MULTIPLE PREGNANCY

Dr Amal Barakat
JU/5th Year Medical Students
November/2023

MULTIPLE PREGNANCY

- A pregnancy with more than one fetus is called a multiple pregnancy

TERMINOLOGY

- Two offspring – twins //Twins are by far the most common form of multiple births in humans
- Terms used for the number of offspring in a multiple birth, where a number higher than three ends with the suffix **-*uplet***:
- High Order Multiple Pregnancy
- three offspring – triplets
- four offspring – quadruplets
- five offspring – quintuplets
- six offspring – sextuplets
- seven offspring – septuplets
- eight offspring – octuplets
- nine offspring – nonuplets
- ten offspring – decuplets

Incidence and Epidemiology

- **DZ twins** arise in about 1% to 1.5% of pregnancies, and MZ twins occur in 0.4% of pregnancies.
- The incidence of multiple gestation **continues to increase in developed countries,** and now accounting for more than **3%** of all live birth
- **DZ twins** are **more common** than **MZ twins**, **69 and 31 %** of twins, respectively.
- Rates of spontaneous DZ twinning are greatly affected by racial, ethnic, geographic, maternal age, family history.
- The **incidence of MZ twins** is relatively **stable** worldwide at **3 - 5 /1000** births

Rising multiple birth rate is due mainly to:

- **Rising use of drugs used in induction of ovulation & Increasing use of Assisted Reproduction Techniques including (IVF).**
- ***Up to 24% of successful IVF procedures result in multiple pregnancies***
- Ovulation induction: risk of twining:

➢10% for Clomiphene Citrate tab

➢15-30% for Human Menopausal Gonaodotrophins (HMG) Injections

- IVF 20-45% risk of twins. It depends on the patient age & number of embryos transferred.
- **Increasing maternal age at conception: Older women are more likely to become pregnant with multiples.**

MATERNAL COMPLICATIONS

- **Multiple gestations are associated with significantly higher risks for:**

  - ✓ **Hypertension**
  - ✓ **Placental abruption**
  - ✓ **Preterm labor**
  - ✓ **Preeclampsia (26%);**
  - ✓ **HELLP syndrome (9%)**
  - ✓ **Anemia (24%)**
  - ✓ **Preterm premature rupture of membranes (preterm PROM) (24%)**
  - ✓ **Gestational diabetes (14%)**
  - ✓ **Acute fatty liver (4%)**
  - ✓ **Chorioendometritis (16%)**
  - ✓ **Postpartum hemorrhage (9%)**
  - ✓ **Miscarriage**
  - ✓ **Operative Delivery**
  - ✓ **Postnatal illness**

MATERNAL COMPLICATIONS

- **The risk of pre-eclampsia for women with twin pregnancies is almost three times that for singleton pregnancies, while the risk for triplet pregnancies is increased nine-fold.**
- **In addition, maternal mortality associated with multiple births is 2.5 times that for singleton births.**

FETAL COMPLICATIONS

- Abortions (^^ 1st and second Trimester)
- Prematurity with its complications
- Monochorionicity with its complications
- Intra Uterine Growth Restriction (14-25%)
- Stillbirth
- Increase in infant mortality rates
- Increase in Long- term morbidity (especially neurodevelopmental disability and chronic lung disease)
- The incidence of severe handicap among neonatal survivors of multiple gestation is also increased.
- Major congenital abnormalities are 4.9% more common in multiple pregnancies than in singleton pregnancies.

PRETERM & TWIN PREGNANCY

- **Preterm birth** occurs in more than **50% of twin** and **75% of triplet** gestations.

- Duration of pregnancy becomes shorter with increasing numbers of fetuses.

- The mean duration of pregnancy is **35.3 weeks for twin gestations**, **31.9 weeks for triplets,** and **29.5 weeks for quadruplets.**

- The higher incidence of preterm birth in multiple pregnancies is associated with an increased risk of neonatal mortality and long- term morbidity (especially neurodevelopmental disability and chronic lung disease).

PRETERM & TWIN PREGNANCY

- A **cervical length measured by vaginal ultrasound of less than 20 mm** in a **twin pregnancy** at **20 to 24 weeks** gestation was associated with a **10-fold** positive likelihood ratio for preterm birth before **32 weeks** gestation.

- **Cervicovaginal fetal fibronectin** assay can be used to predict preterm labor.

PRETERM & TWIN PREGNANCY

- **Interventions to prevent preterm labor** and **prolong pregnancy** for patients with multiple gestations :
  - ✓prophylactic **cervical cerclage** (????)
  - ✓Supplemental **progesterone** (????)
  - ✓**Bedrest (????)**
  - ✓**Tocolytic drugs** (????)

Zygosity

- **Dizygotic (DZ),** resulting from the fertilization of two separate ova during a single ovulatory cycle.
- DZ twins have dichorionic-diamniotic (DCDA) placentas.
- Dizygotic twins are always diamniotic, dichorionic (i.e., have 2 sacs and 2 placentas).
- The 2 placentas may fuse but do not have vascular connections.

Factors influencing the incidence of DZ twins are:

- **Factors influencing the incidence of DZ twins** are:
  - ✓**Use of fertility stimulating drugs(**twin births increased from 1/53 infants in 1980 to 1/30 infants in 2009)
  - ✓**Maternal age (**One-third of the increase in multiple births in recent decades has been attributed to increasing age at childbirth)
  - ✓**Race/geographic area** (1.3/1000 Japan, 8/1000 United States and Europe, 50/1000 Nigeria)
  - ✓**Parity**
  - ✓**Family history**
  - ✓**High BMI & Maternal height**

Dizygotic Twin

- Arises from two zygotes (Two ova fertilized by two separate sperms)
- They are genetically non-identical
- They are always Dichorionic/Diamniotic with 2 sacs/2 placenta
- They can be of same or different sex

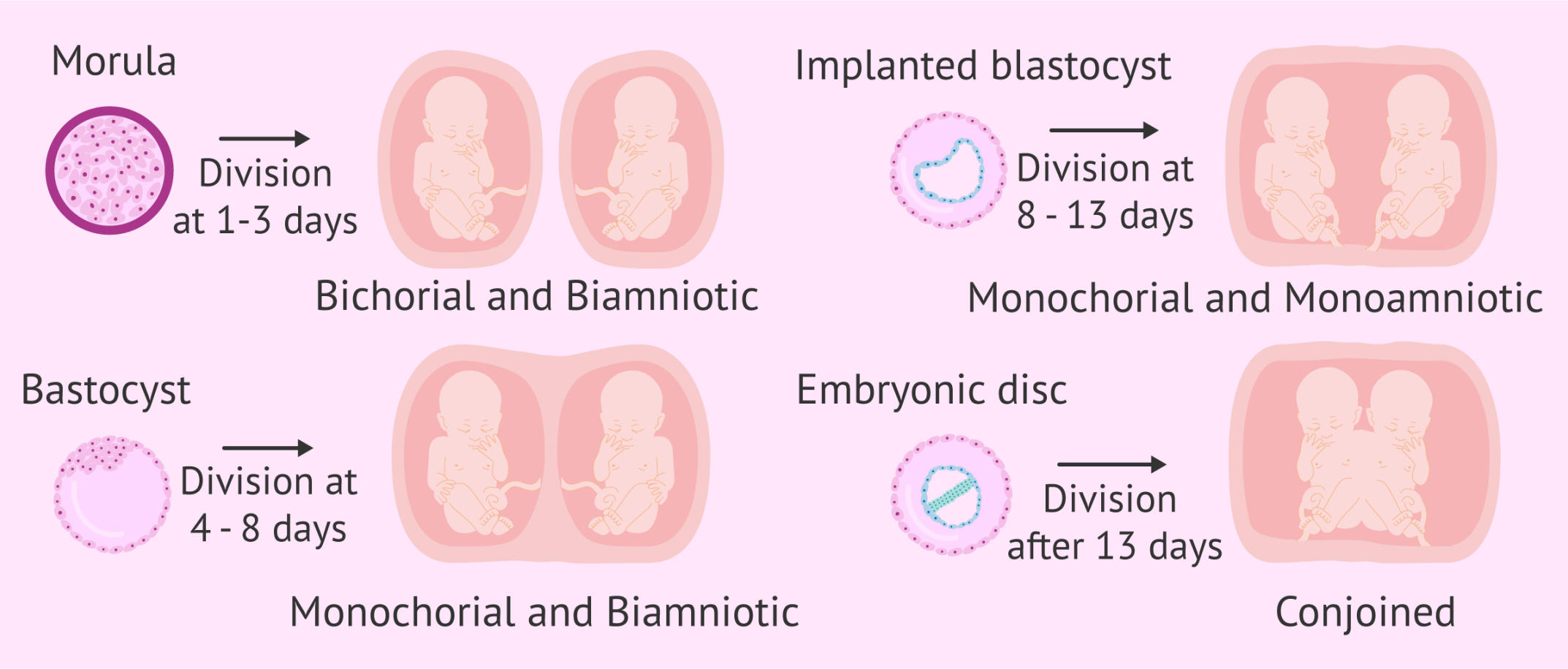
Zygosity

- **Monozygotic (MZ),** resulting from a single fertilized ovum that subsequently divides into two separate individuals.
- The **incidence of MZ twins** is relatively **stable** worldwide at **3 - 5 /1000** births.
- Monozygotic (identical) twins do not run in families.
- Monozygotic twins have different amnionicity and chorionicity depending on the stage of cleavage of the single fertilized ovum.

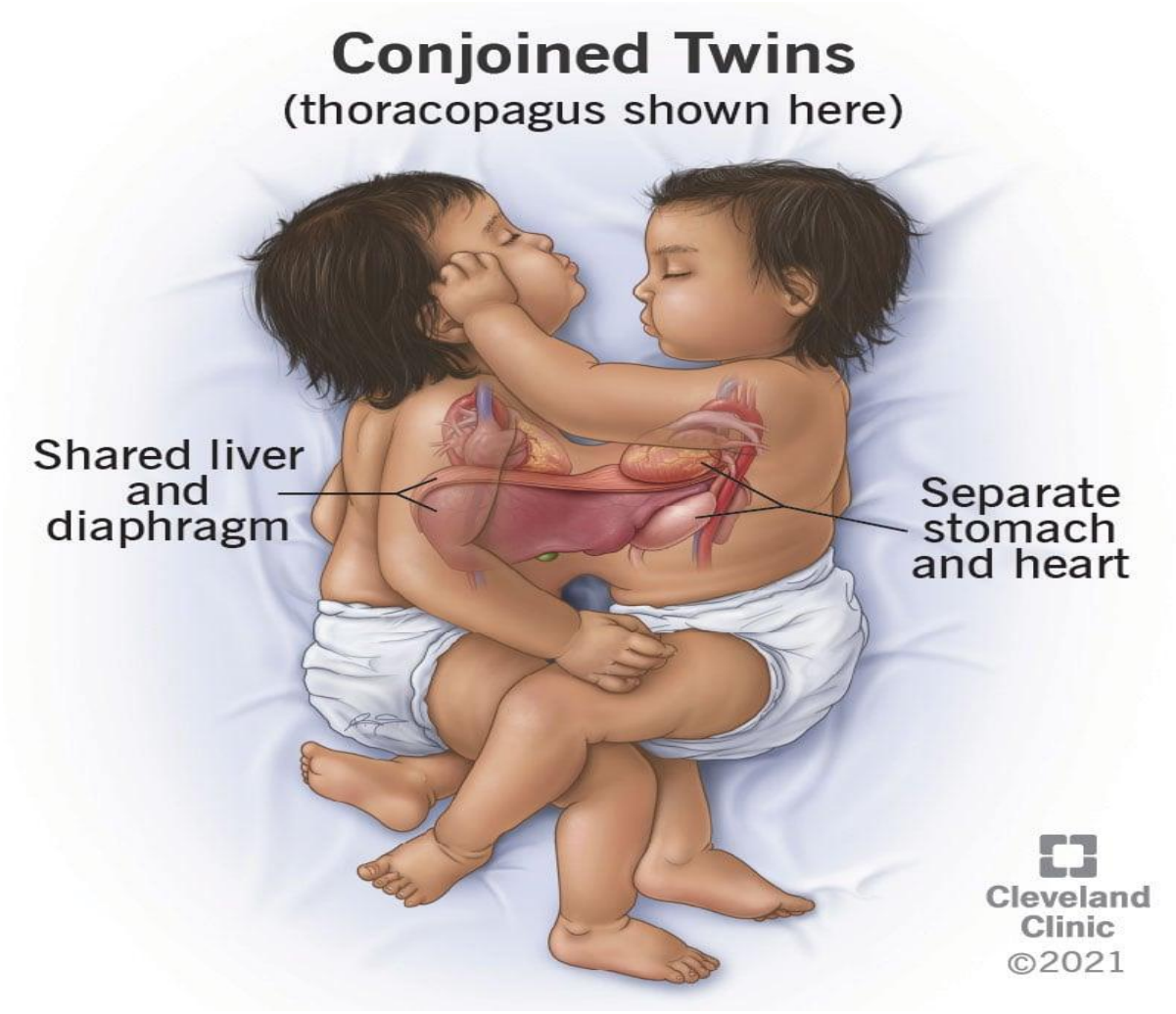
Monozygotic Twins

- **Monozygotic twins have different amnionicity and chorionicity depending on the stage of cleavage of the single fertilized ovum**
- **In MZ Twin the timing of egg division determines placentation**
  - **Diamniotic, dichorionic (DCDA) placentation occurs with division prior to the morula stage (within 3 days post fertilization). This occurs in 29% of the cases.**
  - **Diamniotic, monochorionic (MCDA) placentation occurs with division between 4-8 days postfertilization. This occurs in 70% of the cases.**
  - **Monoamniotic, monochorionic (MCMA) placentation occurs with division between 8-12 days postfertilization. This occurs in 1% of the cases.**
  - **Division at or after day 13 results in conjoined twins. This is an extremely rare condition occurring in up to 200,000 births**

In MZ twins, the timing of egg division determines placentation



Division at or after day 13 results in conjoined twins.



Conjoined Twin

- A subset of **monozygotic twin gestations** in which **incomplete embryonic division** occurs **13 to 15 days** after conception, resulting in varying degrees of fusion of the two fetuses.
- Classified according to the **anatomical site of union** (eg, chest, head).(Thoracopagus, Craniopagus, Ischiopagus)
- **Associated congenital defects** unrelated to the area of fusion are common, as is stillbirth.
- **Delivery of viable infants is always by cesarean.**

Diagnosis

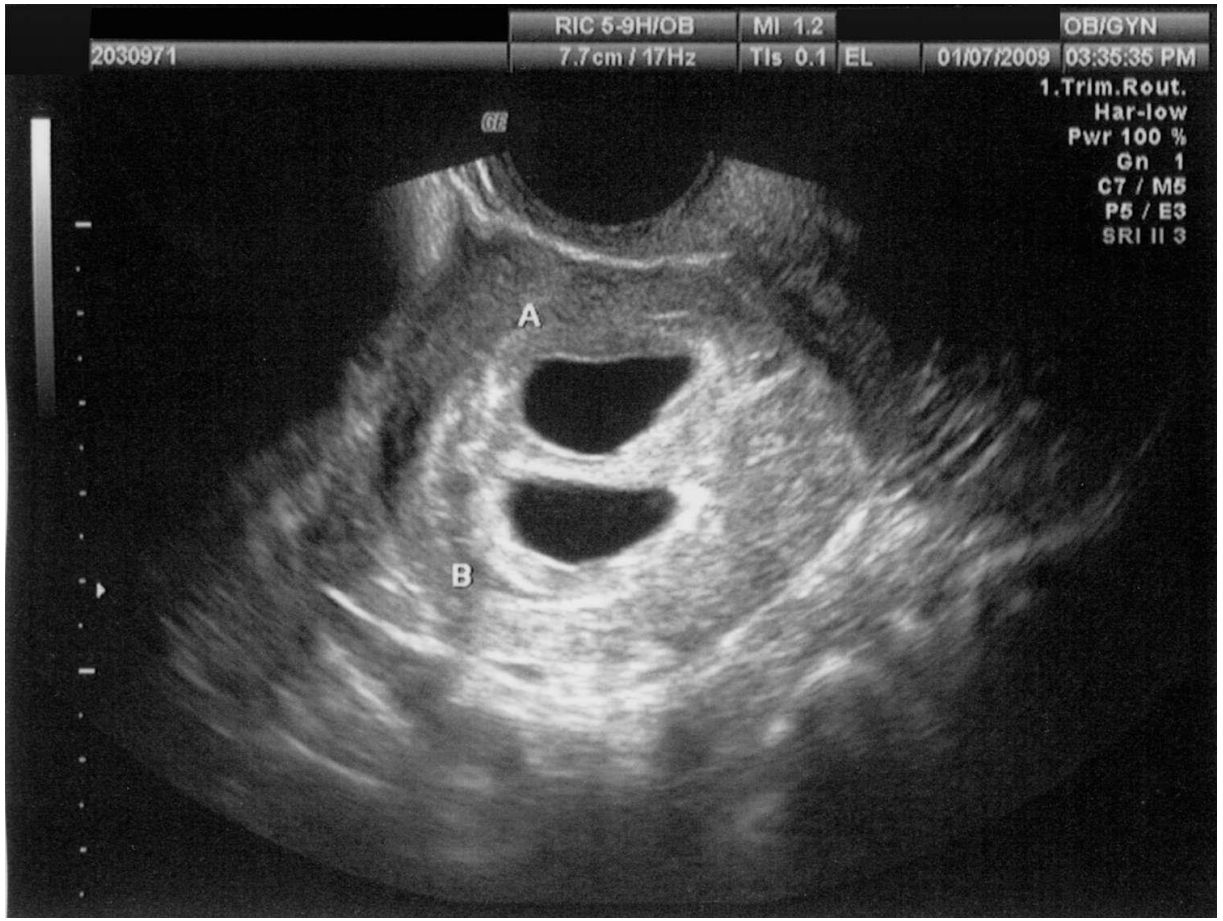
- History
  - Exaggerated symptoms of pregnancy
  - Symptoms due to overdistention (dyspnea, palpitations, leg swelling, varicose veins, hemorrhoids)
  - Inspection:
  - General: pallor, excessive gain weight, leg edema, V/S
  - Fundal height larger than expected gestational age
- Palpation: Multiple fetal pools & grips
- Auscultation of Fetal heart sounds: different FHA
- TAS & Abdominal Ultrsound: are the gold standard for diagnosis of MFP & Follow up

Ultrasound in Twin pregnancy

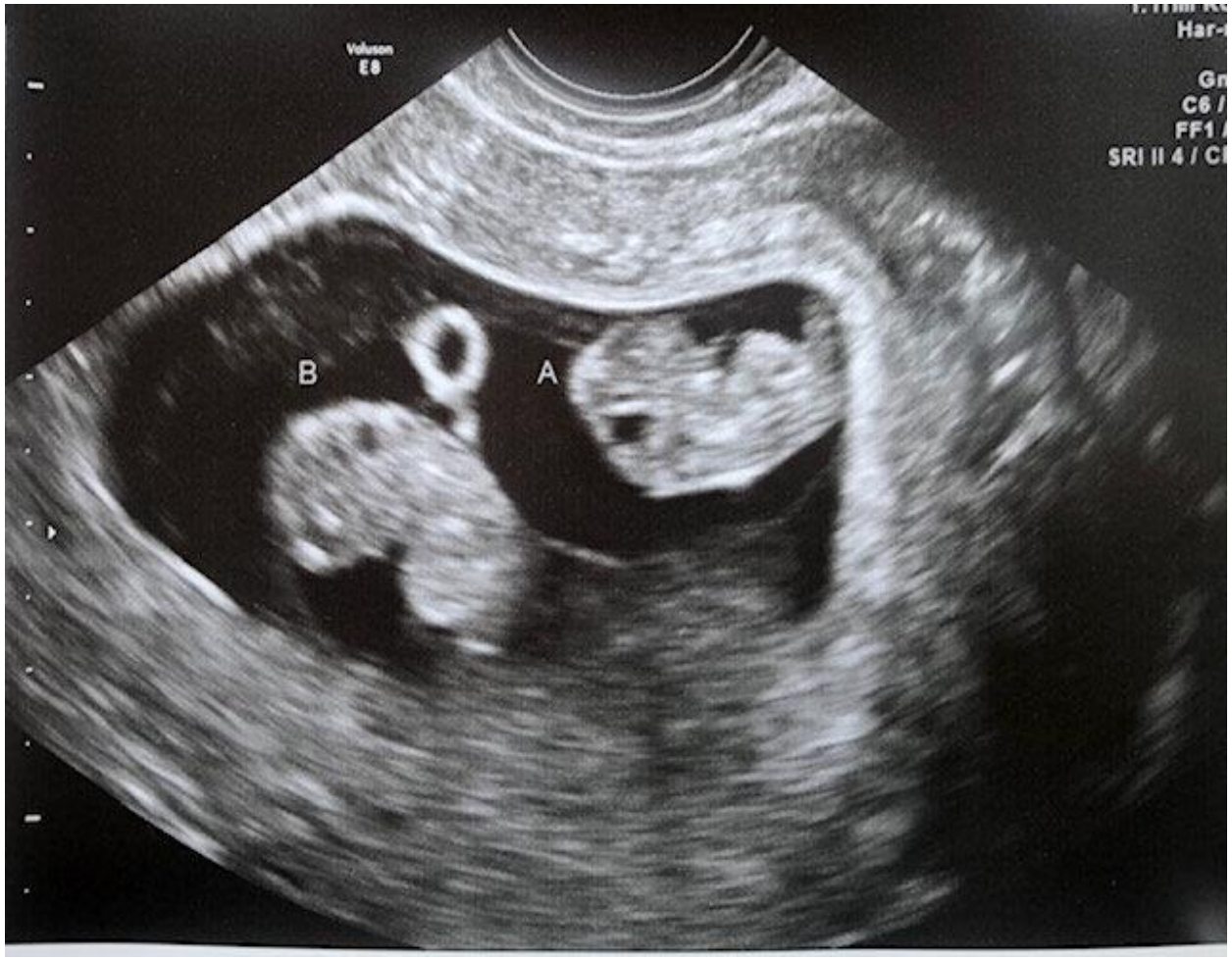
- **Diagnosis**:
  - **Clearly separate gestational sacs**, each surrounded by a **thick echogenic ring**, is suggestive of **dichorionicity.**

- Visualization of **multiple gestational sacs with yolk sacs by 5 weeks**, or **multiple embryos with cardiac activity** by **6 weeks**.

Clearly separate gestational sacs, each surrounded by a thick echogenic ring, is suggestive of dichorionicity.



Visualization of multiple gestational sacs with yolk sacs by 5 weeks, or multiple embryos with cardiac activity by 6 weeks.



Ultrasound in Twin pregnancy

- All women with a twin pregnancy should be offered an ultrasound examination at **10–13 weeks** of gestation to assess:
- **viability**, **chorionicity**, **major congenital malformation** and **nuchal translucency**.

- **Careful sonographic surveys** of **fetal anatomy** are indicated in multifetal pregnancies, because the risk for **congenital anomalies** is **increased (3-5 fold higher).**

Ultrasound in Twin pregnancy

- After confirming a diagnosis of multiple gestation we should determine chorionicity.
- The accuracy of ultrasound in the assessment of chorionicity in the first trimester is high and is mainly based on the evaluation of lambda and T-sign

Ultrasound in Twin pregnancy

- **Fetal growth shoud be assessed** by **serial ultrasonography.**
- Intrauterine growth of twins is **similar** to that of singletons until **30 - 32** weeks gestation.
- Assess for **growth discordance (discordance greater than 20% has also been shown to be an important predictor for adverse perinatal outcomes)**
- **Assess cervical length in** multiple gestation to identify those at **increased risk for preterm delivery**.(**16 -24week , A cut-off of 20 mm**)
- A **cervical length of less than 20 mm** in a **twin pregnancy** at **20 to 24 weeks** gestation was associated with a **10-fold** positive likelihood ratio for preterm birth before **32 weeks** gestation.

Chorionicity

- **Chorionicity is the main determinant of the perinatal outcome in twin pregnancies:**
- **perinatal mortality and morbidity are significantly higher in monochorionic versus dichorionic twins.**
- **This is mainly due to complications associated specifically with monochorionicity such as:**
- **Twin to Twin transfusion syndrome (TTTS),**
- **Selective Fetal Growth Restriction (sFGR)**
- **Twin Reverse Arterial Perfusion Syndrome (TRAP)**

Chorionicity

- **The prenatal determination of chorionicity is the first step for an accurate managing of twin gestation.**
- **Knowledge of chorionicity helps in risk assessment, genetic counseling, invasive procedure and management of TTTS and selective IUGR, death of one twin and discordant fetal anomaly.**
- **It is best done in the first trimester, when the diagnostic accuracy approaches 100%.**
- **The most reliable sonographic signs are the lambda and T-sign and the number of the placental masses evaluated before 14 weeks of gestation**

Chorionicity

- **If it is difficult to determine chorionicity even after referral:**
- ***Manage the pregnancy as monochorionic until proved otherwise.***

Fetal gender

- **The identification of discordant fetal gender indicates dichorionic twinning.**
- **The positive predictive value of discordant gender (when correctly identified) is 100%.**
- **However, considering that around 50% of concordant sex twins are dichorionic, the definition of chorionicity needs further sonographic signs.**

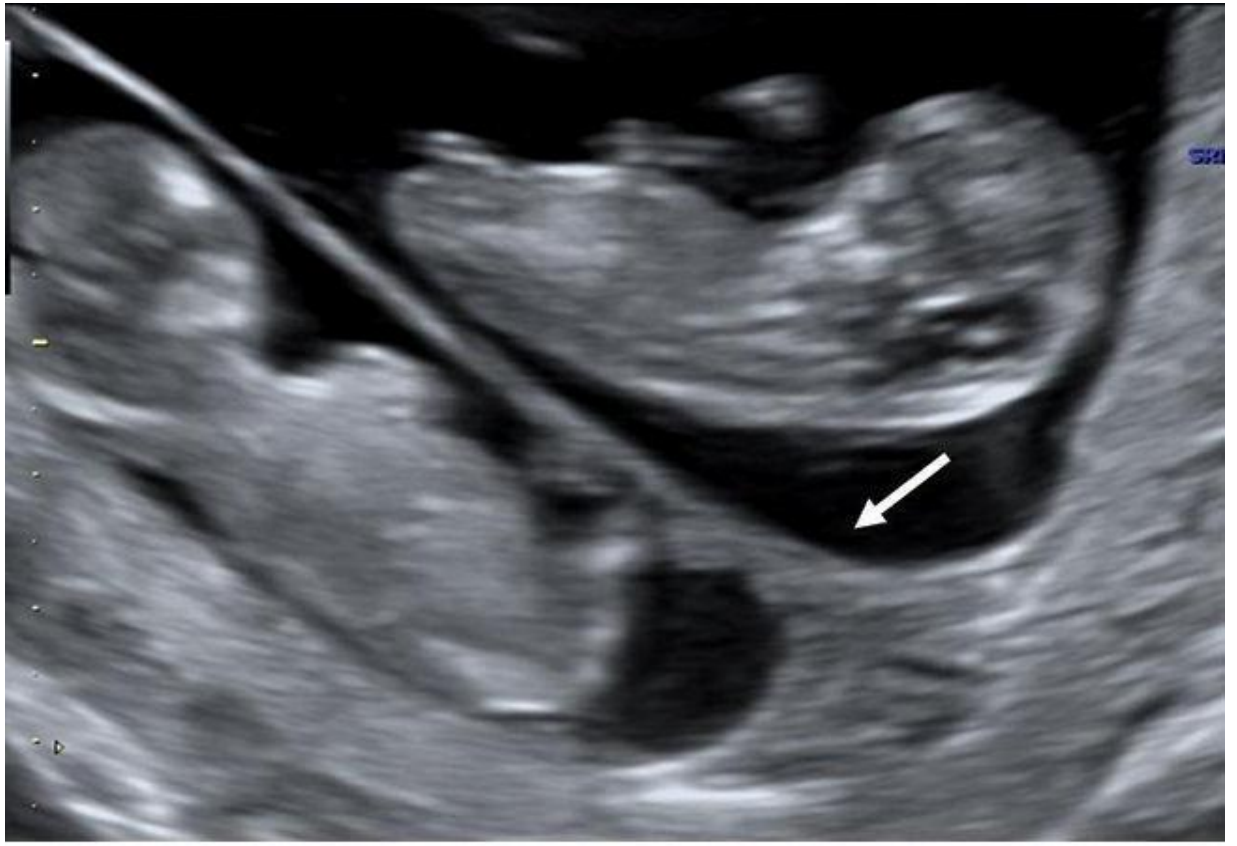
Different sonographic signs may be used to evaluate chorionicity:

- **Different sonographic signs may be used to evaluate chorionicity:**
- 1- number of placental masses
- 2- sex of the fetuses. The identification of discordant fetal gender indicates dichorionic twinning
- 3- Membrane thickness: **membrane thickness of 2 mm** helps in diagnosing **chorionicity**.
- 4- Number of membrane layers: **placentation is MC** if only **two layers** are present; the presence of **three or four layers suggests dichorionicity.**
- 5- characteristics of the intertwine membrane is the most useful and valuable tool: the take-off of the membrane from the placental surface shows the typical “lambda” appearance in dichorionic pregnancy and the typical “T” appearance in the monochorionic ones.

Twin peak sign (the lambda (λ) sign)

- **Seen in Dichorionic Diamniotic twin pregnancy.**
- **This sign is a triangular projection of placental tissue which extends from the placenta between the layers of amniotic and chorionic membranes of each fetus**
- **It is best seen in the first trimester (between 10-14 weeks)**

Twin peak sign (the lambda (λ) sign)

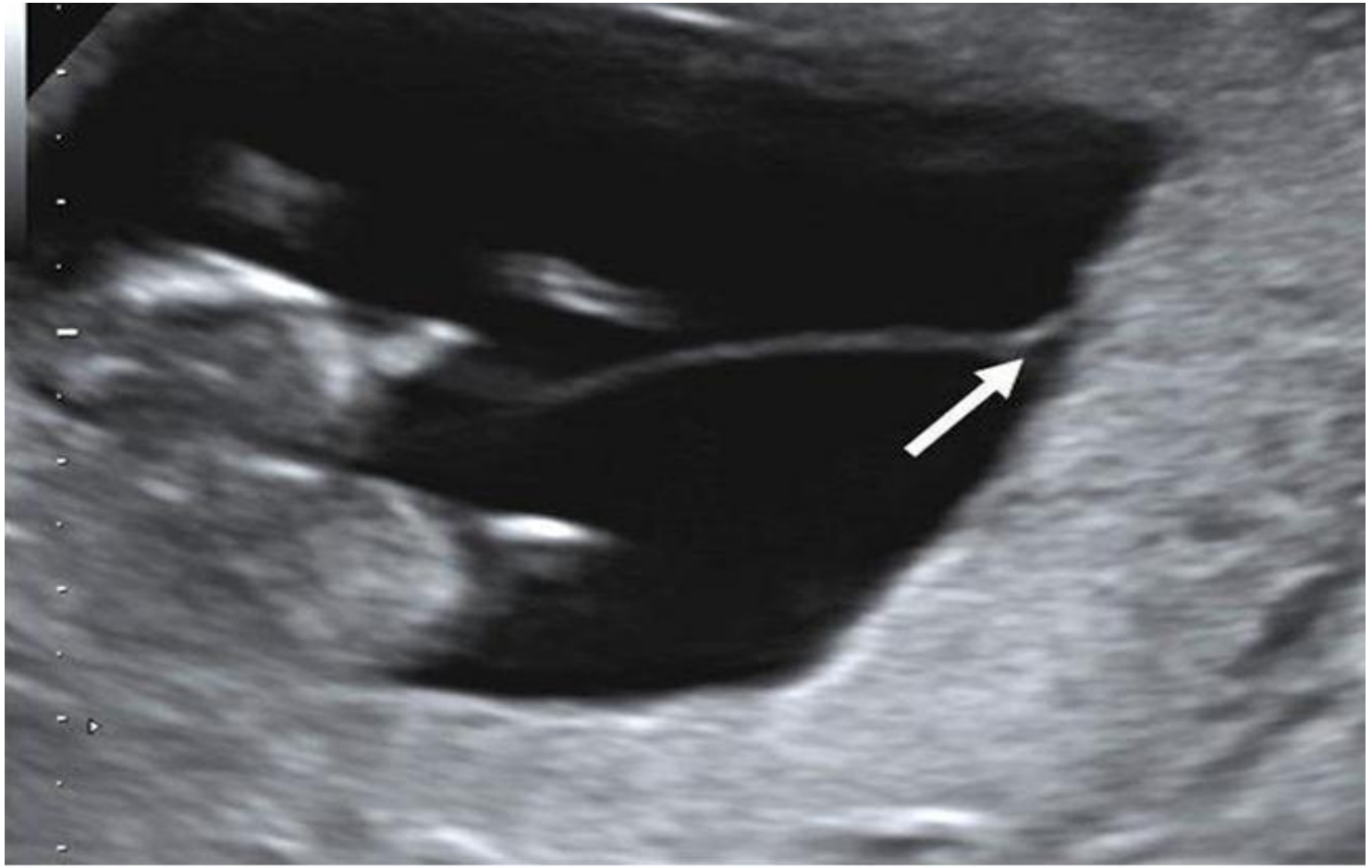


Diagn Prenat. 2014;25:58-64

The T sign

- Seen in Monochorionic Twin
- It refers to the lack of chorion extending between the layers of the intertwin membrane, and the appearance of the **thin intertwin membrane** as it takes-off from the placenta at a **90 degree angle,** denoting a monochorionic pregnancy.

The T sign



Diagn Prenat. 2014;25:58–64

Antenatal Management

- Improved nutrition and better health care
- Adequate rest for the mother
- Extra 300Kcl/day & more protein
- Folic acid, Iron, Calcium supplements
- More frequent Antenatal visits
- Fetal surveillance by Ultrasound every 3-4 weeks interval

Antenatal Care and Fetal Surveillance

- **Serial sonographic assessment of fetal growth** is recommended in multiple gestations.
  - ✓every **3 - 4 weeks** from **18 weeks gestation** in **DC twins**, or every **2 weeks** if **growth restriction or growth discordance (>20%) is discovered.**
  - ✓**MC twins**, as well as all **higher-order multiple gestations**, serial growth scans are performed every **2 weeks** from **16 weeks** gestation.

- When **significant growth discordance** is confirmed, fetal testing should begin intensively. This consists of **twice-weekly NST** supplemented by **biophysical profiles** and **umbilical artery Doppler velocimetry**.

Antenatal corticosteroid prophylaxis for reducing perinatal morbidity

- A single course of corticosteroids is recommended for pregnant women between 24 weeks and 34 weeks of gestation who are at risk of preterm delivery within 7 days, including for those with ruptured membranes and multiple gestations.

Timing and Method of delivery

- The Royal College of Obstetricians and Gynaecologists (RCOG) and National Institute for Health and Care Excellence (NICE) recommend uncomplicated MCDA twins to be delivered between 36 and 37 weeks and DCDA twins to be delivered between 37 and 38 weeks.

- In general, All **twin fetuses** should be **delivered by 39 weeks of gestation** because of the **rising perinatal morbidity and mortality** beyond that date.

- In **MCMA twins** delivery at about 32-34 weeks **should be considered** because of the **increasing risk of perinatal mortality and unexpected fetal loss in the third trimester.**

Timing and Method of delivery

- **Fetal presentations** and size of twin should be determined before choosing the mode of delivery.
- **Electronic fetal heart monitoring** should be available for both.
- **Epidural anesthesia is recommended**

Timing and Method of delivery

- For **vertex-vertex presentation** and in the **absence of obstetric indications for cesarean delivery**, **vaginal birth** should be planned regardless of gestational age.
- There is **no absolute indication** to deliver the **second twin** within a **specified time limit** (**continuous FHM**).
- For **vertex-non-vertex twins**, **Vaginal delivery allowed with breech delivery of the 2nd twin .**
- **If the 2nd twin is significantly larger than the 1st , cesarean delivery is recommended.**
- For **non-vertex 1st twin cesarean delivery is recommended**.

Timing and Method of delivery

- **Higher-Order Multiple Gestations:**
  - ✓**cesarean delivery** under **regional anesthesia** for all patients with three or more live fetuses that are of a viable gestational age is recommended.

- **Monoamniotic twins:**
  - ✓**Cesarean birth is recommended** to avoid complications from **cord entanglement**.

Cesarean section or vaginal delivery??

- **In Summry:**
- **Cesarean delivery in multiple pregnancy is needed when:**
- First twin is in non cephalic presentation
- When it is a Monoamniotic twin pregnancy.
- Higher-Order Multiple Gestations (Triplets, ..)
- If there is medical or obstetric indication

Feto- Fetal Transfusion Syndrome

- FFTS occurs in **15% of MC twin** pregnancies, and accounts for about 20% of stillbirths in multiple pregnancies.
- TTTS occurs almost exclusively in monozygotic twins with monochorionic placentation.
- It can develop at any point during pregnancy but typically emerges in the second trimester.
- Vascular communication is present virtually in all monochorionic twins; in most cases, the blood flow is balanced with no net transfusion of blood from one twin to the other
- **TTTS** occurs because of an **imbalance in blood flow** through **vascular communications in the placenta**, which leads to **overperfusion** of one twin and **underperfusion of its co-twin.**
- **Arterio-venous unidirectional anastomoses** result in net transfusion of blood from the donor to the recipient fetus.

Feto- Fetal Transfusion Syndrome

- **Donor:**
- Anemic
- Growth restricted
- Hypovolemic
- Pale
- Oliguric
- Oligohydramnios, IUGR, Pulmonary hypoplasia
- **Recipient:**
- Polycythemic
- Hypervolemic
- Plethoric
- Polyuric
- Polyhydramnios
- Cardiac Failure

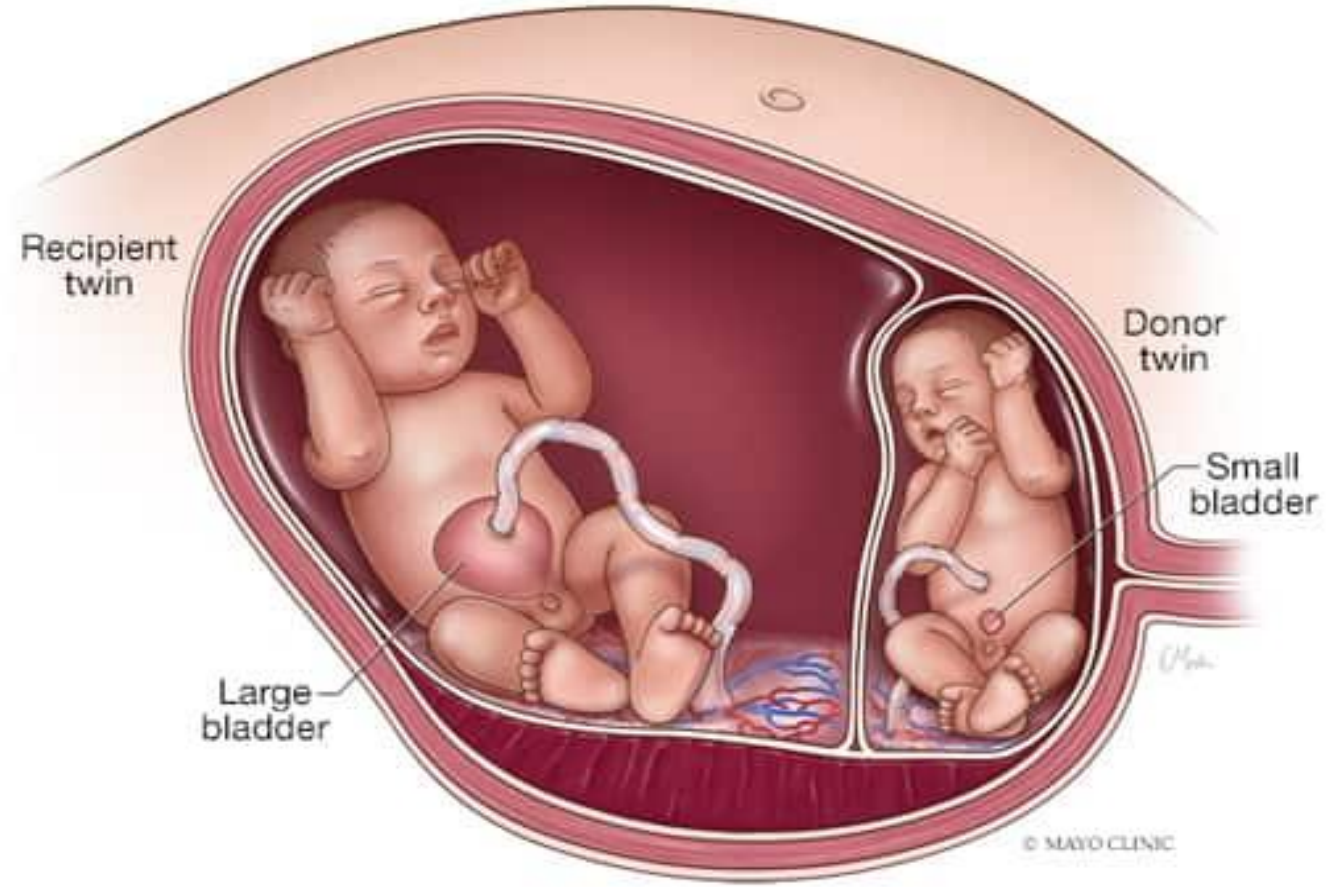
Feto-fetal transfusion syndrome (FFTS)

- **Ultrasonographic criteria for diagnosis of TTTS include** :
  - ✓Presence of a single placenta (Monochorionic placenta)
  - ✓Sex concordance (same sex gender)
  - ✓Significant growth discordance (approximately 20%)
  - ✓Discrepancy in amniotic fluid volume between the two amniotic sacs (usually oligohydramnios and polyhydramnios)
  - ✓Presence of fetal hydrops or cardiac dysfunction
  - ✓Abnormal umbilical artery Doppler findings, such as absent end-diastolic flow in the donor fetus

Feto-fetal transfusion syndrome (FFTS)

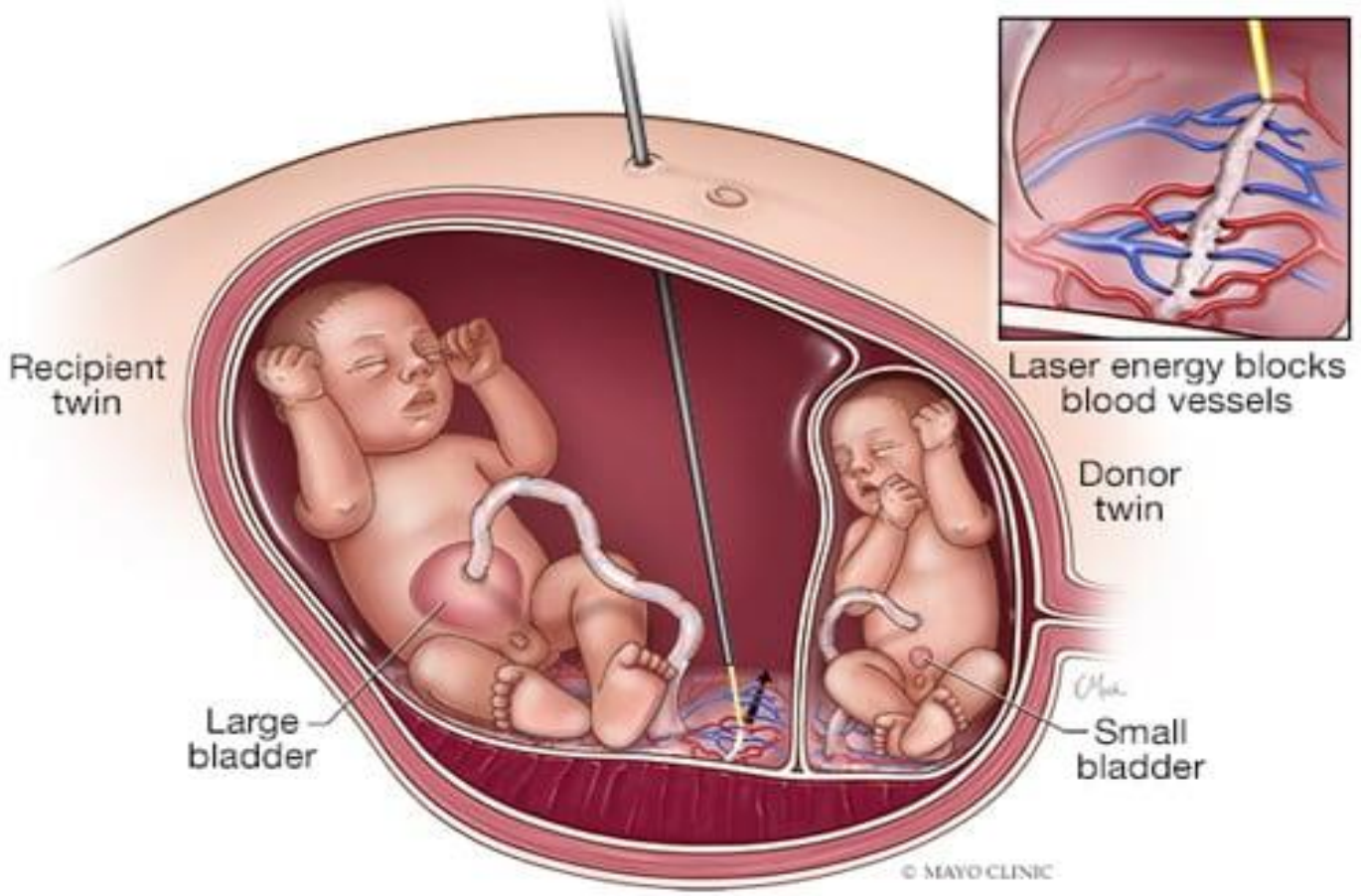
- **The donor fetus** is hypoperfused, demonstrating signs of intrauterine growth restriction, anaemic and oligohydramnios.
- **The recipient fetus** is hyperperfused, hypertensive, demonstrate biventricular hypertrophy and diastolic dysfunction, and polyhydramnios.
- FFTS is associated with a **high risk of fetal/neonatal mortality**, and fetuses who survive are at risk of **severe cardiac, neurologic, and developmental disorders.**
- management approaches for the treatment of **severe TTTS (**24 to 26 weeks) gestation:
  - ✓**Serial reduction amniocenteses**
  - ✓**Amniotic septostomy**
  - ✓**Selective fetoscopic laser coagulation of placental anastomoses.**
  - ✓Fetoscopic Laser Photocoagulation (FLP) is the best treatment option for stages 2 through 4 and is approved by the Food and Drug Administration (FDA) for use during 16 to 26 weeks' gestation.

Feto-fetal transfusion syndrome (FFTS)



Twins with twin-twin transfusion syndrome

Feto-fetal transfusion syndrome (FFTS)

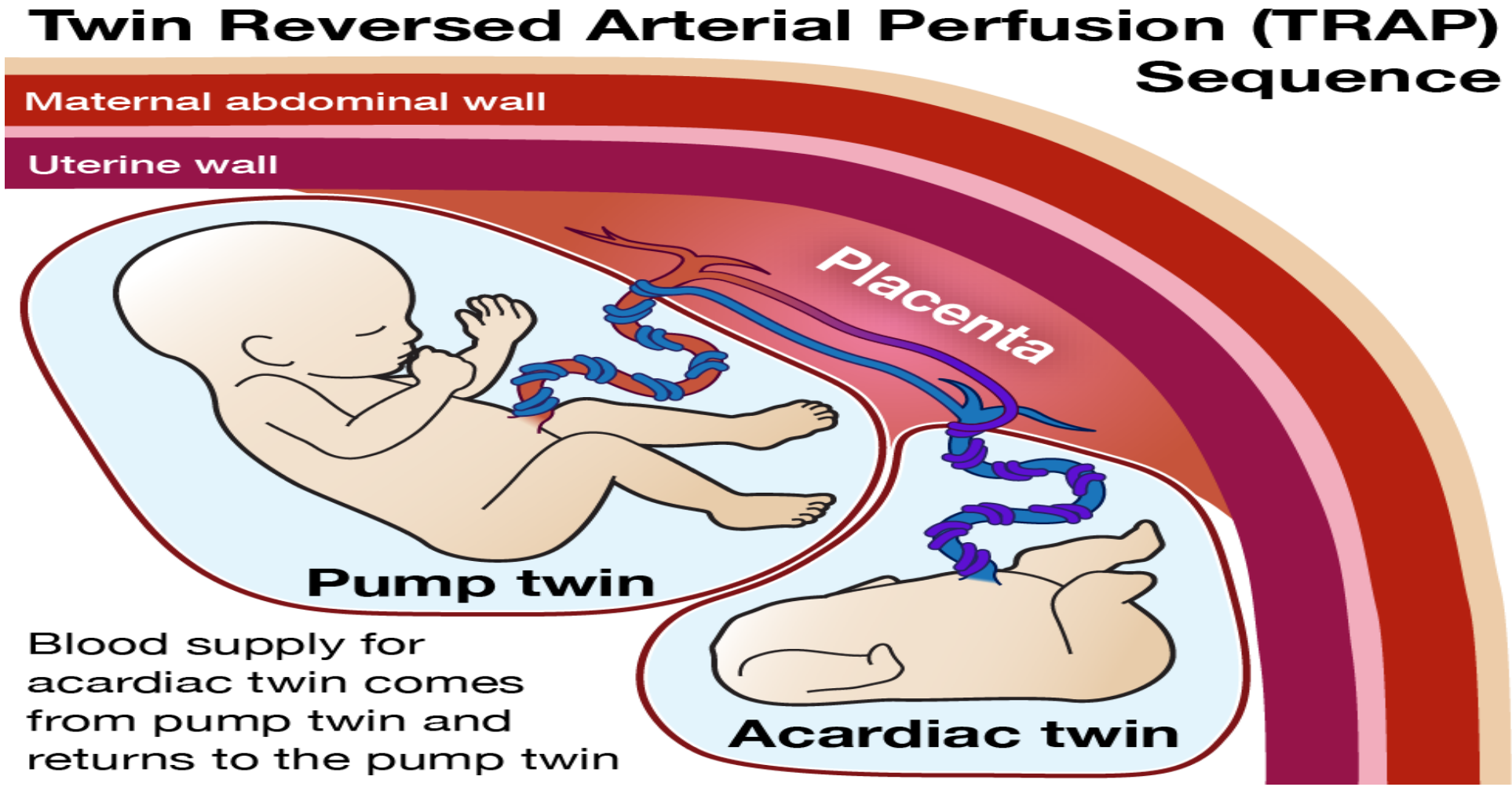


Fetal laser photocoagulation

Twin Reversed Arterial Perfusion Sequence(TRAP)

- Occur in **1%** of **MZ twins.**
- One twin has an **absent, rudimentary, or nonfunctioning heart (acardiac)**.
- **The donor (pump twin)** provides circulation for itself and for the **recipient (perfused twin)** through a **direct arterio-arterial anastomosis** at the placental surface.
- The pump twin is at risk for development of **hydrops** or congestive **cardiac failure.**

Twin Reversed Arterial Perfusion Sequence(TRAP)



Intrauterine Demise of One Fetus

- **The risk to the surviving fetus depends on:**
- 1- The time of death (first trimester or beyond)
- 2- Time interval between the death of one twin to the delivery of the surviving twin.
- 3- Chorionicity & zygocity of twins

Intrauterine Demise of One Fetus in the First Trimester

- Loss of one twin in the first trimester does not appear to impair the development of the surviving twin.
- The dead fetus is completely absorbed.

Intrauterine Demise of One Fetus in the Second Trimester

- The dead fetus may persist as a small, dried and flattened mass known as fetus papyraceous.
- **Fetal death occurring after mid gestation may increase the risk of:**
- **I**ntrauterine growth restriction (IUGR)
- Preterm labor
- Preeclampsia
- Perinatal mortality.

Intrauterine Demise of One Fetus in the Second Trimester

- **Effect on the surviving Twin:**
- After the death of one twin in a MC gestation, approximately 15% of remaining fetuses also die, compared with approximately 3% of remaining fetuses in a DC gestation.
- The risk for significant neurologic morbidity is increased after intrauterine death of one fetus in a MC, but not in a DC gestation.

Intrauterine Demise of One Fetus in the Second Trimester

- **Effect on the mother:**
- Maternal coagulopathy, the most feared complication following twin demise, appears to be uncommon.
- However, coagulopathy has been reported to occur about 3–5 weeks following fetal demise.

Multifetal Pregnancy Reduction(MFPR)

- The incidence of **high order multifetal gestation** (ie, triplets or more) increased dramatically, due to widespread use of assisted reproductive technology (ART).
- These pregnancies are at higher risk of **maternal, fetal, and neonatal complications than singleton pregnancies**
- Higher order multifetal gestations **should be prevented** by better control of ovulation induction and embryo transfer.
- It is recommended to use single embryo transfer in all situations if a top-quality blastocyst is available
- Selective reduction was developed in the mid-1980s, as people in the field of assisted reproductive technology became aware of the risks that multiple pregnancies carried for the mother and for the fetuses.

Multifetal Pregnancy Reduction

- **MFPR** is defined as a first-trimester or early second-trimester procedure for reducing the total number of fetuses in a multifetal pregnancy by one or more.
- Operative techniques that may be used are chemical, thermal, radiofrequency and laser, depending on chorionicity as well as other factors.
- Intracardiac potassium chloride is appropriate to employ when there is independent chorionicity. It carries a lower risk of pregnancy loss.
- Vascular occlusion using radiofrequency ablation, bipolar coagulation or intrafetal laser can be employed in monochorionic fetuses and twin reversed arterial perfusion pregnancies, but carry a higher risk of pregnancy loss.

Multifetal Pregnancy Reduction(MFPR)

- **MFPR** is usually performed between **10 and 13 weeks** of gestation.
- Under **continuous ultrasound guidance**, a **needle** is placed into the thorax of the targeted fetus, **2 to 3 mL of potassium chloride** is injected, and **asystole** is observed for at least **3 minutes.**
- Potassium chloride injection must not be used for MFPR in **a single fetus of a MC pair because of the risk for co-fetal demise or neurologic injury.**
- **A lot of medical, ethical and religious issues where raised against this procedures.**