Multiple Pregnancy

- **Multiple pregnancy** occurs when more than one fetus is carried in the womb in the same pregnancy.

  - **Epidemiology**
    - Incidence has increased since the introduction of ovulation induction techniques and IVF
    - 1 in 90 pregnancies in the UK
    - 1 in 34 babies born in the UK result from a multiple pregnancy
    - Higher multiples extremely rare: twins 1.5%, triplets 0.02%, quadruplets 0.0003%
    - The most recent surviving set of quintuplets were born in the UK in 2011

  - **Risk factors**
    - Assisted reproduction: clomiphene ovarian stimulation (10%), ICSI (10-20%), IVF (25%)
    - Previous multiple pregnancy
    - Maternal family history of multiple pregnancy
    - Increasing maternal age and parity
    - Ethnicity e.g. sub-Saharan African descent

  - **Aetiology & classification of twin pregnancies**
    - **Dizygotic (~70%)**
      - Two separate eggs are released in the same cycle and fertilised by two separate sperm before simultaneously implanting and developing
      - This almost always results in a dichorionic diamniotic (DCDA) twin pregnancy
      - Rarely, blastocysts may fuse and form a monochorionic diamniotic (MCDA) pregnancy
      - If there are two separate eggs involved the twins will always be non-identical
    - **Monozygotic (~30%)**
      - A single egg is fertilised by a single sperm and subsequently divides to form two fetuses
      - The type of monzygotic twin pregnancy is dictated by when the embryo splits into two
        - ≤3 days → dichorionic diamniotic (DCDA) twin pregnancy 20-30%
        - 3.7 days → monochorionic diamniotic (MCDA) twin pregnancy 60-70%
        - 8-12 days → monochorionic monamniotic (MCMA) twin pregnancy <1%
        - >12 days → conjoined twin pregnancy very rare
      - These twins come from the same genetic material and will be identical and the same sex
    - **Rarer twin types**
      - Heterotopic twin pregnancy: one intrauterine twin and one ectopic twin
      - Parasitic twin pregnancy: a type of conjoined twinning involving one viable twin and one non-viable parasitic twin, which becomes incorporated into its sibling as vestigial tissue
      - Partial molar twin pregnancy: one viable twin and one molar pregnancy. This generally results from one twin having triploidy or complete paternal uniparental disomy
      - Chimerism/mosaicism: one viable fetus consisting of genetic material from two twins. This may result in intersex disorders if one twin is female and the other male.
    - **Higher order multiples** are increasingly difficult to classify, but use the same ideas as above

  - **Symptoms**
    - There may appear to be nothing unusual about the pregnancy
    - There is increased incidence of hyperemesis gravidarum due to ↑↑ levels of beta-hCG
    - Other early pregnancy symptoms may also be exaggerated e.g. nausea, fatigue, mastalgia...

  - **Signs**
    - Examination may also be unremarkable – most cases are diagnosed on first trimester ultrasound
    - Abdominal examination may reveal a larger-than-expected fundal height, or the uterus may be palpable above the symphysis pubis earlier than usual
    - Auscultation may reveal two fetal heartbeats

  - **Differential diagnosis**
    - Hyperemesis/exaggerated pregnancy symptoms: singleton pregnancy, multiple pregnancy, gestational trophoblastic disease (hydatidiform mole, choriocarcinoma, trophoblastic tumours)
    - Large-for-dates fundal height: wrong dates, polyhydramnios, multiple pregnancy, fibroid uterus
    - >1 fetal poles on USS or >1 fetal heartbeats: no real alternative diagnoses!

- **Investigations**
  - USS to diagnose twin pregnancy and establish choriocarcinoma and amnioncits
  - Fetal abnormalities are much more common in multiple pregnancies, e.g. chromosomal disorders and anatomical defects (risk ↑↑ with increasing maternal age and monozygotic twinning)
    - Nuchal translucency screening can be used to identify individual twins at risk of trisomy
    - Detailed anomaly scans should be performed
    - Chorionic villosity biopsies and amniocentesis can be used for prenatal diagnosis, but samples may be contaminated by tissue belonging to the other fetus

- **Management**
  - **Antenatal management**
    - Multiple pregnancies are high risk and require consultant-led antenatal care
    - Mothers should take iron and folate supplements to prevent anaemia and NTDs
    - If one fetus is shown to be abnormal on testing, targeted selective termination can be offered. This can result in complications for the surviving twin in monozygotic twins.
    - Fetal growth and well-being should be monitored on a regular basis:
      - Regular third trimester growth scans to assess growth and placental function
      - Monochorionic twins require close monitoring throughout pregnancy
      - Establish presentation of leading twin by 34 weeks
    - Maternal health should be closely monitored due to ↑↑ risk of complications (see below)

  - **Delivery**
    - Women should be booked to deliver in a specialist unit with special care baby facilities
    - Vaginal delivery can be considered an option as long as there have been no complications and the first twin has a confirmed cephalic presentation
    - Induction of labour can be offered at 38 weeks (many deliver earlier than this)
    - The second twin is prone to intrapartum hypoxia during vaginal delivery and is therefore at increased risk of perinatal morbidity and mortality
    - Caesarean section should be offered, especially if the first twin is non-cephalic, the twins are monochorionic, or there are higher multiples e.g. triplets, quadruplets
    - Caesarean section appears to be more beneficial for the second twin

  - **Complications**
    - **Fetal complications**
      - Congenital abnormalities: chromosomal anomalies, NTDs, cardiac defects, GI atresia
      - “Vanishing twin syndrome”: first trimester loss and reabsorption of one twin
      - Miscarriage
      - Intrauterine death of one twin: can kill the other twin if MC, and may precipitate labour
      - IUGR affects up to 25% of twin pregnancies
      - Twin-to-twin transfusion syndrome (TTTS) affects up to 25% of MC twins
        - Placental vascular anastomoses preferentially redistribute blood to the twin
        - This endangers both donor and recipient twins (getting too little/too much blood)
        - This can be treated with laser ablation of anastomases or selective termination
      - Polyhydramnios
      - Preterm labour and prematurity: 40% deliver before 37 weeks, 10% before 32 weeks
      - During labour: malpresentation (only 45% are both cephalic), cord entanglement, head entrapment or “locked twins”, fetal distress of second twin
      - Perinatal morbidity and mortality is at least 3x that of singletons

  - **Maternal complications**
    - Hyperemesis gravidarum
    - Anaemia
    - Gestational diabetes
    - Pre-eclampsia risk is up to 5x that of singleton pregnancies
    - Placenta previa and antepartum haemorrhage
    - Postpartum haemorrhage due to ↑↑ risk of uterine atony and iatrogenic birth trauma
    - Operative delivery is often required to expedite delivery of the second twin
    - Post-natal depression rates are much higher

  - **Social complications (support groups are available)**
    - Financial strain of providing for two babies +/- other pre-existing children
    - Physical and psychological demands of breastfeeding and twin parenthood in general

- **Prevention**
  - most IVF centres offer elective single embryo transfer (ESET) to reduce risk of multiples

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