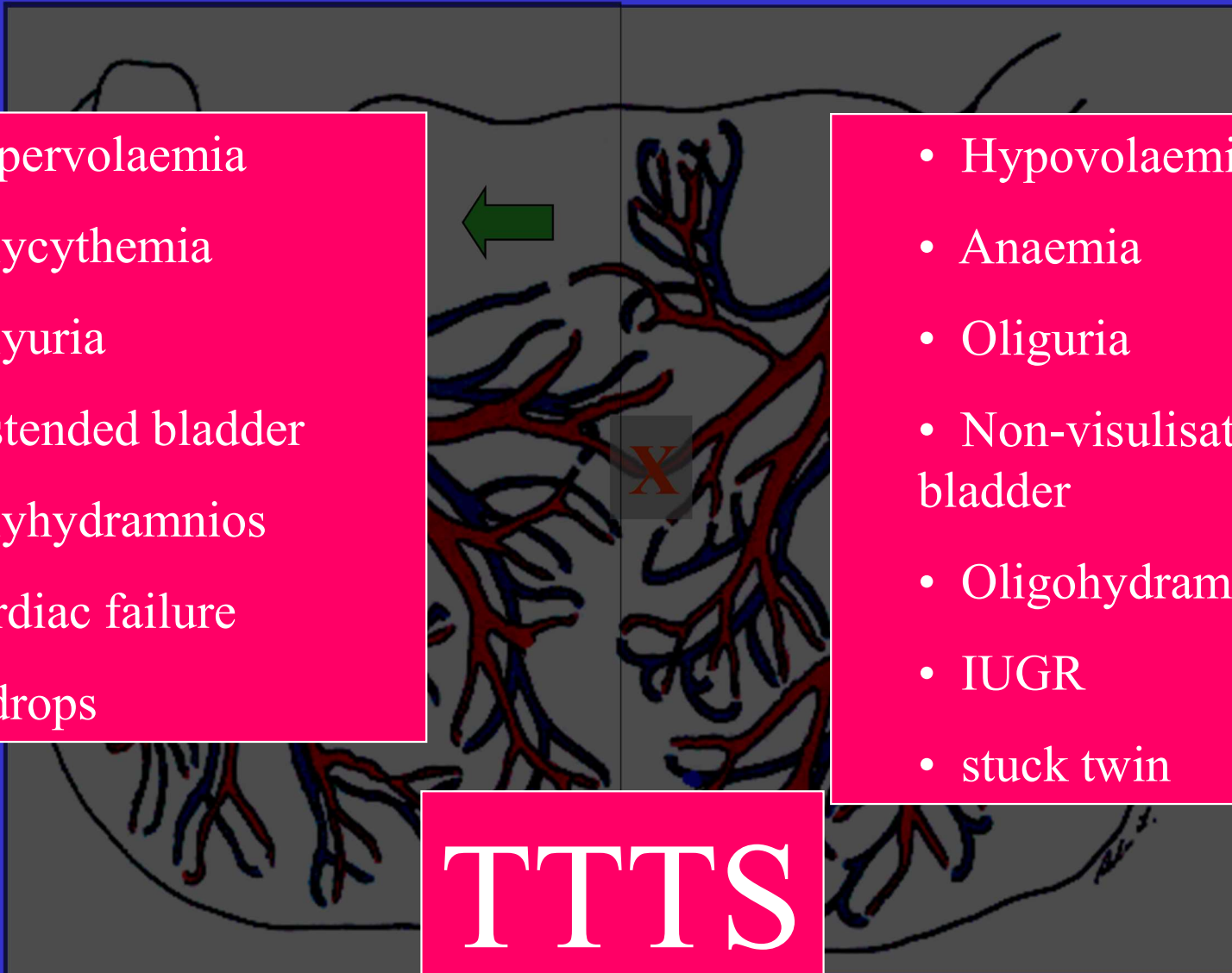
Pathophysiology

- Hypervolaemia
- Polycythemia
- Polyuria
- Distended bladder
- Polyhydramnios
- Cardiac failure
- hydrops



- Hypovolaemia
- Anaemia
- Oliguria
- Non-visualisation of bladder
- Oligohydramnios
- IUGR
- stuck twin

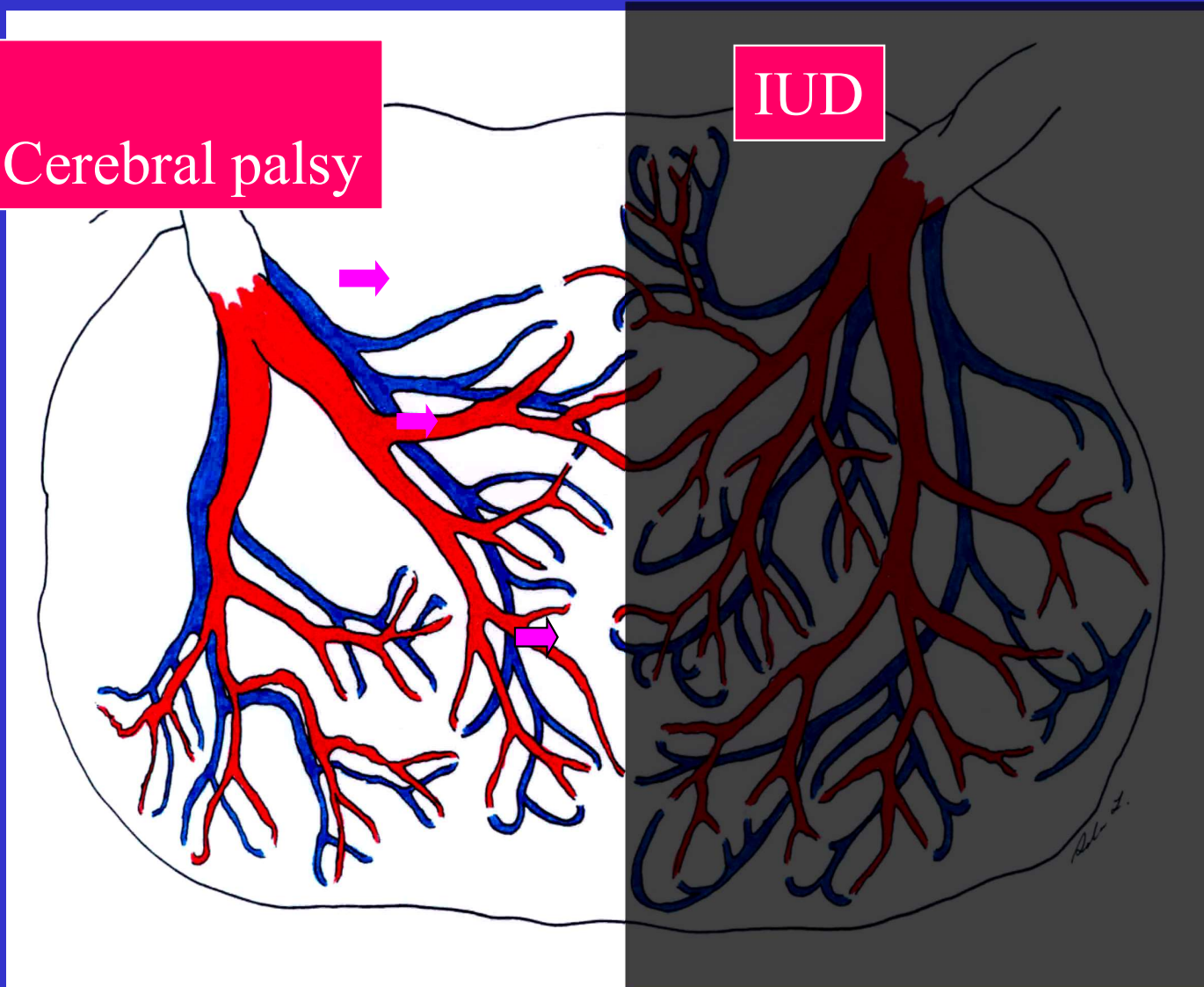
TTTS



Pathophysiology (MC twin)

IUD

5-30% Cerebral palsy



Diagnosis of TTTS

- MC Twin
 - Before 16 weeks
 - Same sex
 - Single placenta
- Polyhydramnios (Deepest pocket $\geq 8\text{cm}$)
- Oligohydramnios (Deepest pocket $\leq 2\text{cm}$)
- Both fetuses are affected

Staging of TTTS

Stage	Poly- Oligo-	Absence of Bladder	Critically Abnormal Doppler	Hydrops	IUFD
I	+	-	-	-	-
II	+	+	-	-	-
III	+	+	+	-	-
IV	+	+	+	+	-
V	+	+	+	+	+

Twin Twin Transfusion Syndrome

Staging

Stage one

Stage two

Stage Three

Stage four

Prognosis

Abnormal doppler

Cardiac Decomposition

Ductus venosus Doppler



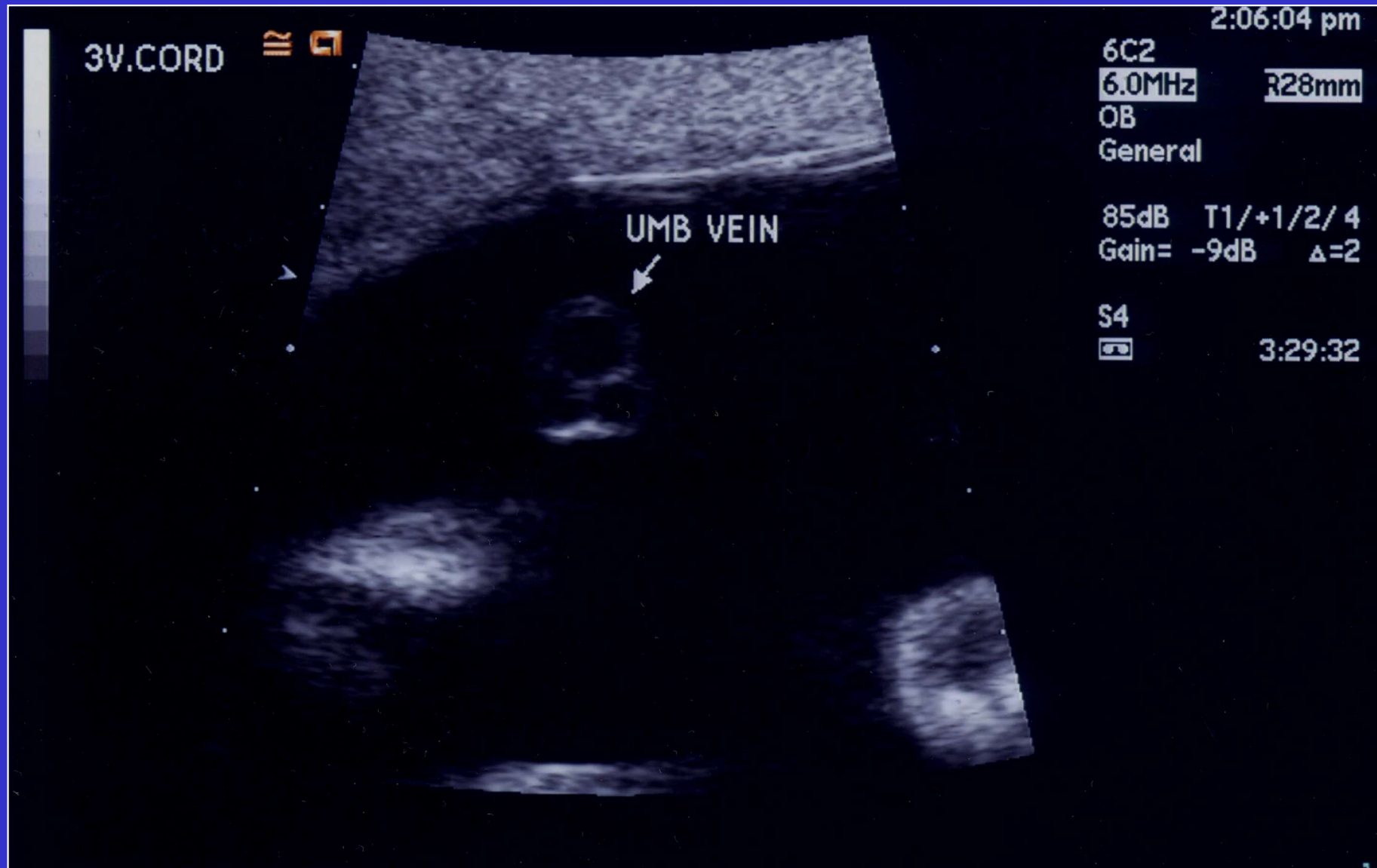
TTTS



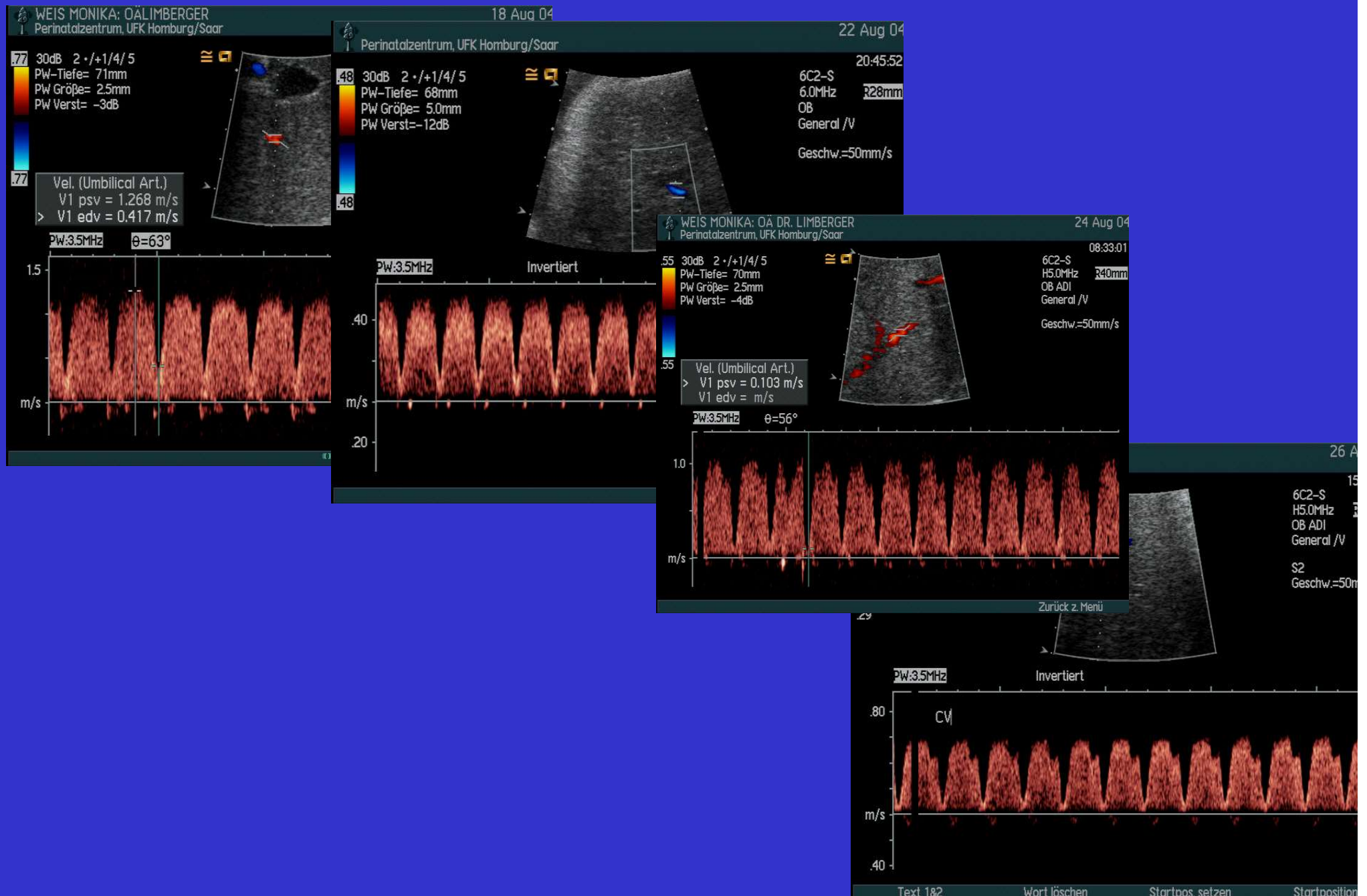
TTTS



TTTS



Twin Twin Transfusion Syndrome

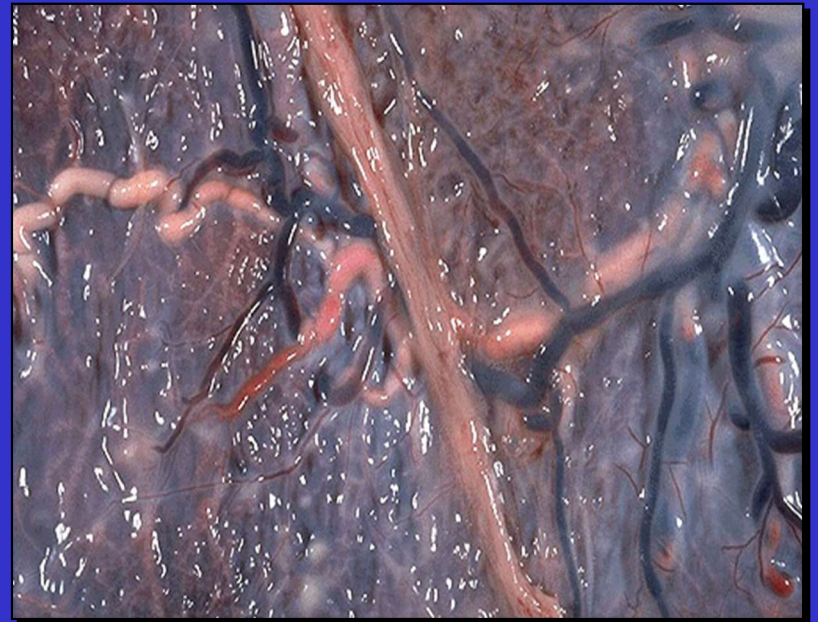


Twin Twin Transfusion Syndrome

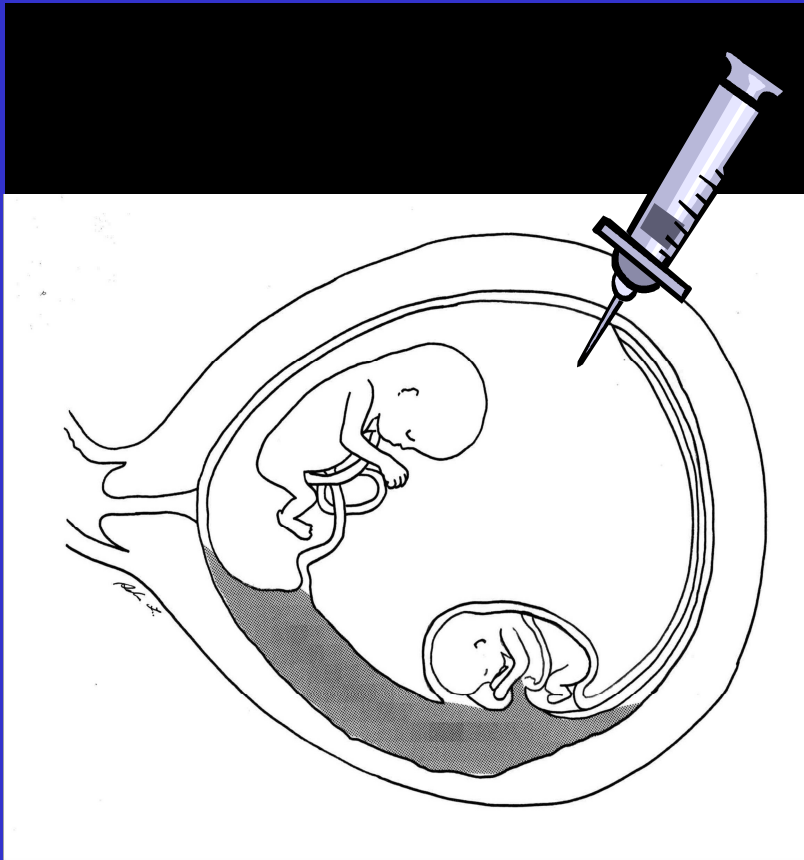
Euro fetus

Repeat Amnioreduction

Laser Coagulation of the vessels



Serial Amnioreduction



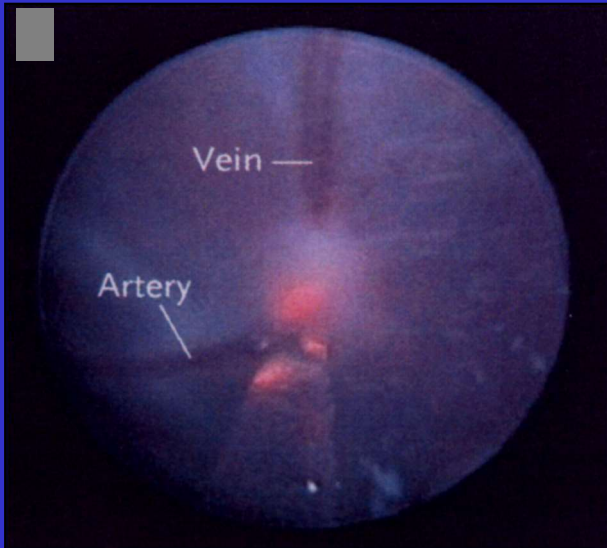
- Simple procedure
- Technically easy
- Low cost
- Available in the majority of obstetric units

Serial Amnioreduction

- Not targeted to the origins of disease – placental vascular anastomosis
- Cannot prevent the effect of single IUD on the other co-twin
- Usually needs multiple procedures
- Only effective in early stages of TTTS
- Procedure-related risk of PPROM / delivery: 4% / procedure
- 16-20% of survivors have cerebral palsy

TTTS – Treatment

Fetoscopic Laser Photocoagulation



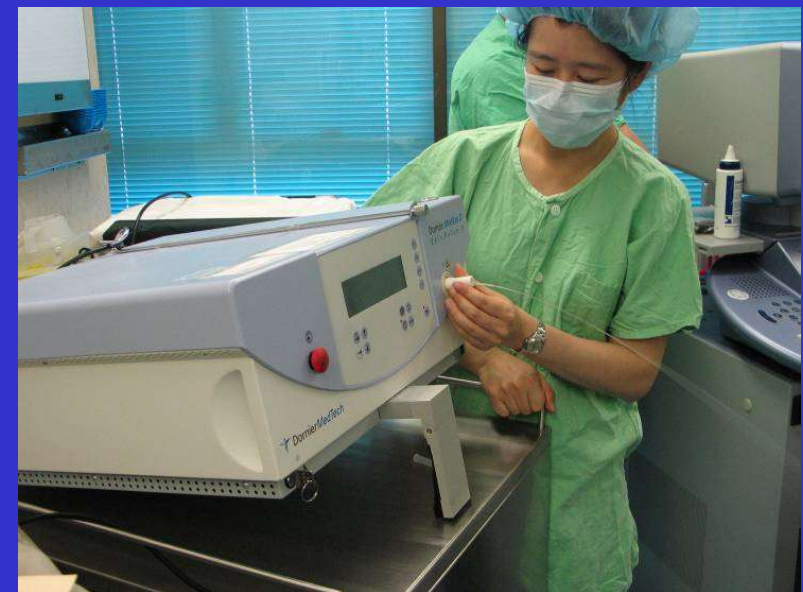
- Targeted to the disease origin
- Single treatment
- Prevents adverse effect on the co-twin even one twin dies
- Effective for late stages TTTS
- Survivor has lower incidence of cerebral palsy

- Technically demanding
- More expensive equipments
- Long learning curve
- If un-equal sharing of placenta, may precipitate death of one twin
- Risk of PPROM or preterm delivery: 5%

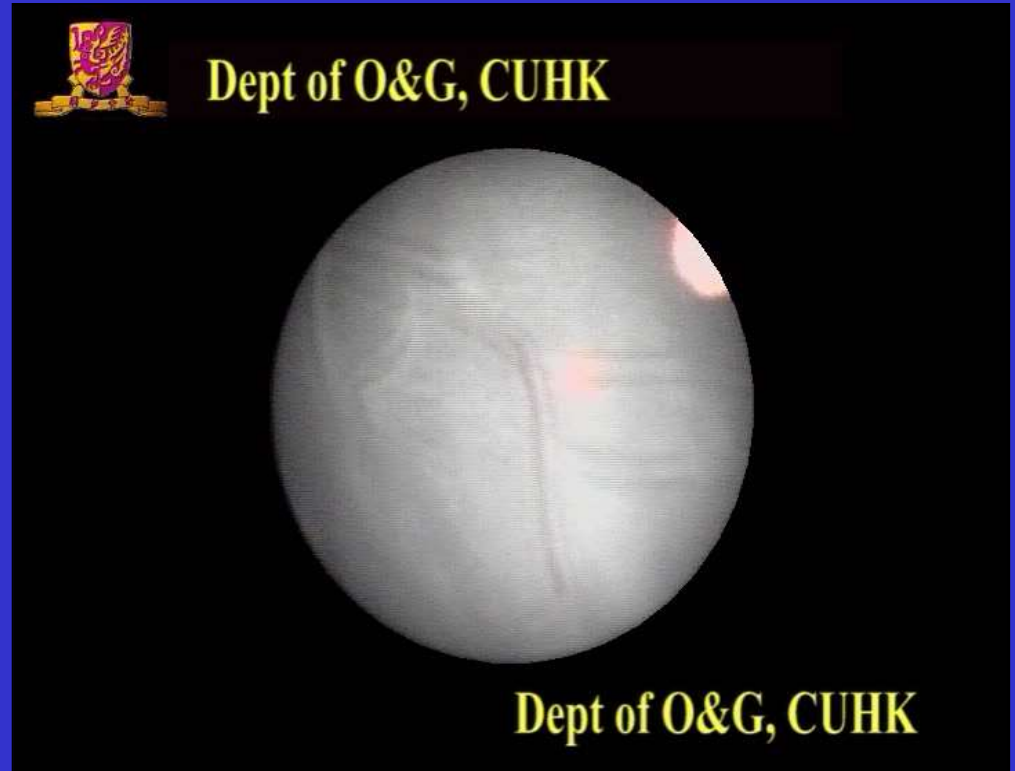
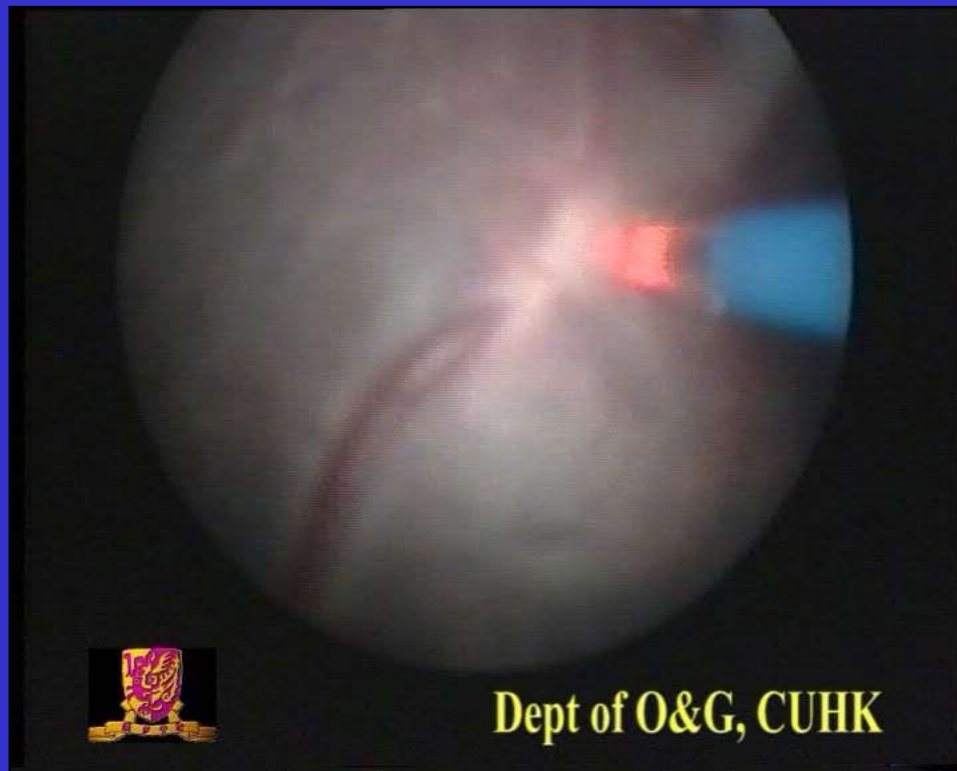
Laser Treatment: Indication

- Severe early onset TTTS
- <26 week
- TTTS Stage II or above
 - Polyhydramnios $\geq 8\text{cm}$
 - Oligohydramnios $\leq 2\text{cm}$
 - Non-visualisation of bladder

TTTS – Laser Therapy



TTTS – Laser Therapy



What to do after laser therapy ?

1th World Congress

Twins Pregnancy – a Global Perspective

Venice – April 16 – 18, 2009

Vanishing twins syndrome;

1th World Congress

Twins Pregnancy – a Global Perspective

Venice – April 16 – 18, 2009

Delivery:

**Monochorionic Twins: deliver at 33 -34 weeks
Of gestation**

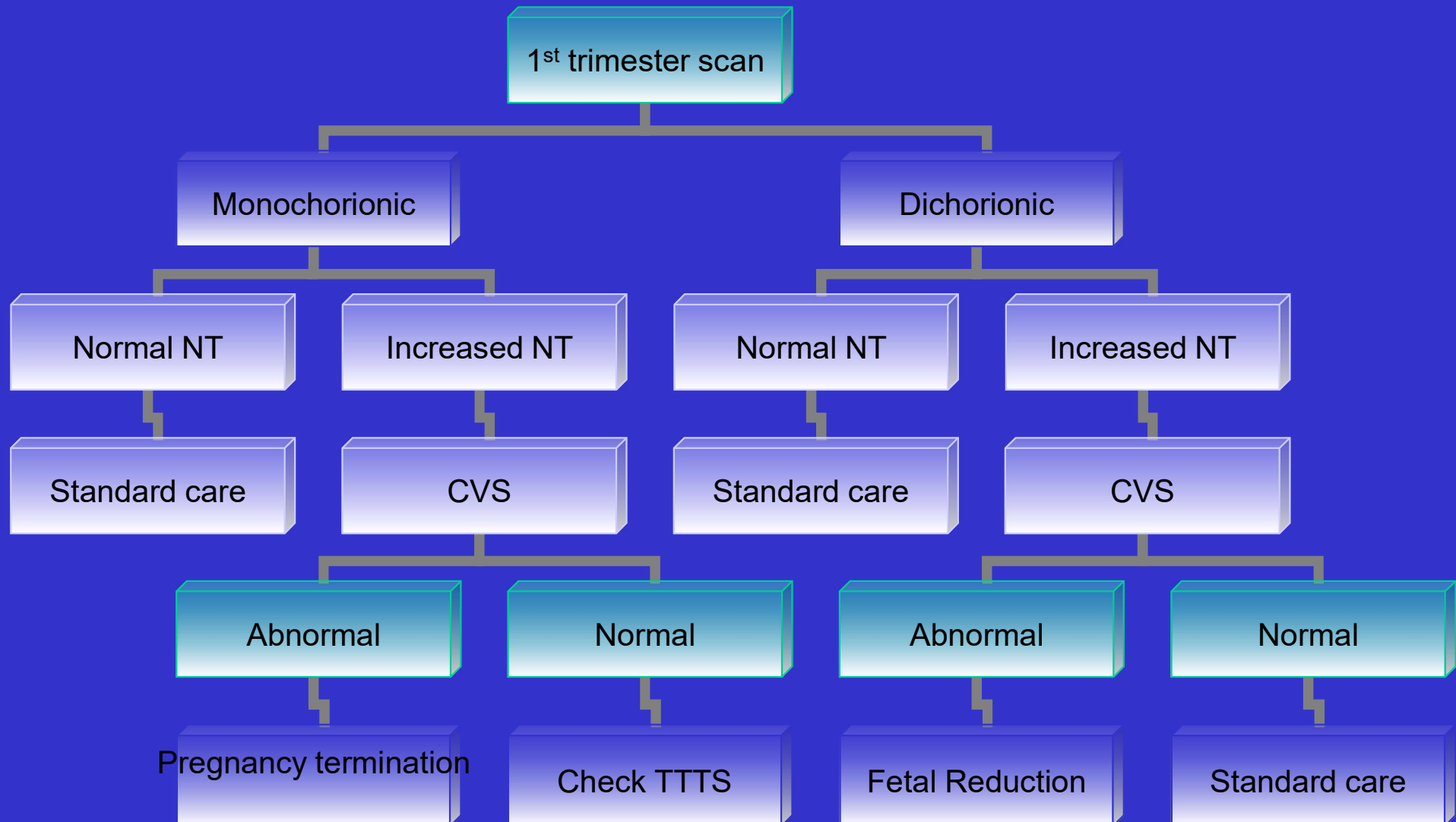
Vanishing twins syndrome;

Incidence:

**Recognition by sonographic community;
(Two much Vodka)**

Relationship to CP

Strategy in prenatal diagnosis in twins



Antenatal Management: Prevention of Preterm Birth

**NOT shown to decrease incidence of
preterm birth**

X Routine hospitalization for bed rest

X Prophylactic activity restriction/Work leave

X Prophylactic routine cervical cerclage

X Prophylactic tocolysis

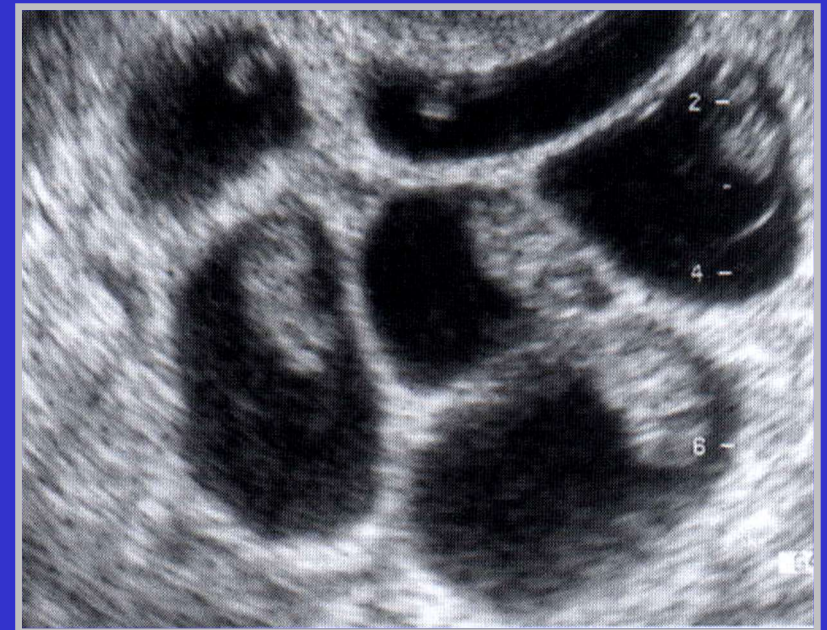
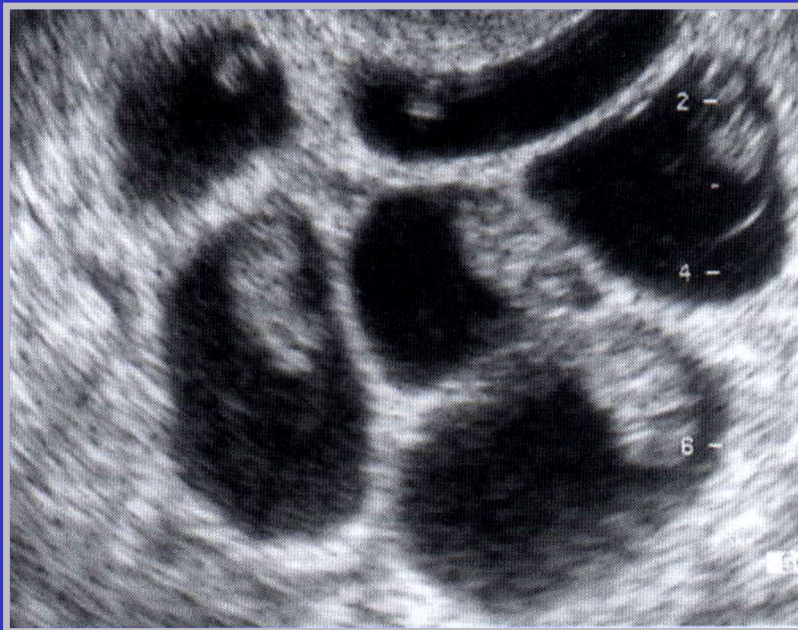
X Specialized twin clinics

X Home uterine activity monitoring

Take Home Message:

HIGH-ORDER MULTIPLE PREGNANCY

Multiple Fetal Reduction



Take Home Message:

Chorionicity Not Zygosity

**No first trimester US report should read
normal twins pregnancy**



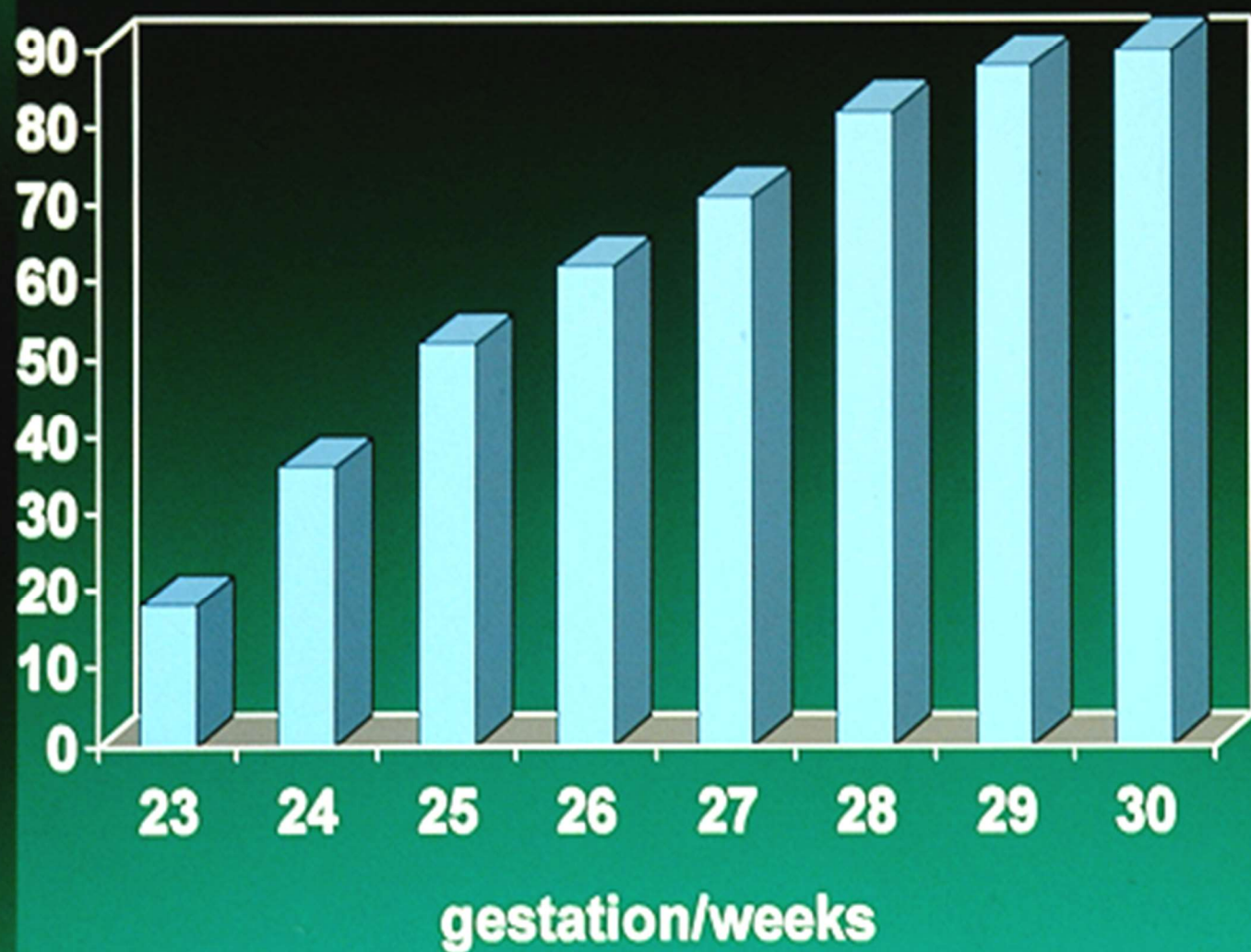
**Table for two.
No reservations.**

**Thank
you !**



The Campesinos

Survival by gestational age



Rennie 1996, n=11069

**EMBRYOS THAT UNDERGO
2 CLEAVAGES
IMPLANT BETTER THAN
2 CELL EMBRYOS**



- Cleavage stage of an embryo:*
- *timing of the transfer relative to insemination of the oocytes*

Staessen et al., *Fertil Steril* 1992

Austin et al., *J of Assisted Reprod & Genetics* 1996



**NO CORRELLATION BETWEEN
THE EMBRYONIC STAGE OF
DEVELOPMENT
&
THE INCIDENCE OF MULTIPLE
PREGNANCIES**

Risk of multiple gestation following ET

VARIABLES THAT DO NOT CORREALATE

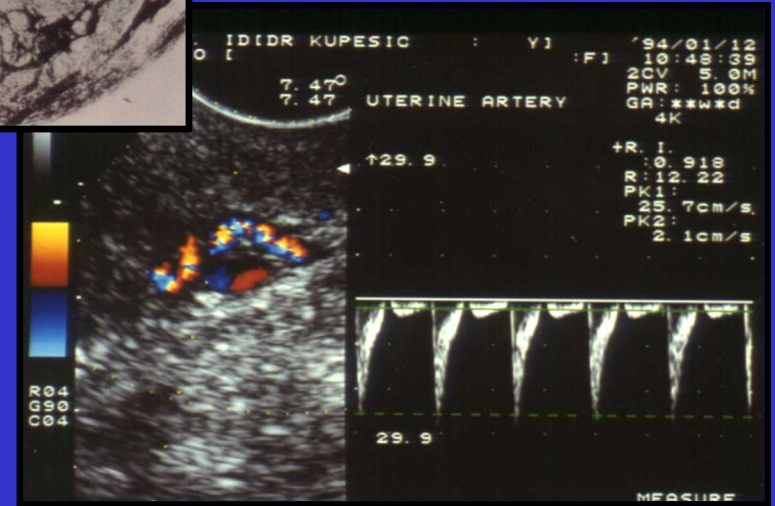
- infertility diagnosis
- stimulation protocol
- peak estradiol level
- number of oocytes retrieved
 - fertilization rate
 - cleavage stage

ONLY SIGNIFICANT VARAIBLE

- the number of embryos transferred

Optimal uterine receptivity

PI = 2 - 3



ON THE DAY OF ET

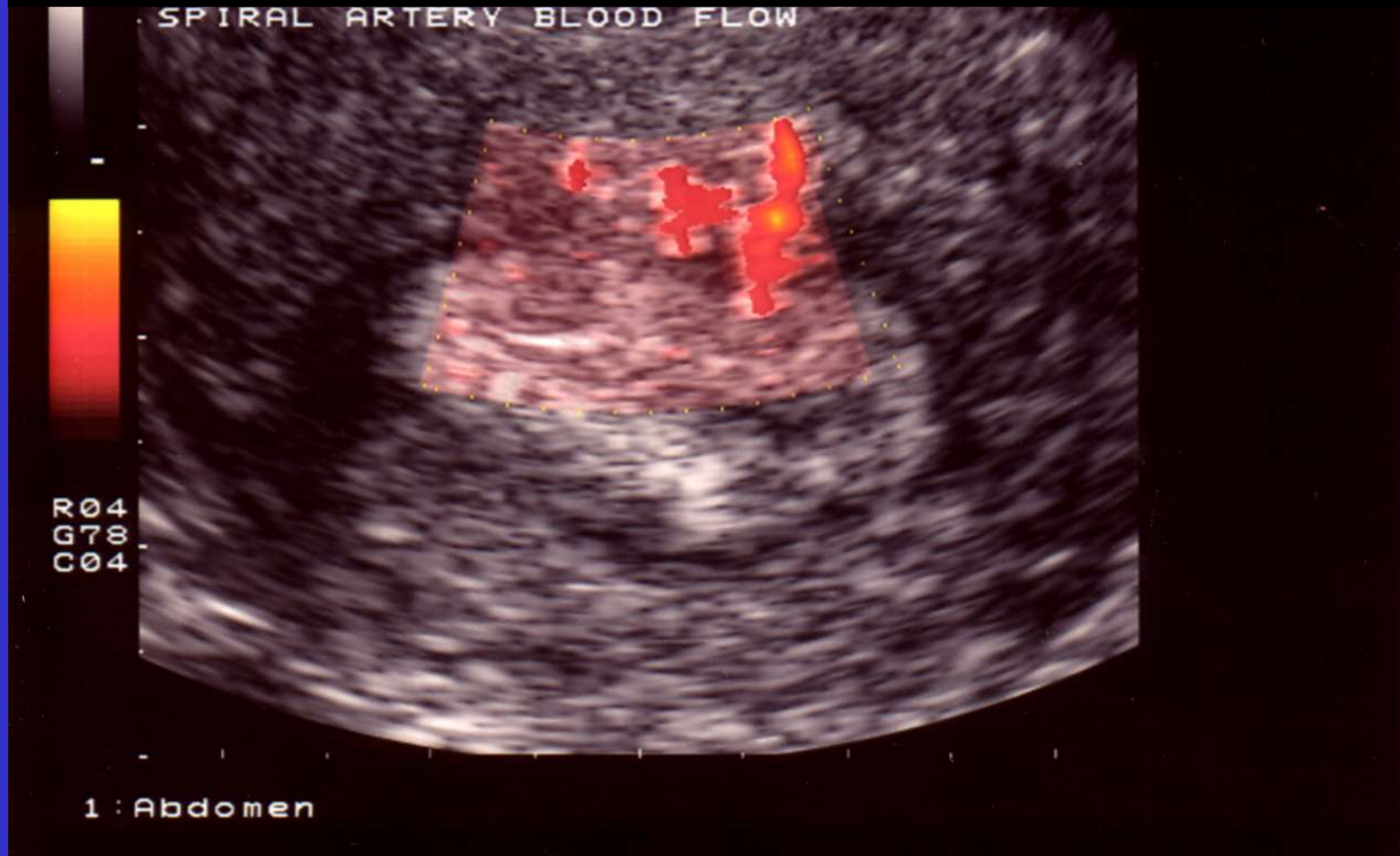
Kupesic et al, *Fertil Steril* 1992

Steer et al., *Fertil Steril* 1992

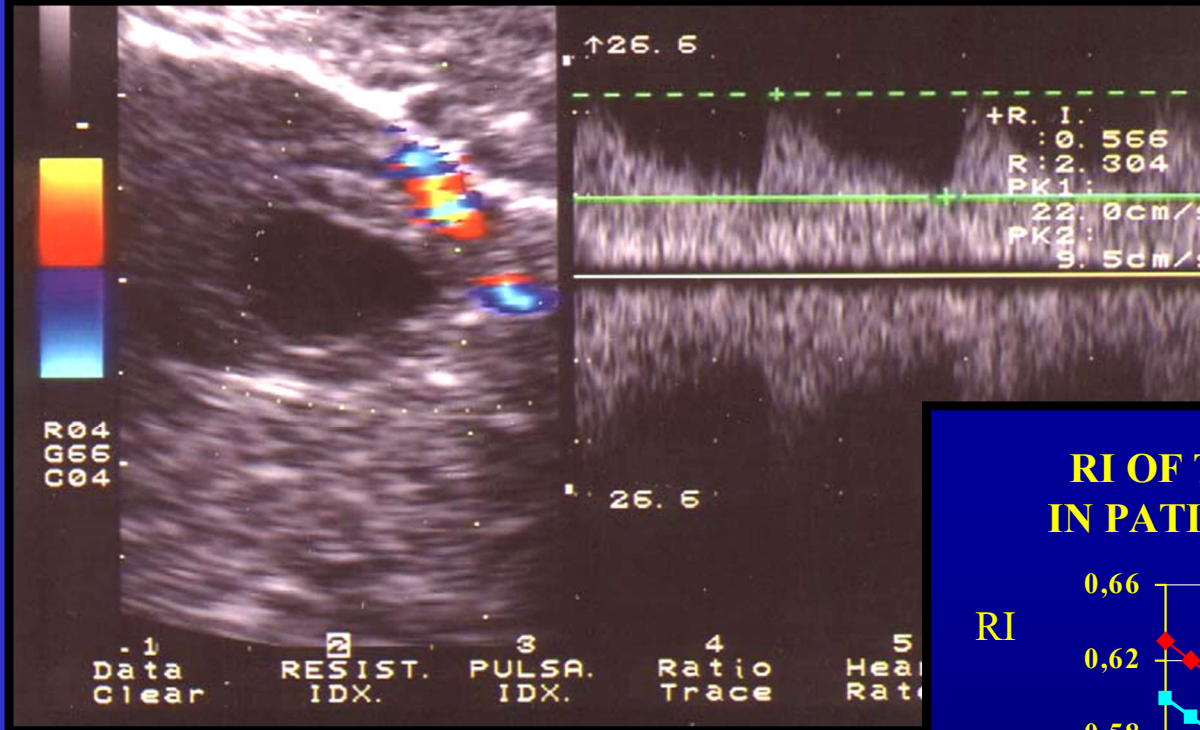
ON THE DAY OF HCG ADMINISTRATION

Tsai et al., *J Ultrasound Med* 1996

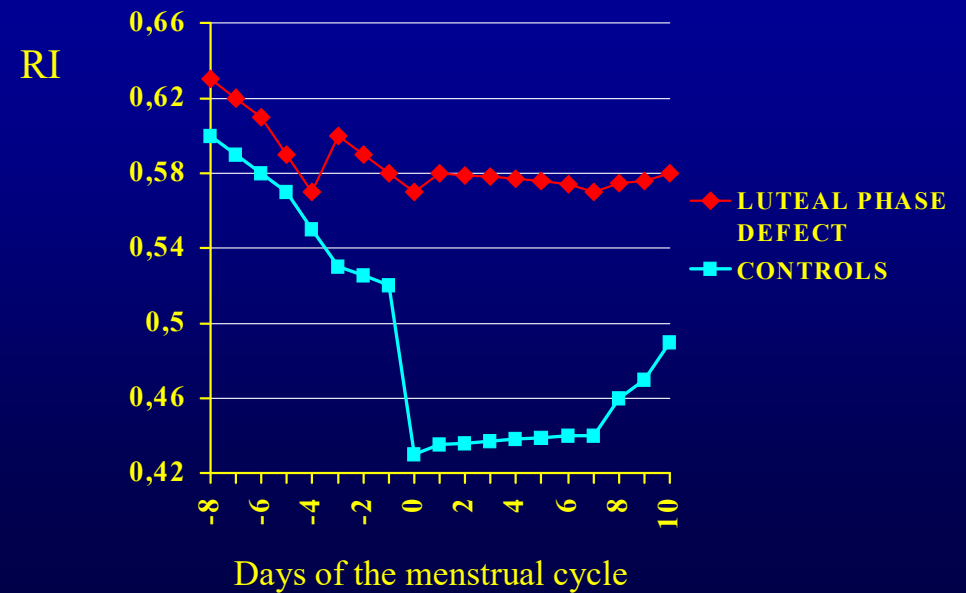
SPIRAL ARTERY BLOOD FLOW



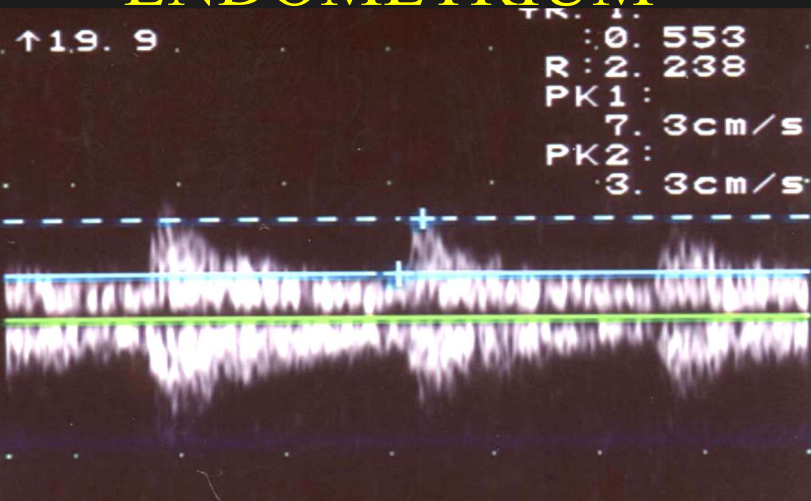
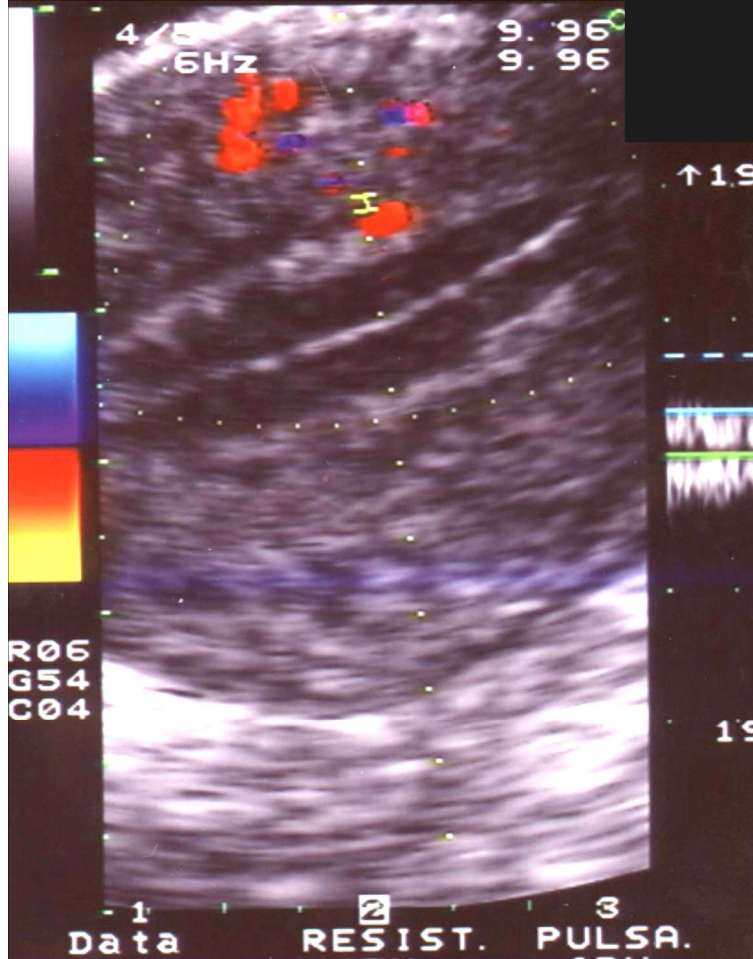
CORPUS LUTEUM BLOOD FLOW



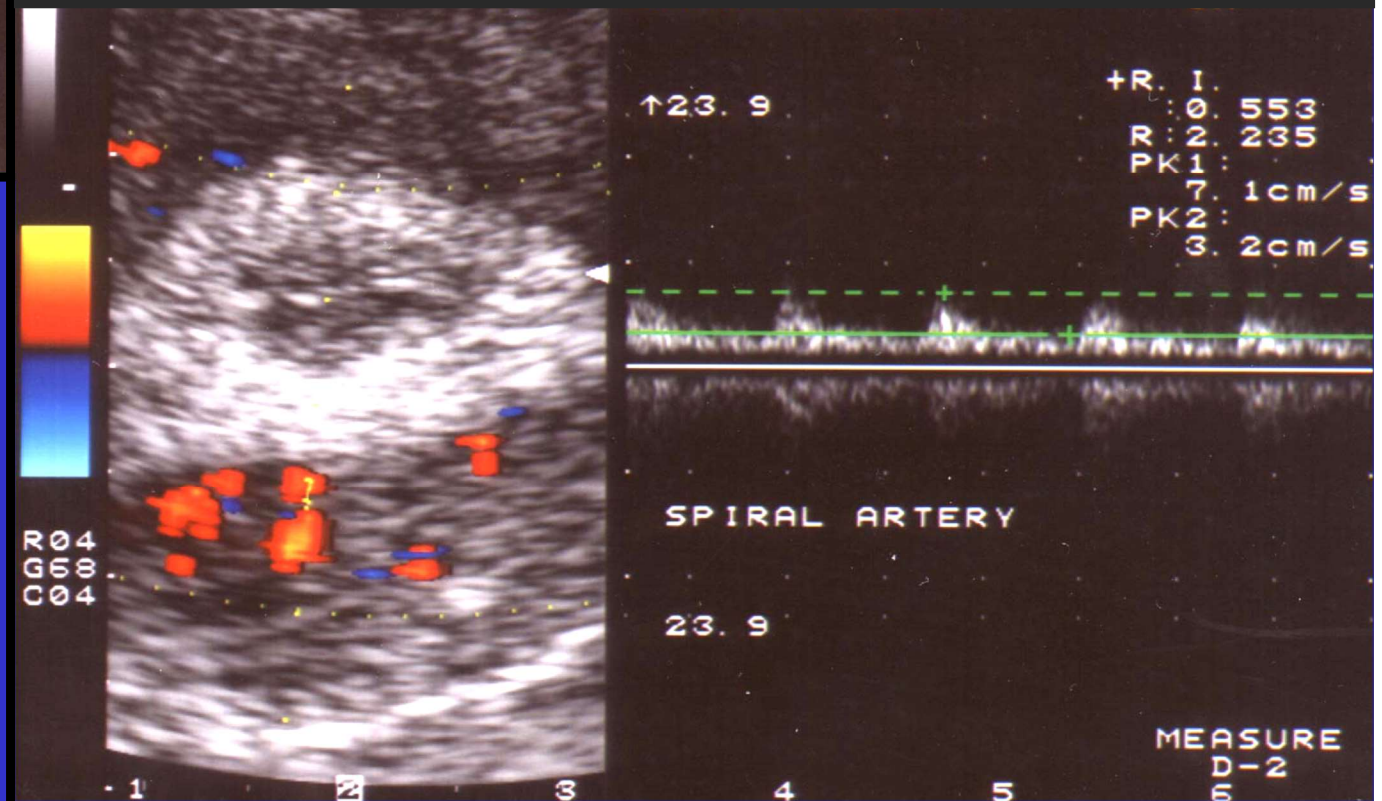
RI OF THE INTRAOVARIAN BLOOD FLOW IN PATIENTS WITH LPD AND IN CONTROLS



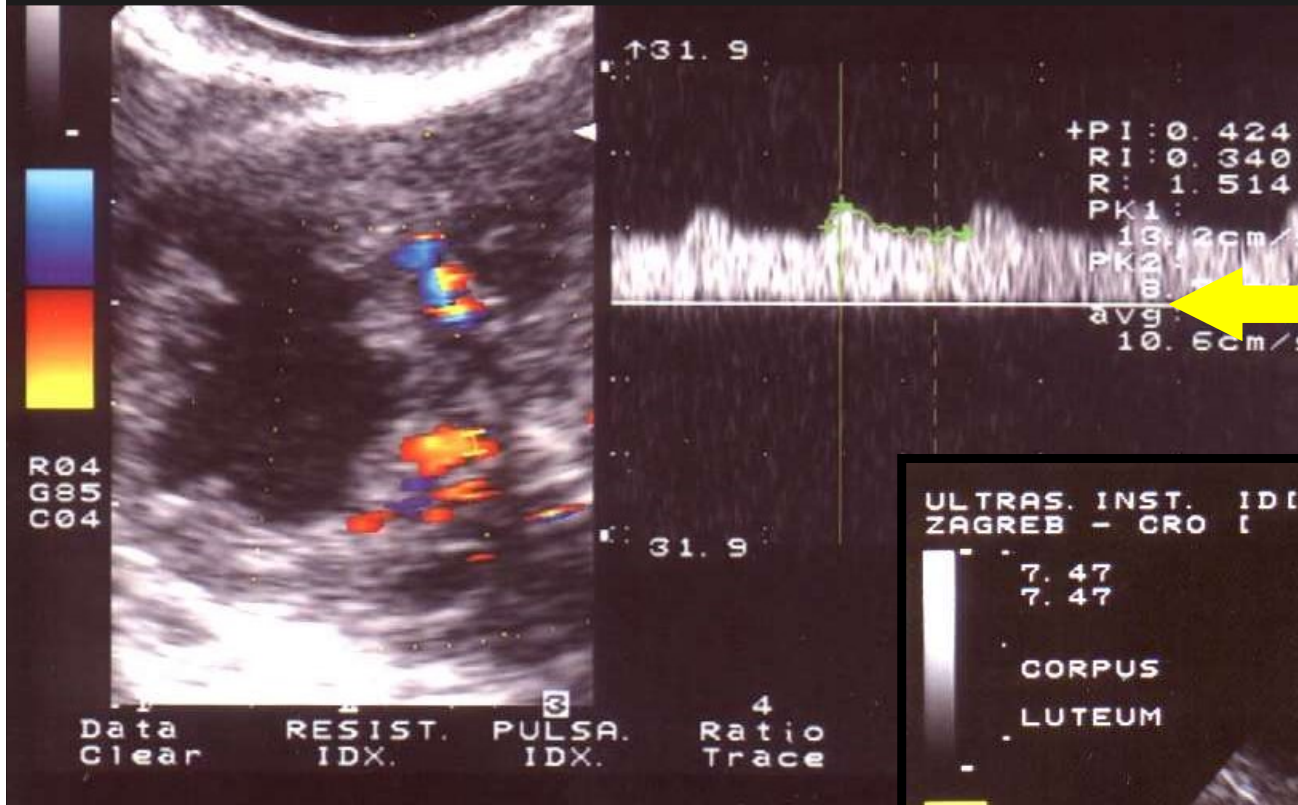
TRIPLE-LINE ENDOMETRIUM



SECRETORY ENDOMETRIUM

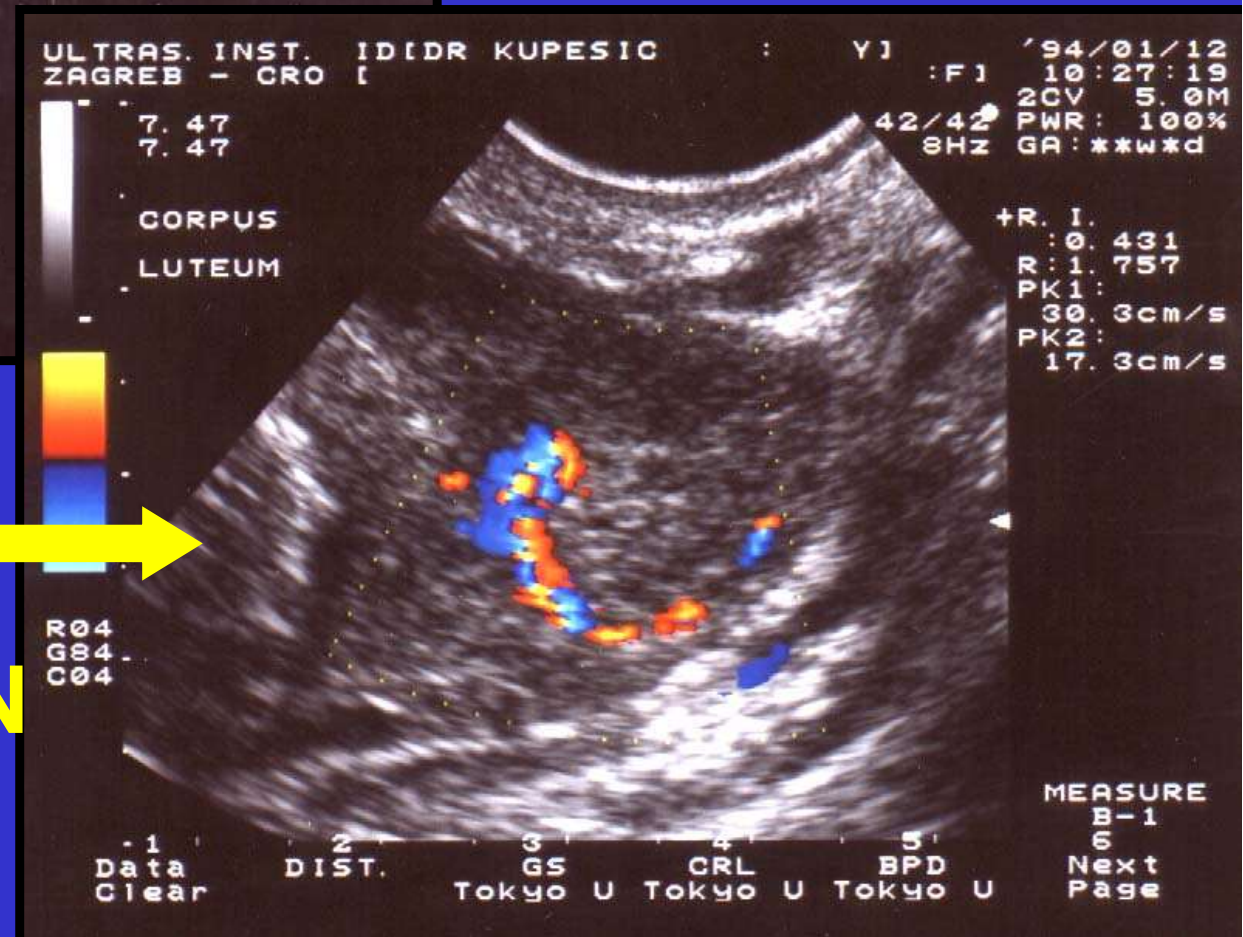


CORPUS LUTEUM



ORGANIZATION

VASCULARIZATION

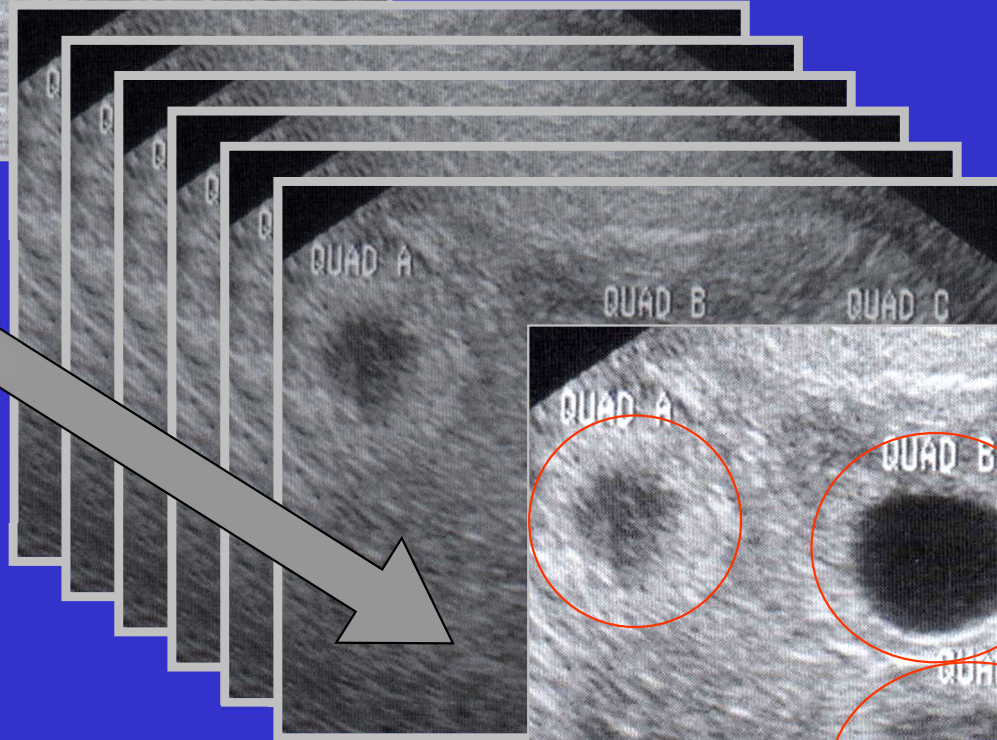
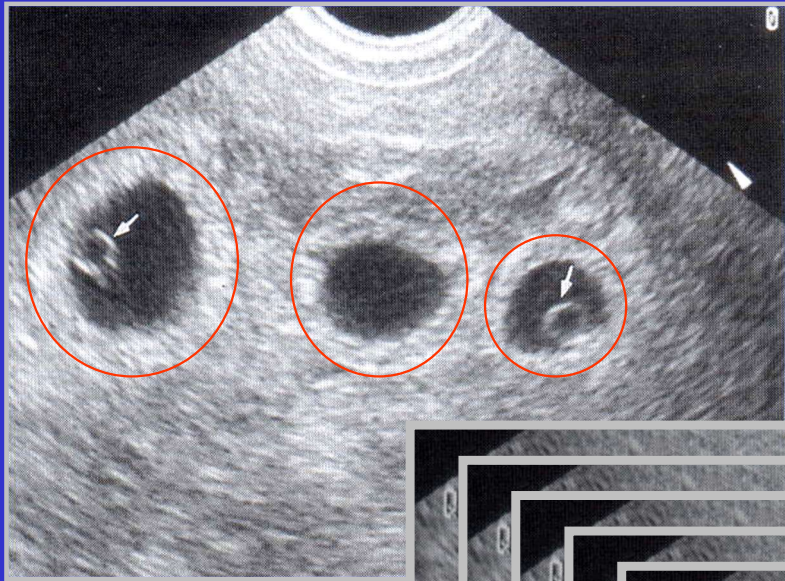


In consideration with:

- ***cause of infertility***
- ***number of previous attempts***
 - ***stimulation results***
 - ***uterine configuration***
 - ***endometrial thickness***
- ***uterine and ovarian perfusion***
 - ***uterine contractility***

... be carefull !!

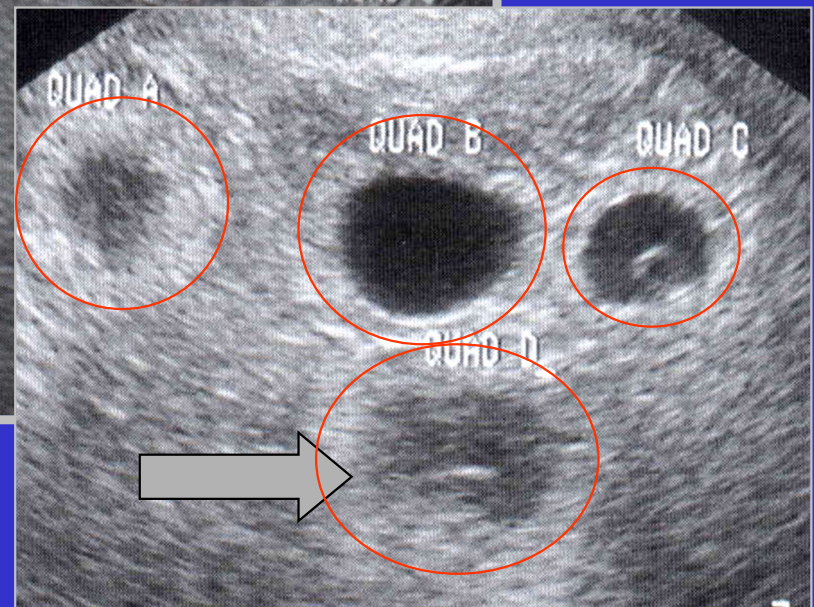
**Triplets or
quadruplets?**



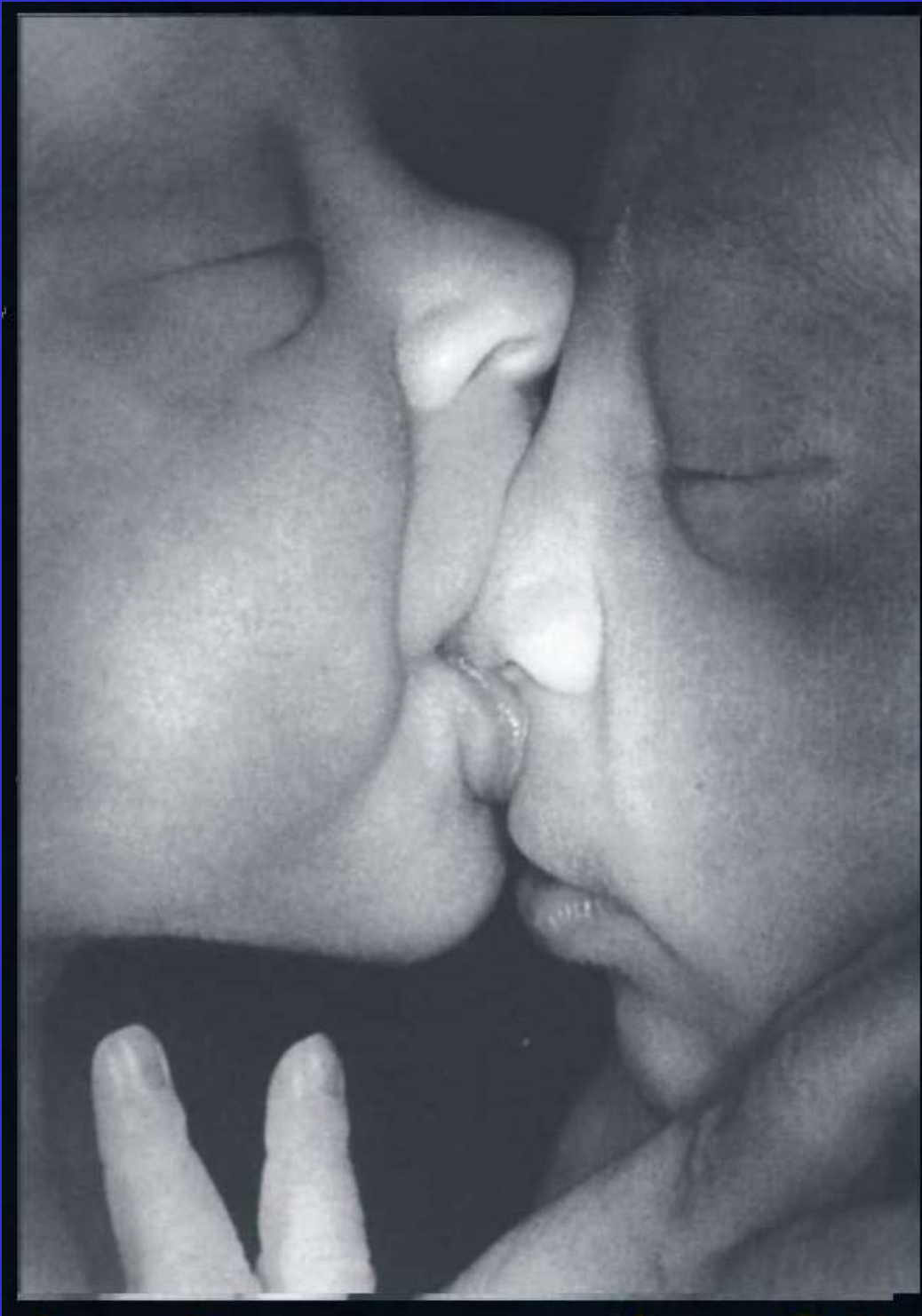
*probe
movement*

2D

limitations



TWINNING = SHARING



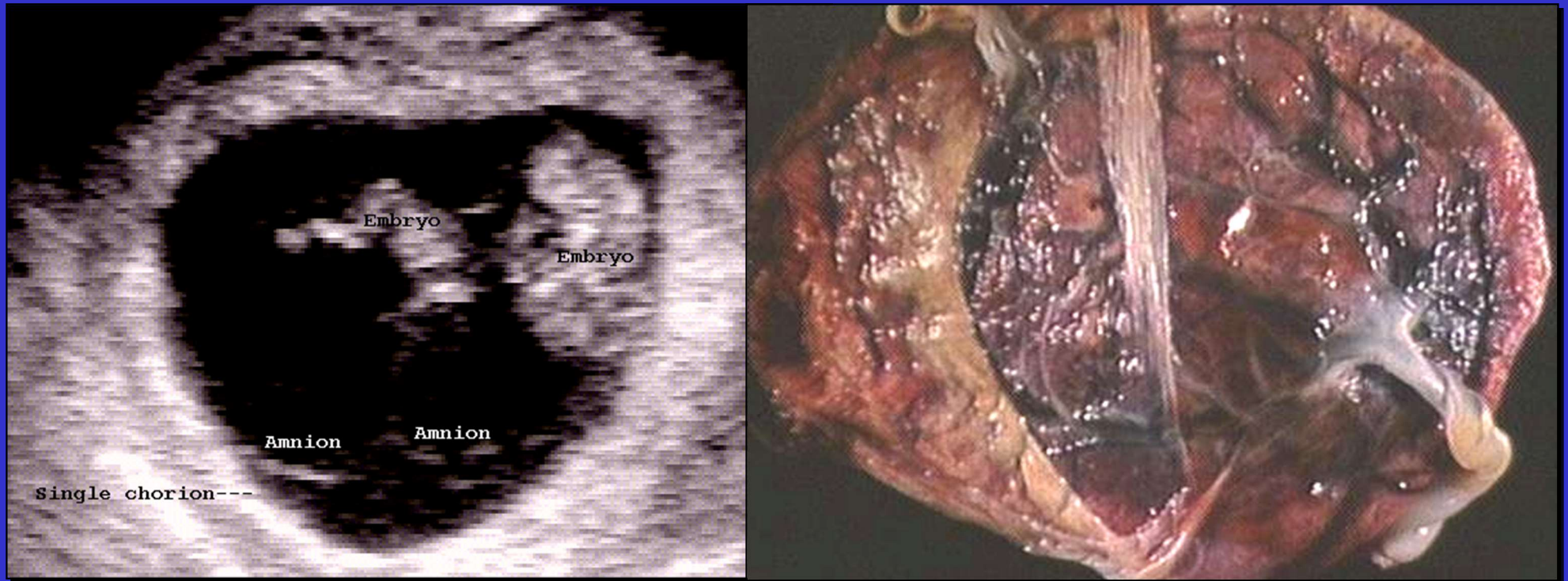
moreno pena , immaculada RAB 4-8L/Obstetric C. Gutenberg Dra Medic
9509-04-07-28-5 GA=28w0d 2.3/10.1cm / 4Hz 28.07.2004 18:10:20

TWINNING = SHARING

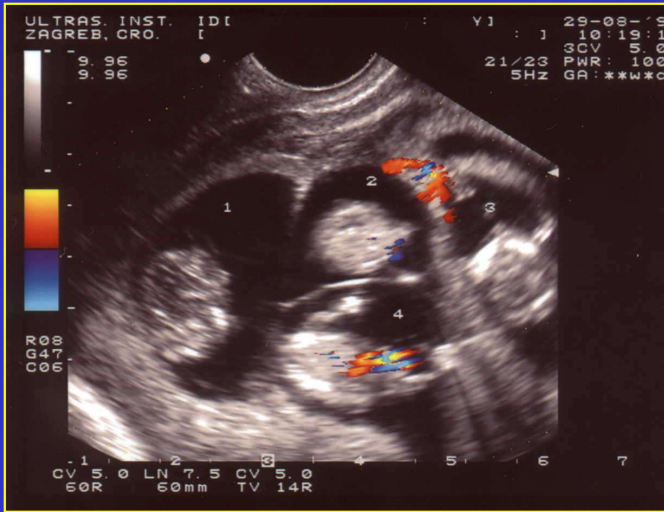


I. The same maternal supply

TWINNING = SHARING



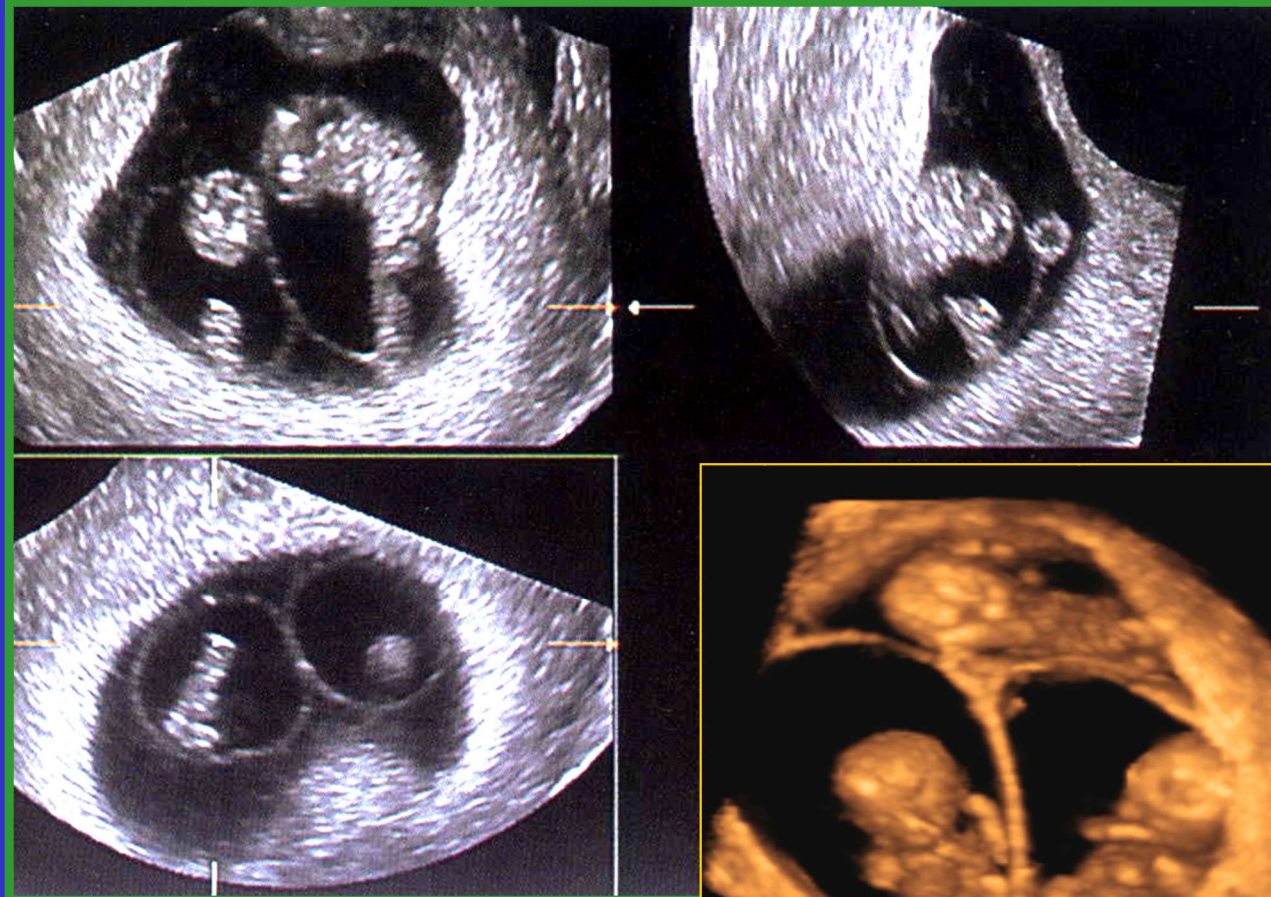
IIIa. The same chorion



754 PATIENTS UNDERGOING IUI

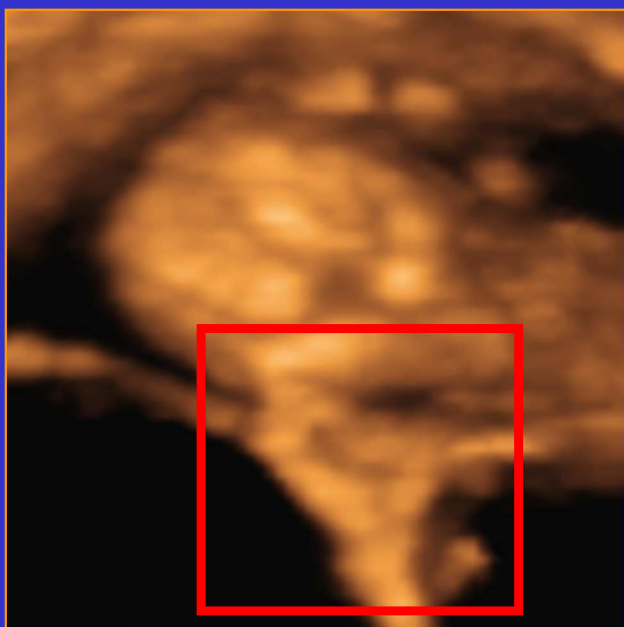
- **32 % (98/305) TWIN GESTATIONS**
- **13 % (39/305) HIGHER-ORDER MULTIFETAL GESTATION**

2D multiplanar imaging

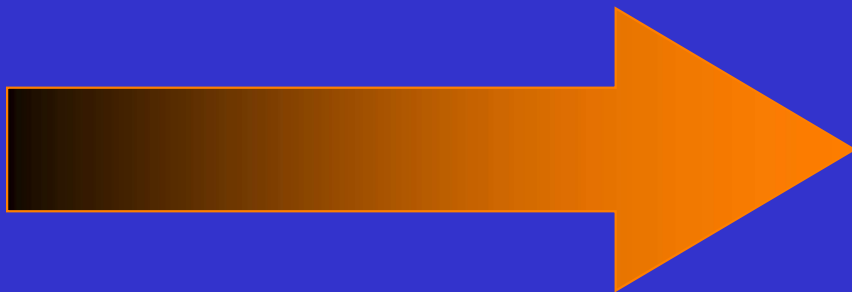


TRIPLETS

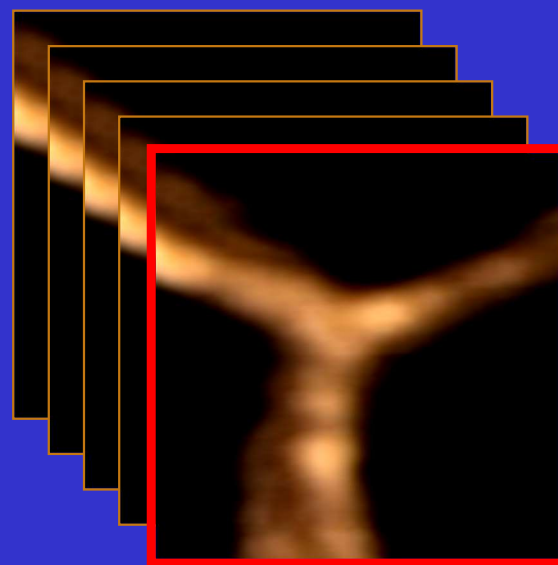
- volume scanning
- volume rendering
- spatial reconstruction *3D reconstruction*
- plastic imaging



TRIPLETS



MERCEDES - SIGN



Objective #2: Prenatal Diagnosis

- **The triple test is inaccurate**
- **The risk of having at least one fetus with TRISOMY 21 at 32 yrs is similar to the risk at 35 yrs in singletons**

Reducing the risk of invasive prenatal diagnosis: Nuchal translucency



Objective #3:

Maternal complications

Cardiopulmonary

- PET, PIH
 - Beta-mimetics
-

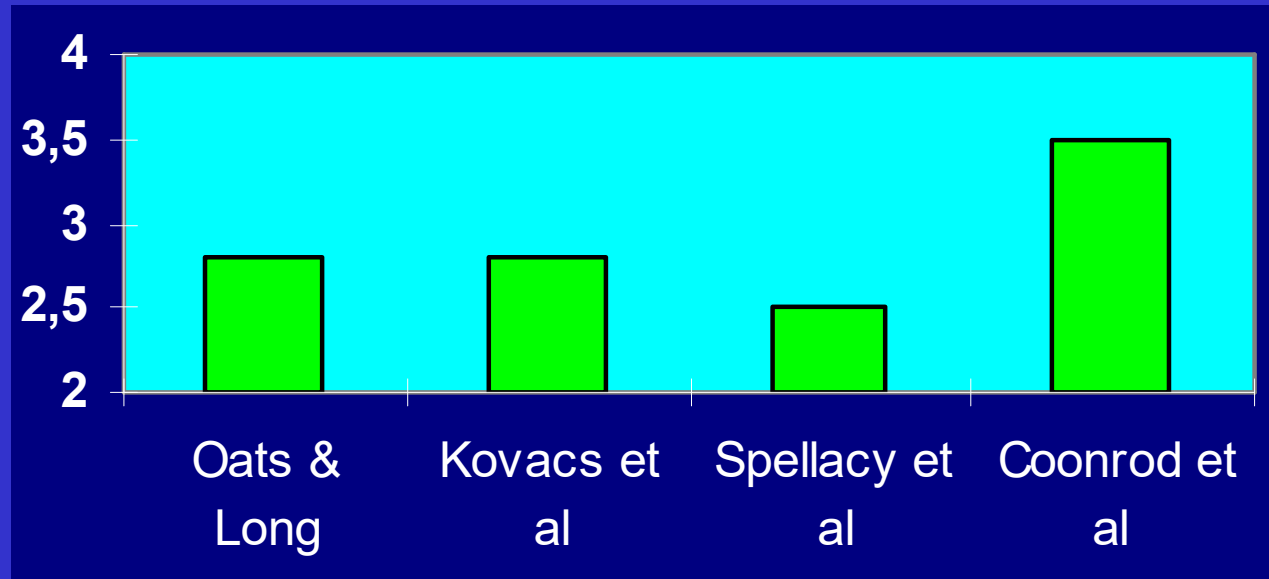
Hematological

- Anemia

Obstetrical

- PTL - PTD
- C/S
- Abruption
- PPH

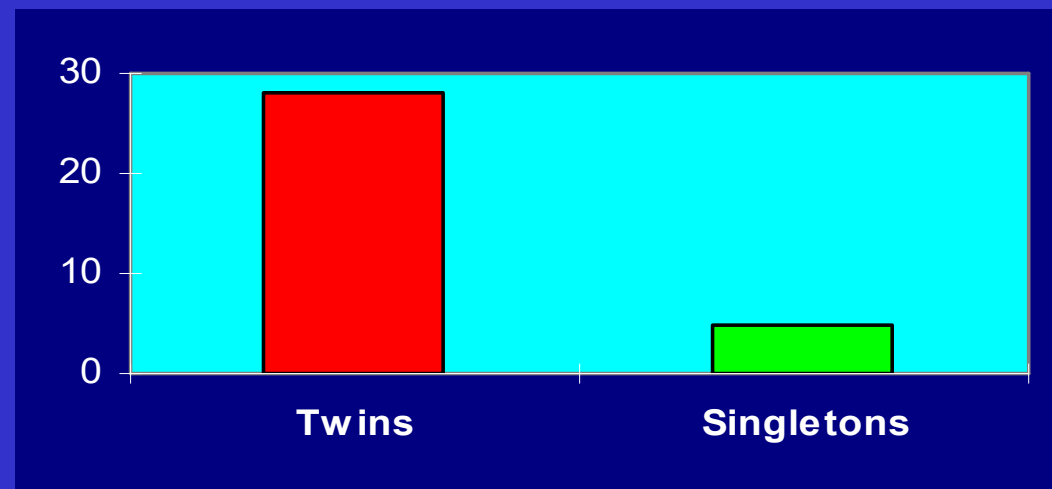
Hypertensive disorders



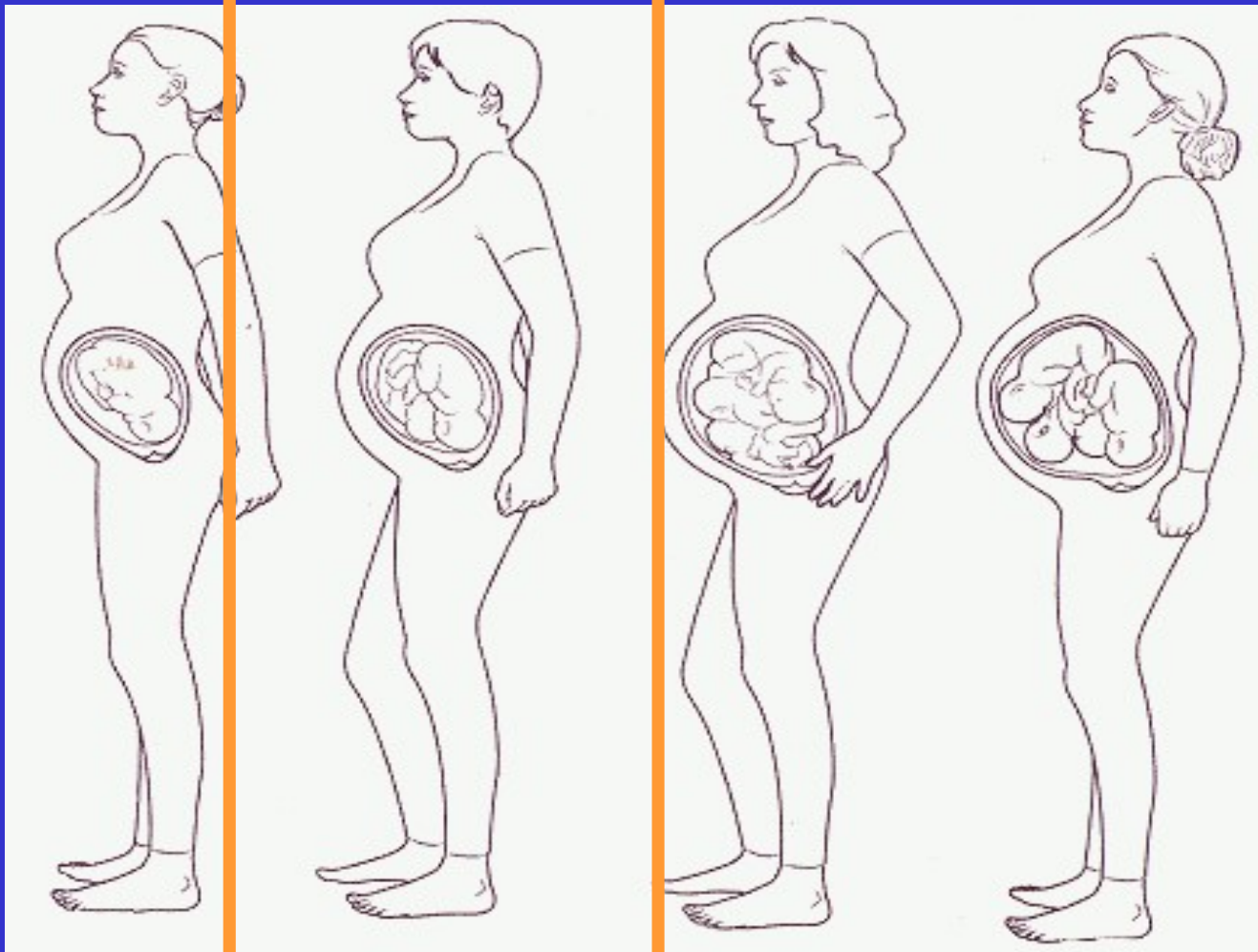
**RR in twins
is 2.5 - 3.5**

**RR of eclampsia
in twins is 6.0**

Douglas & Redman, 1994

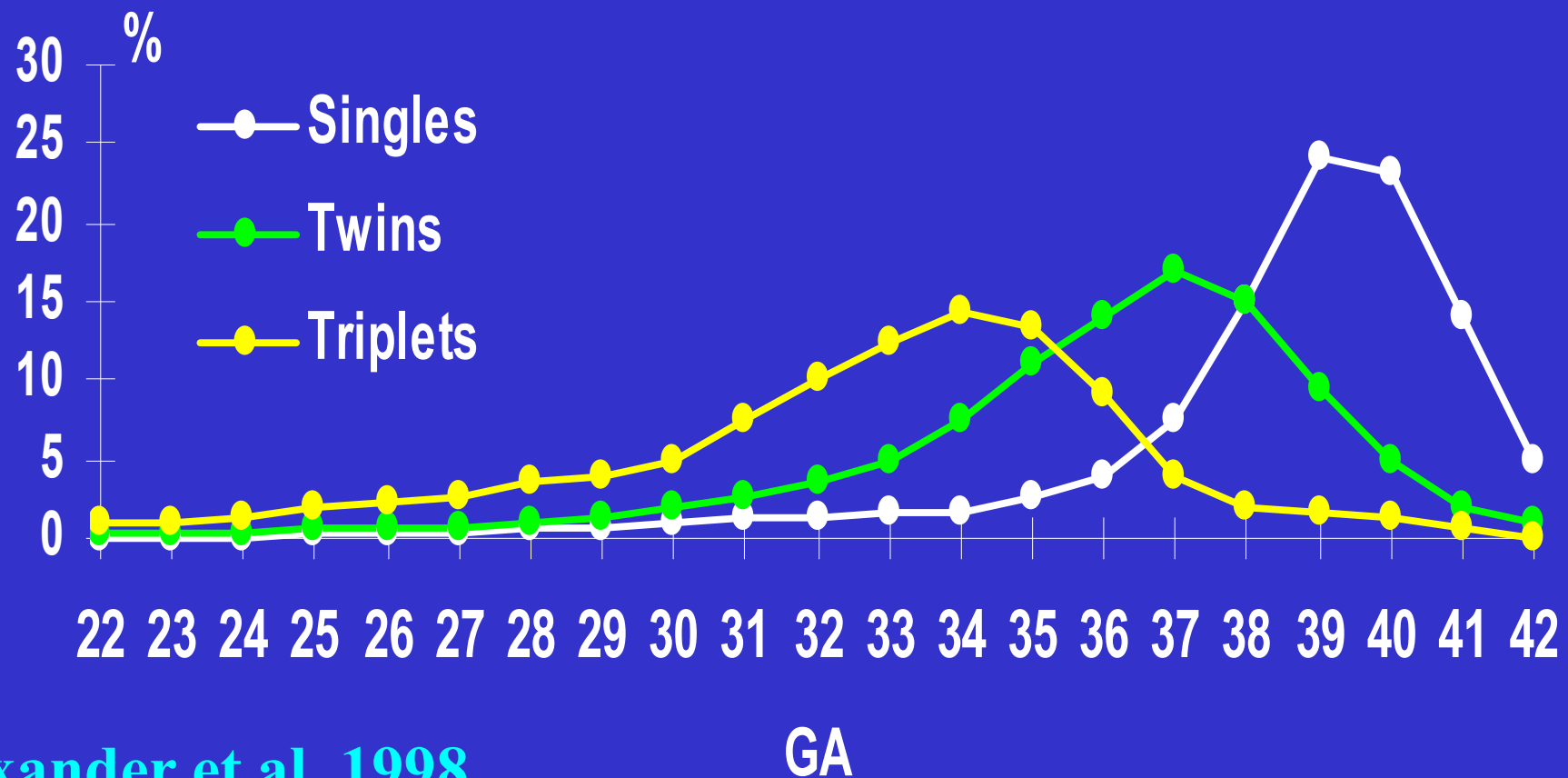


Objective #4: Reducing prematurity



Gestational Age by Plurality

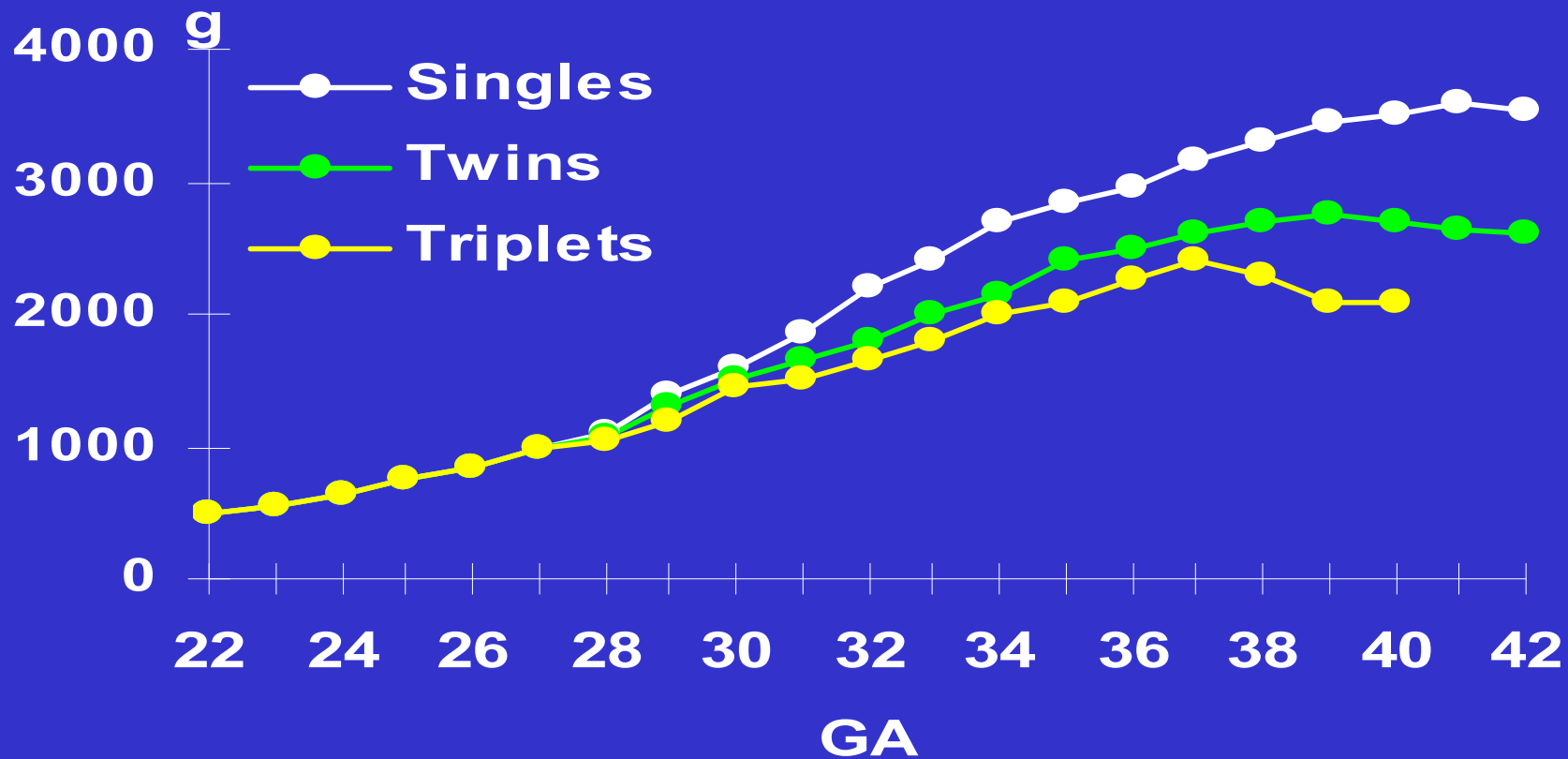
[U.S resident live births, 1991-5]



Alexander et al, 1998

50th Birth Weight Percentile by Gestational Age and Plurality

[U.S resident live births, 1991-5]

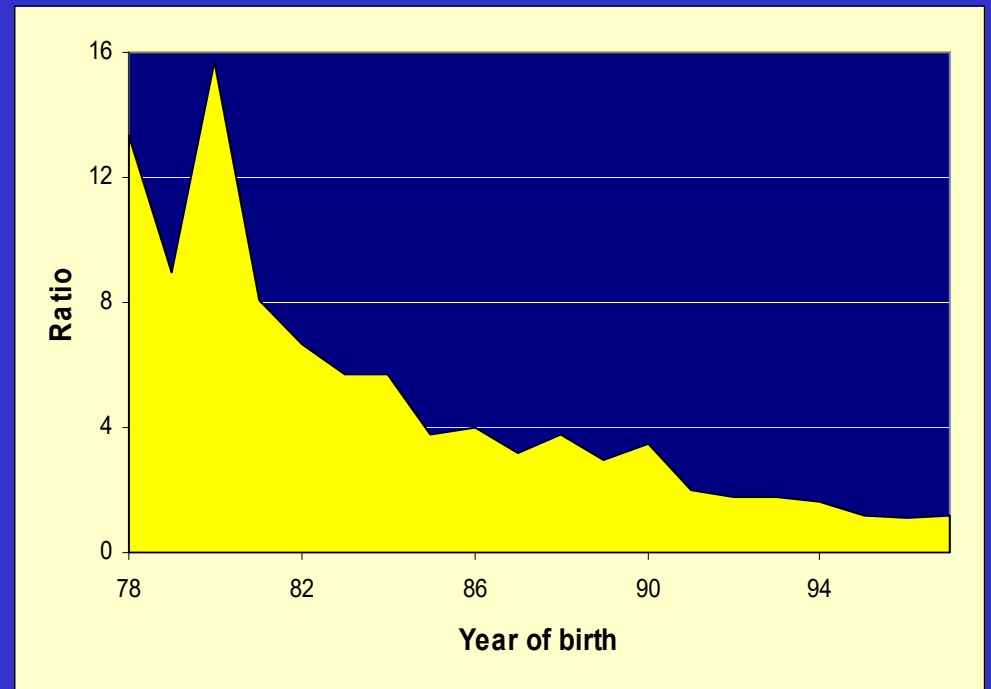
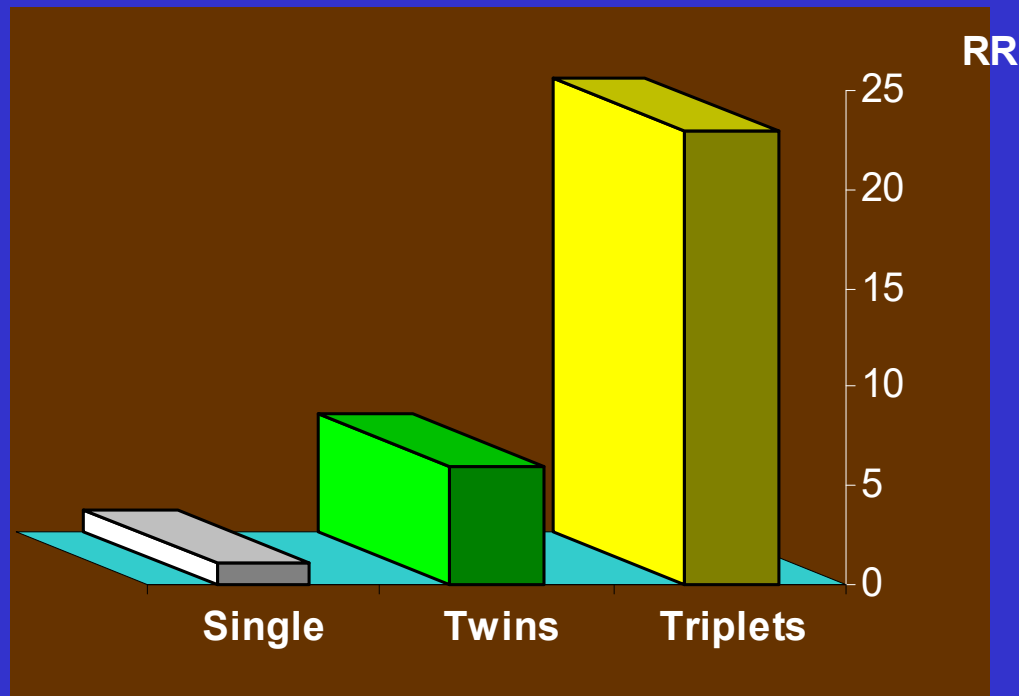


Alexander et al, 1998



Objective #5: Reducing IMP

iatrogenic multiples and CP



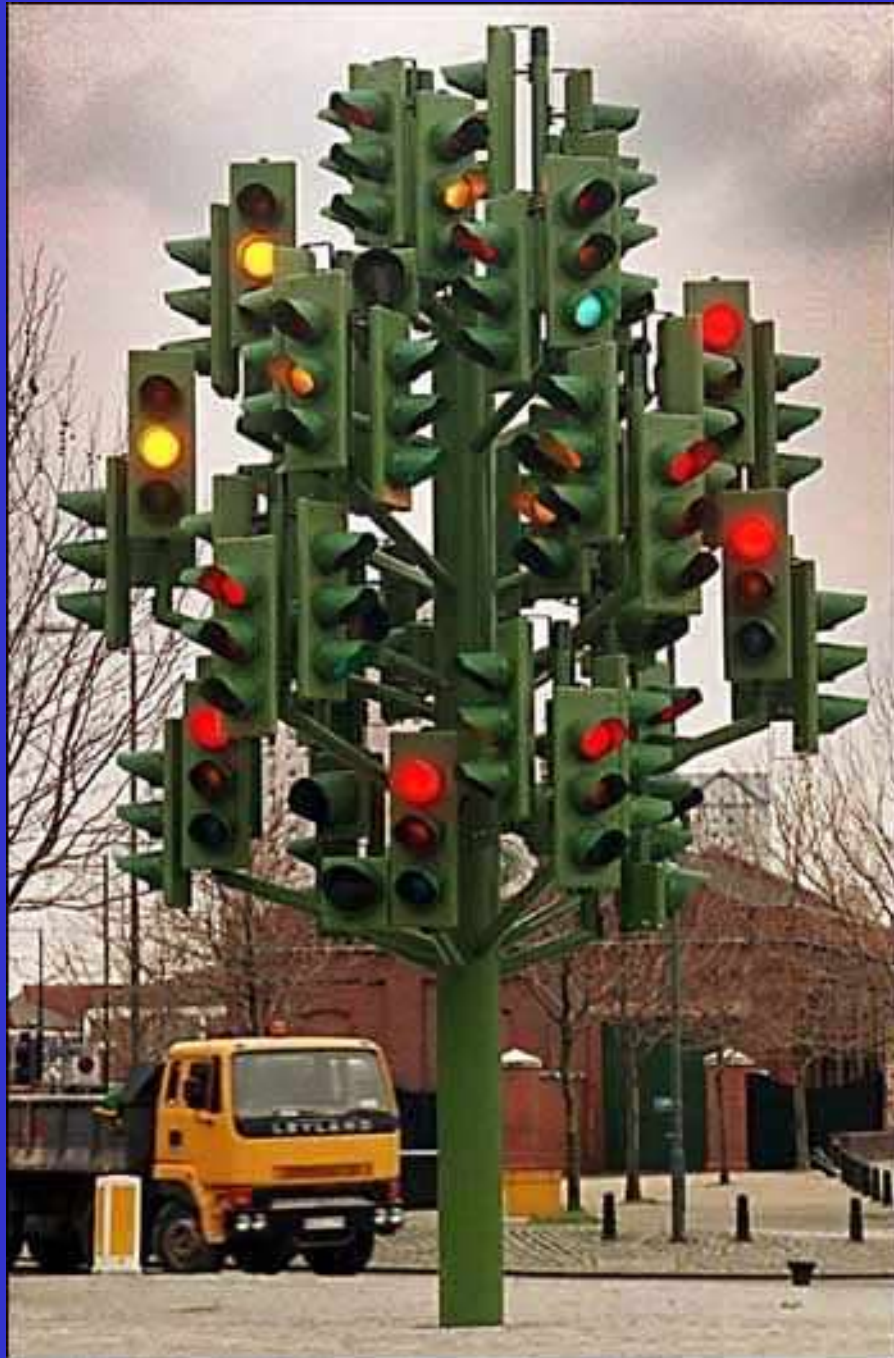
Blickstein & Weissman, NEJM 1999

"LET GO, I
TELL YA"

"WAH! WAH!
I WANT MY
TWIN!!!"

PUFF! PUFF! PUFF!
PUFF! PUFF! PUFF!
PUFF! PUFF! PUFF!

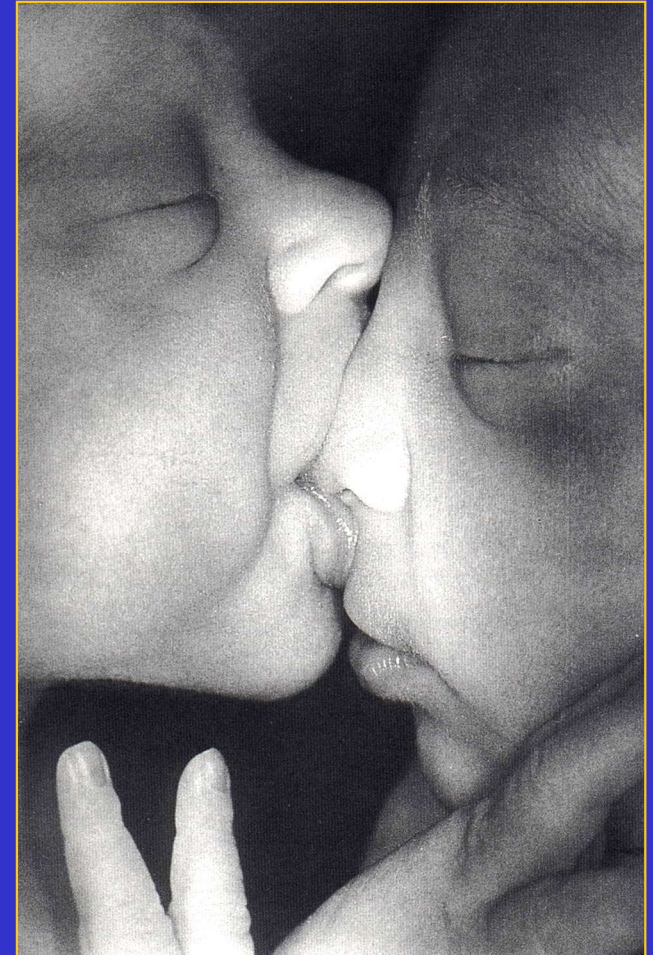




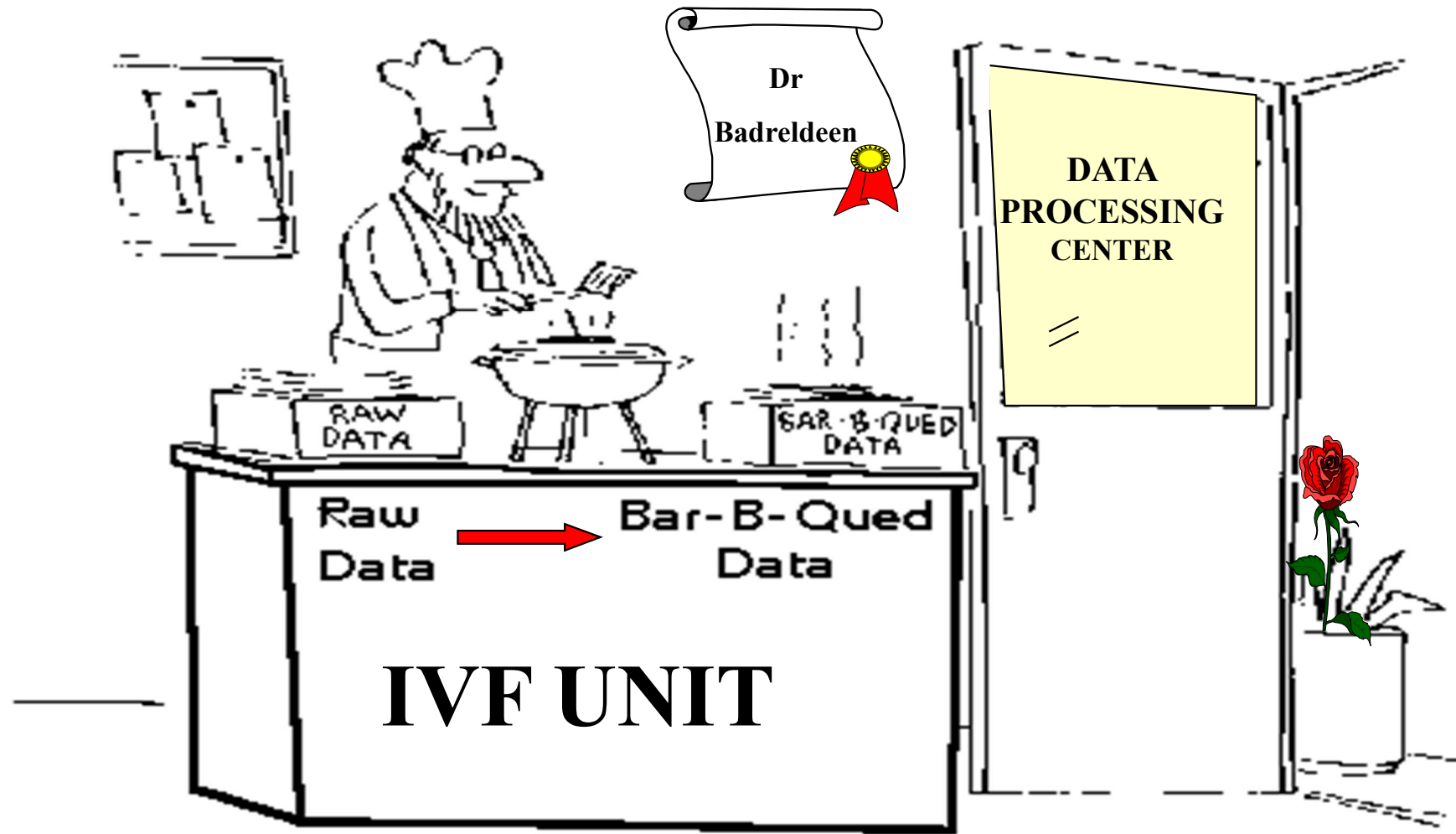
**Decision
making in
twin delivery**

Reasons for CS in twins:

- **Infertility**
- **Age**
- **S/p CS**
- **Size and age of fetus**
- **Maternal complications**



“DATA PROCESSING CENTER” at Hamad Medical



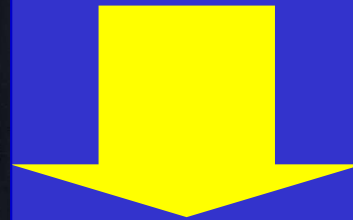


**HOW TO AVOID
MULTIPLE PREGNANCY
USING METHODS OF
ASSISSTED REPRODUCTION?**

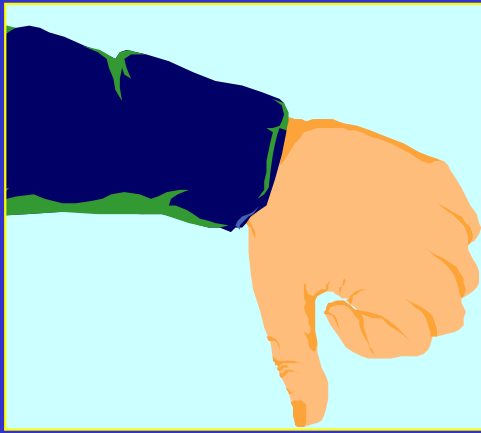
***ASSISTED REPRODUCTION
TECHNIQUES
AND MULTIPLE PREGNANCY***

- 1. Direct impact on the incidence of multiple pregnancy***
- 2. Increased number of patients undergoing infertility treatment***

HIGH MULTIPLE PREGNANCY RATE



- ∞ HIGH RATE OF CESAREAN SECTIONS
- ∞ HIGH PREMATURITY RATE
- ∞ HIGH RATE OF PERINATAL MORTALITY



PROBLEMS ASSOCIATED WITH THE LITERATURE REVIEW

- VITAL STATISTICS RECORD LIVE BIRTHS,
NOT TOTAL PREGNANCIES
- VARIOUS DEFINITIONS USED FOR “PREGNANCY”
- DENOMINATORS VARY FOR CALCULATION OF
“PREGNANCY RATES”
- MULTIPLE REPORTS ARISING FROM THE SAME
DATA BASE

TRIPLET PREGNANCIES

9 % conceived spontaneously
50 % after ovulation induction
38 % after IVF or GIFT



Elster et al., *Obstet Gynecol* 1991

QUADRUPLET PREGNANCIES

6 % conceived spontaneously
69 % after ovulation induction
25 % after IVF-ET or GIFT



Collins & Bleyl,
Am J Obstet Gynecol 1990

FACTORS RESPONSIBLE FOR MULTIPLE PREGNANCIES AFTER OVARIAN STIMULATION & IUI WITH GONADOTROPINS

- ♫ YOUNG WOMEN < 30 YEARS
- ♫ MORE THAN 6 FOLLICLES
- ♫ E2 > 1000 pg/ml

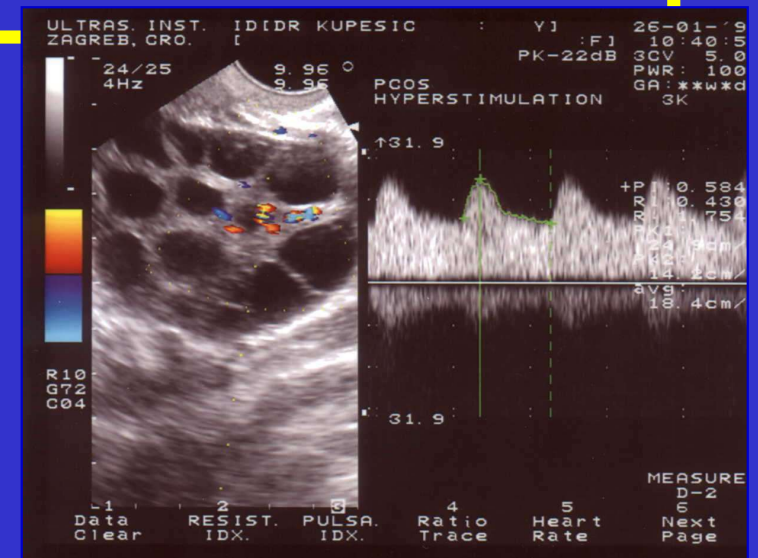


Higher risk of multiple gestation

Ovulation induction

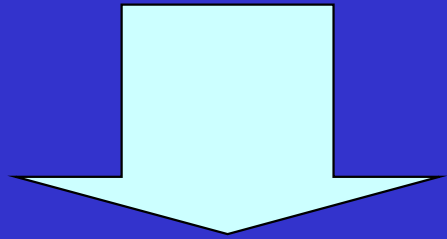


- CLOMIPHENE CITRATE (7-9 % MP)
- hMG / FSH (25-40 % MP)



Kupesic et al., J Perinat Med 1999.

**INSEMINATING DOSE OF SPERM
REDUCED TO LESS THAN
20 MILLION OF MOTILE SPERM**



Reduced risk of
multiple pregnancy



Sperm characteristics & ovarian induction cycles characteristics in predicting the occurrence of multiple conception in patients undergoing IUI

♫ **SPERM WITH AN AMPLITUDE OF LATERAL HEAD MOVEMENT > 4 microm**

♫ **PEAK E2 LEVEL > 583 pg/ml**

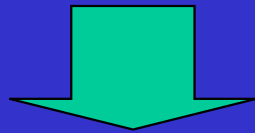


Significant risk factors for multiple pregnancy

TRANSFERS OF

2

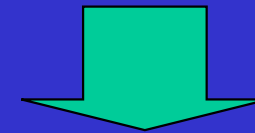
**AVERAGE
EMBRYOS**



TRANSFERS OF

3

**AVERAGE
EMBRYOS**



8 %

MPR*

23 %

42 %

PR

48 %

*** P < 0.05**

*“No more than **two** embryos should ever be placed in the uterus, though under very special circumstances, such as repeated failures of implantation, occasionally **three** embryos may be replaced.”*

The Croatian Society Human Reprod & MAR, 2000.

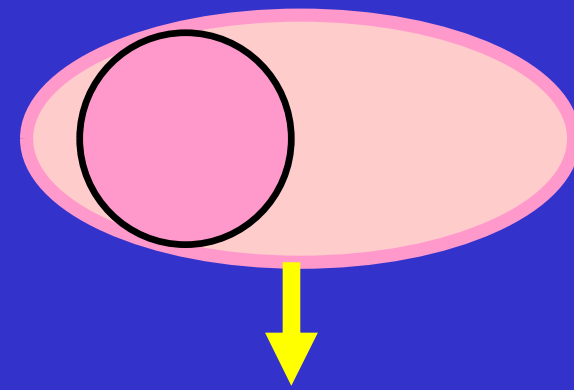
CRYOPRESERVED EMBRYOS

- **AVOID THE PROBLEM OF MULTIEMBRYO TRANSFER**
- **INCREASE PREGNANCY RATE**

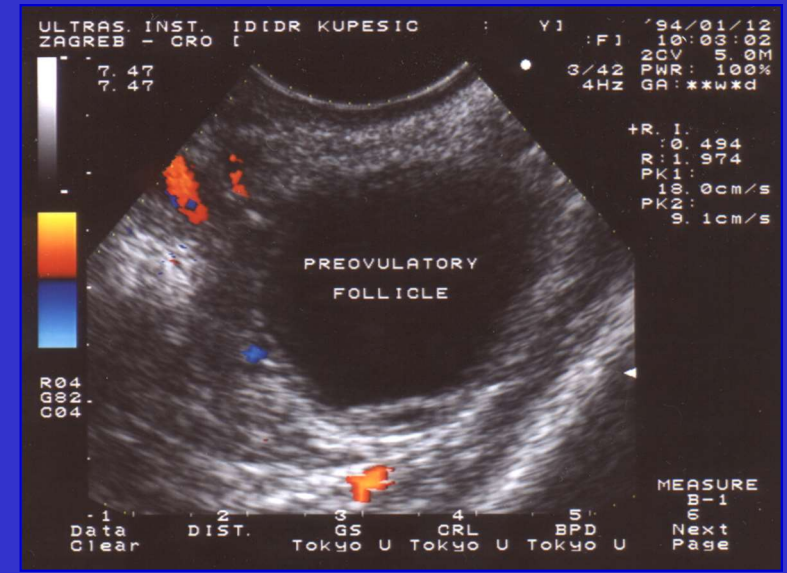


- the uterine milieu may be more receptive to implantation if cryopreserved embryos transferr into the natural, unstimulated endometrium

"Natural cycle" IVF-ET (30%)



- no ovarian stimulation
- collection of only a single oocyte per attempt



- REDUCES THE COST PER CYCLE
- THE RISK OF MULTIPLE GESTATION IS VIRTUALLY ELIMINATED

TUBAL EMBRYO TRANSFER OUTCOME BY NUMBER OF EMBRYO TRANSFERRED

<i>No.embryos transferred</i>	<i>Pregnancies /transfer (%)</i>	<i>Multiple pregnancies (%)</i>
1	20	0
2	29	0
3	45	21
4	38	57
Total	40	31



TWINNING = SHARING



II. The same uterine milieu

Aberrant growth



6 months

Conjoined twins







1th World Congress

Twins Pregnancy – a Global Perspective

Venice – April 16 – 18, 2009



**Diagnosis of Congenital Heart Disease in Twins
and High Order Pregnancy**



Diagnosis of Congenital Heart Disease in Twins and High Order Pregnancy



**Professor Badreldeen Ahmed FRCOG MD (Newcastle)
Hamad Medical Corporation Feto – maternal Unit
Women's Hospital – Doha – Qatar.**

Does Multiple gestation increases CHD

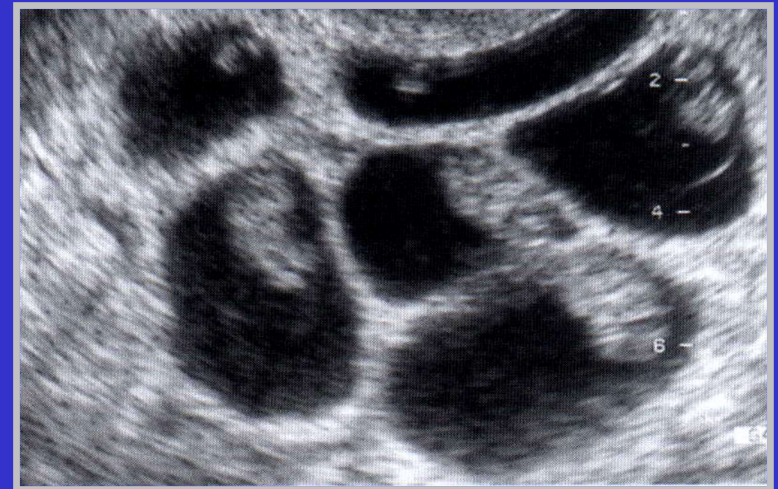
It Should: (in utero insult)

May be: (Sweden birth Register)

NO:

Yes: (Hansen et al NEJM 2002)

Yes: (Merlob et al EJMG, 2005)





Fetal Echocardiography clinic

Salwa Morcos, El Sissi, M Darwal, Reema Kamal, M Numan,

N Salih; Najat Khneyab; Z Mansori; Baderedeem Ahmed

Hamad Medical Corporation, Doha, Qatar

Twins and High Order Pregnancy

Multiple pregnancy	Numbers
Twins	125
Triplets	24
Quadruplets (eight viable GS)	4
Quintuplets (Fetal reduction)	2

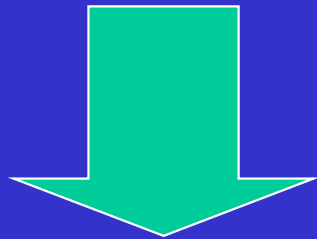
Types of Congenital Heart Disease and Pregnancy Outcome

Congenital heart defect is 4%

Number	Gestational age	Prenatal diagnosis	Type of twin	Chromosomes	Postnatal diagnosis
1	21 weeks	Hypo plastic heart	DD	Not A viable	Hypo plastic heart
2	22 weeks	Hypo plastic heart	DD	Not A viable	Hypo plastic heart
3	20 weeks	Hypo plastic heart	MD	Not A viable	Hypo plastic heart
4	21 weeks	Atrioventricular septal defect	MD	Not A viable	Atrioventricular septal defect
5	23 weeks	Atrioventricular septal defect	DD	Not A viable	Atrioventricular septal defect
6	22 weeks	Ventricular Septal defect	MD	Not A viable	Ventricular Septal defect
7	21 weeks	Ventricular Septal defect	DD	Not A viable	Ventricular Septal defect

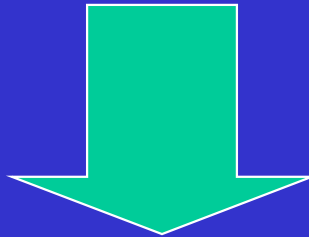
Diagnosis of Congenital Heart Disease in Twins and High Order Pregnancy

High risk population



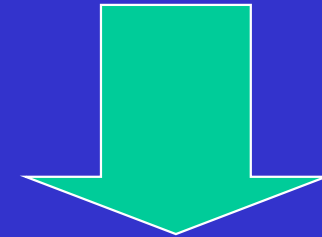
14%

Twins and high order pregnancies



4%

Low risk population



<1%

Twins pregnancy and high order pregnancy is an indication for Fetal echocardiography?

Diagnosis of Congenital Heart Disease in Twins and High Order Pregnancy

Twins pregnancy and high order pregnancy is an indication for Fetal echocardiography?



00 4D TRIPLE bicor triamn sem 11 compri



QUADRUPLETS

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2009

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December 12 – 16, 2009

E-mail: jadranka.cerovec@hko.hr

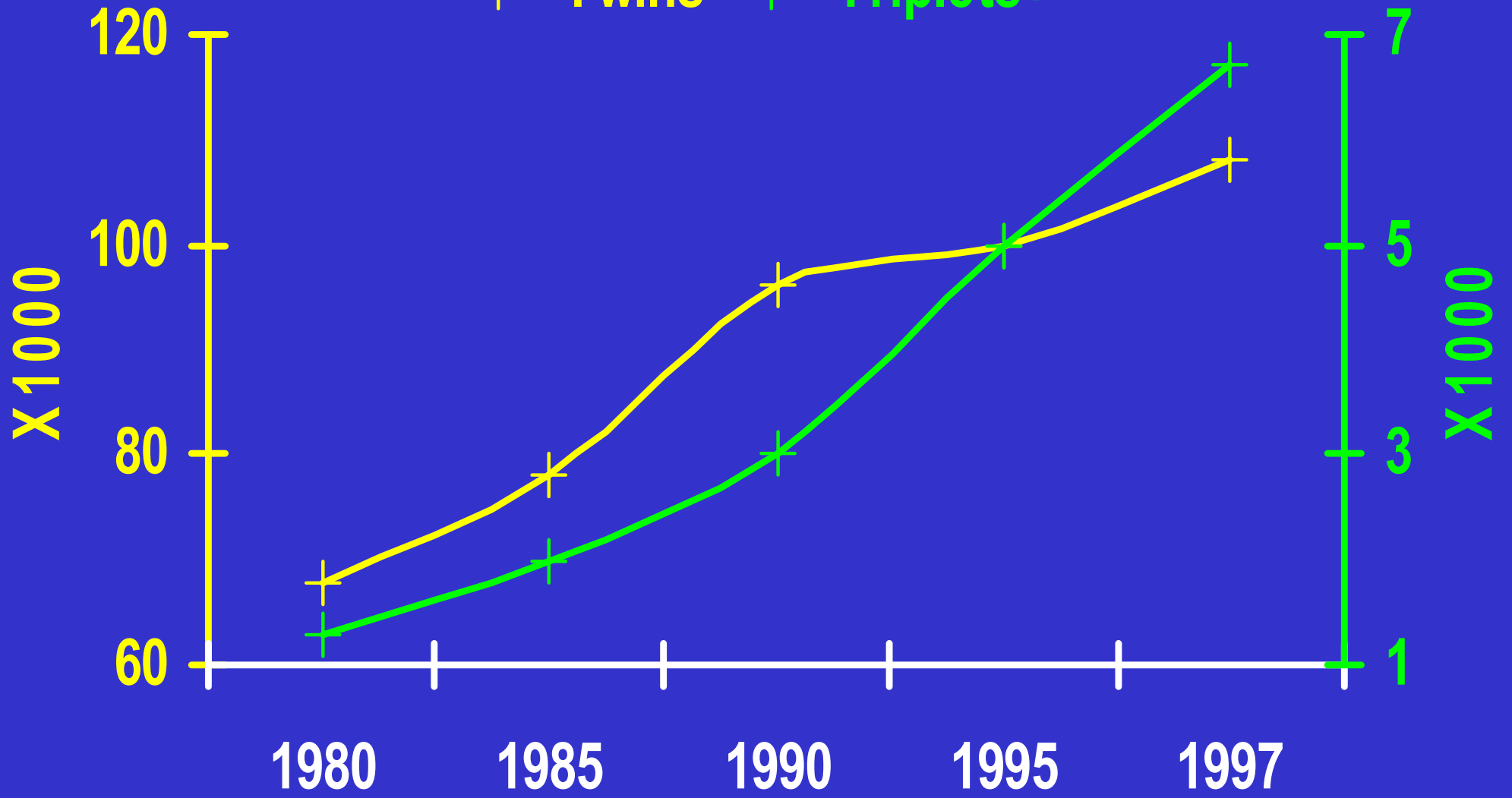
1th World Congress

Twins Pregnancy – a Global Perspective

**Science is a lot of little Guys, cutting out frogs
on foundation Grants.**

USA, 1980-1997

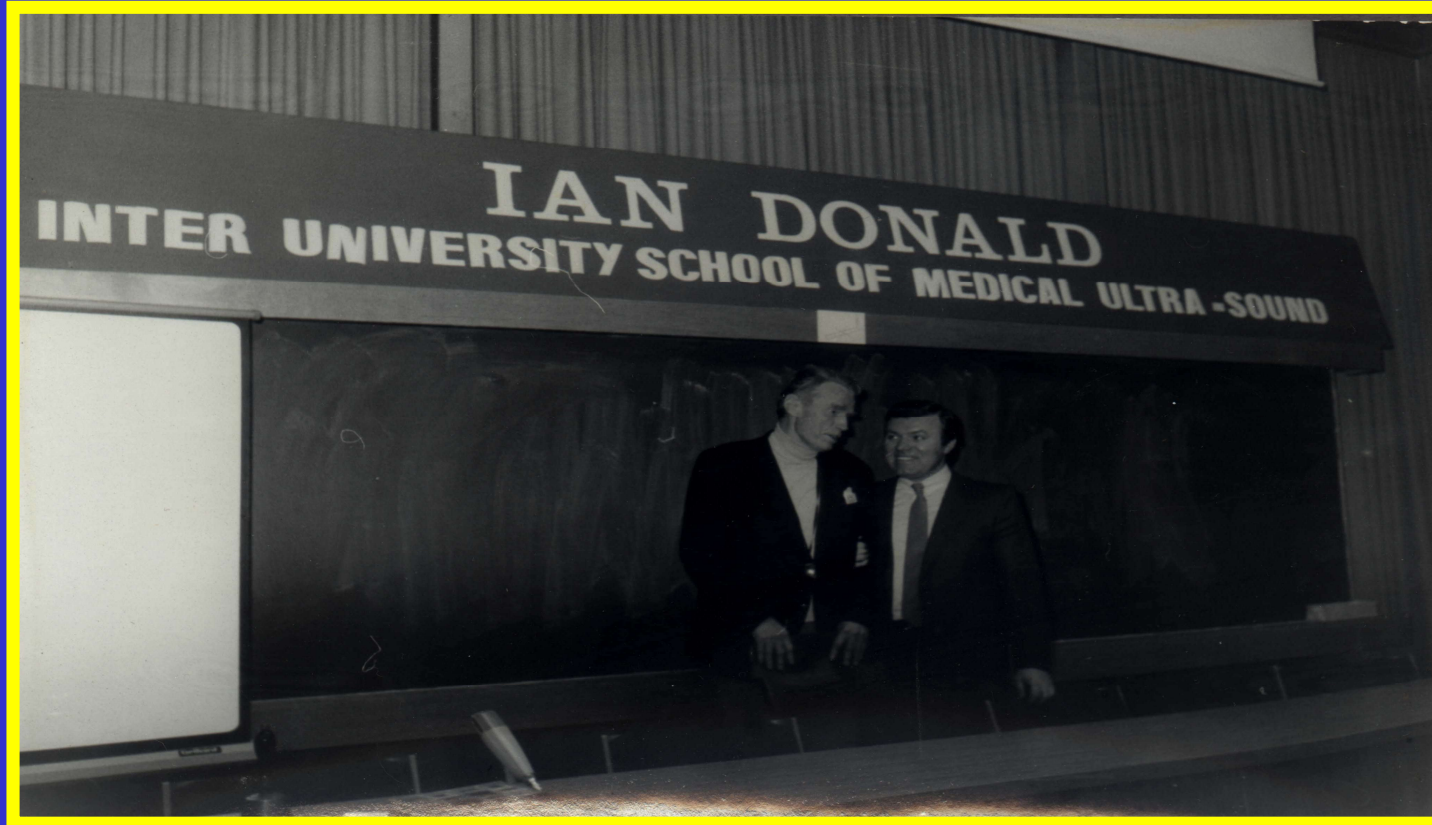
—+— Twins —+— Triplets+



Croatia, 1982-2000 (Rate)

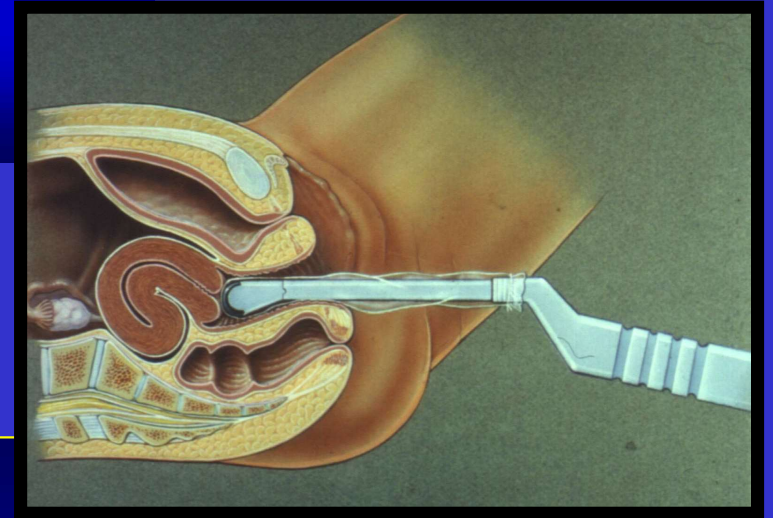


Twin Birth: Double Trouble or Double Joy?

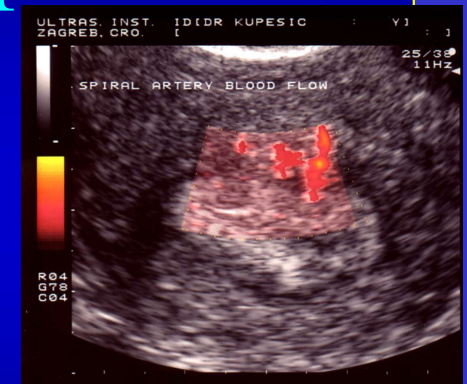


Badreldeen Ahmed FRCOG MD (Newcastle – UK)

PROBABILITY OF (MULTIPLE) PREGNANCY AFTER ET



- ♠ PATIENT'S AGE
- ♠ THE CAUSE OF INFERTILITY
- ♠ ENDOMETRIAL THICKNESS
& VASCULARITY
- ♠ AVERAGE EMBRYO MORPHOLOGY
SCORE



HIGH-QUALITY EMBRYOS

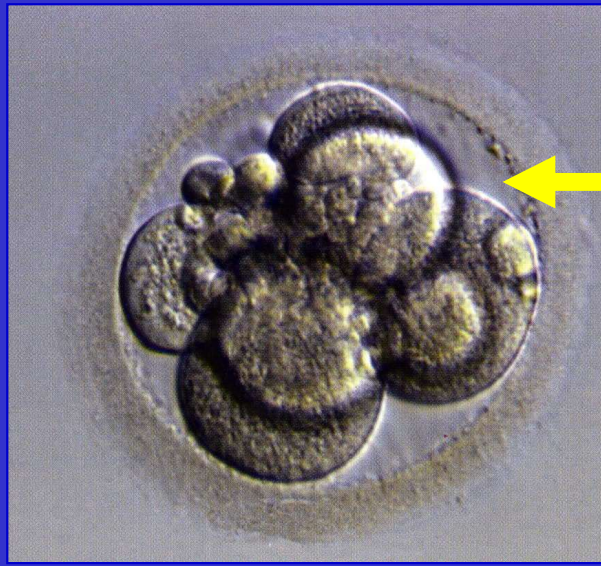
- equal-sized blastomeres
- no fragmentation

*Higher
pregnancy rates*



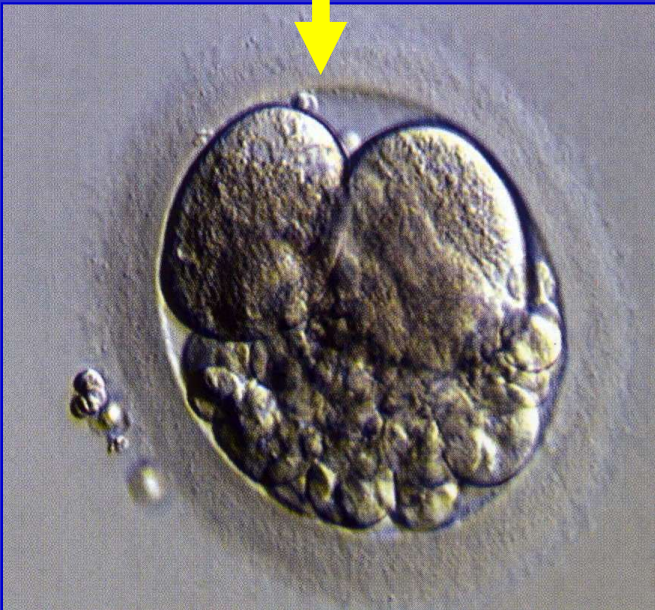
DEFRAGMENTATION

Veeck L., *Ann NY Acad Sci*
Puissant et al., *Hum Reprod*



EMBRYO
grade 3

EMBRYO
grade 4
(near 50 % of fragmentation)



EMBRYO
grade 5
(near 80 % of fragmentation)

