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المرحلة الرابعة

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term refers to the gestational period from 37+0 to 41+6 weeks. Preterm births occur between 24+0 and 36+6 weeks. Although births earlier than this are referred to as miscarriages, occasional survivors are seen after delivery at 23 weeks, which has become the ‘grey zone’ for viability. A ‘late’ or second trimester miscarriage occurs between 12 and 23 weeks gestation. A more practical definition of late miscarriage is one occurring between 17 and 23 weeks.
Prevalence

There is no evidence that the incidence of preterm birth is declining. In fact, the rate appears to be slowly increasing, in part due to an increasing incidence of multiple pregnancy.

In most countries, including the UK, there are no formal records of miscarriages. The exact incidence of late miscarriages is unknown, but is estimated to be approximately 1 per cent.

Preterm births contribute significantly to perinatal mortality, half of which results from babies born before 32 weeks.
Parents are particularly anxious about the risks of later disability and handicap. These risks are especially significant below 26 weeks gestation. When assessed at six years of age, nearly half the survivors at 23–25 weeks gestation have a moderate or severe disability. Furthermore, many of these disabilities only become apparent after two to three years of age. Survival with no disability is only seen in 1, 3 and 8 per cent of live births at< 24, 24 and 25 weeks, respectively.
Classification

Mildly preterm births at 32+0 to 36+6 weeks (incidence 6.1 per cent).

Very preterm births at 28+0 to 31+6 weeks (incidence 0.9 per cent).

Extremely preterm births at 24+0 to 27+6 weeks (incidence 0.4 per cent).
Aetiology

Infection

Subclinical intrauterine infection of the choriodecidual space and amniotic fluid is the most widely studied aetiological factor underlying spontaneous preterm births. The uterine cavity is normally sterile but the vagina contains commensal bacteria. Depending on the bacterial load and cervical resistance, the bacteria may ascend through the cervix and reach the fetal membranes. This may activate the decidua, increase prostaglandin release and trigger contractions. Alternatively, it may weaken the membranes, leading to rupture. Early-onset neonatal sepsis, maternal postpartum endometritis
Over-distension

The commonest cause of uterine over-distension is multiple gestation. Polyhydramnios has a similar effect. Overstretching of the myometrium (and possibly the membranes) leads to increased contractile activity and premature shortening and opening of the cervix.
Vascular

Disturbance at the uteroplacental interface may lead to intrauterine bleeding. The blood can track down behind the membranes to the cervix and be revealed. Alternatively, it may track away from the cervix and be concealed. Either way, the blood irritates the uterus, leading to contractions, and damages the membranes, leading to early rupture.
Surgical procedures and intercurrent illness

Serious maternal infective illnesses such as pyelonephritis, appendicitis and pneumonia are associated with preterm labour presumed to be due either to direct blood-borne spread of infection to the uterine cavity or indirectly to chemical triggers, such as endotoxins or cytokines.

Amniocentesis is a pregnancy-specific procedure associated with an increased risk of late miscarriage and early birth. It is most commonly performed at 15–18 weeks gestation. It is associated with a 0.5 per cent chance of subsequent pregnancy loss before viability.
Abnormal uterine cavity

A uterine cavity that is distorted by congenital malformation may be less able to accommodate the developing pregnancy. Associated abnormal placentation and cervical weakness may also contribute. Fibroids in a low position may also lead to complications. However, fibroids are common and most pregnancies are successful despite their presence.
Cervical weakness

Due to previous surgical damage or a congenital defect, the cervix may shorten and open prematurely. The membranes then prolapse and may be damaged by stretching or by direct contact with vaginal pathogens. These same pathogens may ascend and trigger contractions. Often referred to as ‘cervical incompetence’, weakness may be a better term. The evidence suggests that gradations of deficiency exist, rather than an ‘all-or-nothing’ phenomenon.
Idiopathic

In many cases, especially mildly preterm births between 34 and 36 weeks, no cause will be found. In these cases, the physiological pathways to parturition may simply have been turned on too early.
The Preterm Parturition Syndrome

- Uterine Over Distension
- Cervical Insufficiency
- Stress-Nutrition
- Vascular
- Infection
- Hormonal
- Allergic Disorder
- Unknown
Risk factors for preterm labour/PPROM

Non-modifiable, major
- Last birth preterm: 20 per cent risk
- Last two births preterm: 40 per cent risk
- Twin pregnancy: 50 per cent risk
- Uterine abnormalities
- Cervical anomalies:
  - cervical damage (cone biopsy, repeated dilatation)
  - fibroids (cervical)
- Factors in current pregnancy:
  - recurrent antepartum haemorrhage
  - intercurrent illness (e.g. sepsis)
- any invasive procedure or surgery
Non-modifiable, minor
- Teenagers having second or subsequent babies
- Parity (0 or> 5)
- Ethnicity (black women)
- Poor socioeconomic status
- Education (not beyond secondary)

Modifiable
- Smoking: two-fold increase of PPROM
- Drugs of abuse: especially cocaine
- Body mass index (BMI) <20: underweight women
- Inter-pregnancy interval <1 year
Clinical features of preterm labour

History

Less than 50 per cent of all women presenting with symptoms suggesting a risk of early delivery will deliver within 7 days. Too much emphasis is often placed on the contraction frequency. In isolation, it correlates poorly with the risk of preterm birth. Markers of intensity, such as analgesic requirements or simple bedside clinical impression, may add refinement. Vague complaints such as increased discharge, pelvic pressure or low backache are sometimes reported, with the latter two often showing a cyclical pattern. Nonetheless, the diagnosis of preterm labour remains notoriously difficult unless contractions are accompanied by advanced dilatation (3 cm), ruptured membranes or significant vaginal bleeding.
General examination is important to assess overall health. This will include pulse, blood pressure, temperature and state of hydration. Abdominal examination may reveal the presence of uterine tenderness, suggesting abruption or chorioamnionitis. Speculum examination by an experienced clinician may yield valuable information; pooling of amniotic fluid, blood and/or abnormal discharge may be observed. A visual assessment of cervical dilatation is usually possible and has been shown to be as accurate as digital examination findings. Digital exams should be limited, as they are known to stimulate prostaglandin production and may introduce organisms into the cervical canal.
Differential diagnosis

- Urinary tract infection
- Red degeneration of fibroid
- Placental abruption
- Constipation
- Gastroenteritis
Fetal fibronectin (fFN) is a ‘glue-like’ protein binding the choriodecidual membranes. It is rarely present in vaginal secretions between 23 and 34 weeks. Any disruption at the choriodecidual interface results in fFN release and possible detection in the cervicovaginal secretions. Bedside fibronectin testing offers a rapid assessment of risk in symptomatic women with minimal cervical dilatation. If performed correctly, the test has a greater predictive value than digital examination. Only 1 percent of those women who test negative for fibronectin will deliver within 1 week. Aggressive intervention can be avoided in these women.
Cervical length measurement by transvaginal ultrasound has also been shown to improve diagnostic accuracy. A normal cervix measures approximately 35 mm in length. Significant cervical shortening is often accompanied by dilatation and funnelling of the membranes down the cervical canal. Although measurements can be repeated frequently and with little expense, skilled ultrasonographers and suitable machines with transvaginal probes are required.
Normal cervix.
Cervical length and funnelling on ultrasound
Uterine contractions are present and cervical length is...

- >30 mm: No preterm labor
- 20–30 mm: Negative fetal fibronectin
- <20 mm: Positive fetal fibronectin
  - Preterm labor
Repeat vaginal examination in 1–4 hours should be considered essential in the absence of specialized tests. The interval between assessments should be guided by the severity of the symptoms.
Clinical features of preterm pre-labour rupture of the membranes PPROM

History

The most reliable diagnostic feature of PPROM from the history is the report of a ‘gush of fluid’ vaginally, usually followed by a more-or-less continuous dribble. Ask about frequency, urgency, leakage and dysuria, as Incontinence or a urinary tract infection (UTI). The presence of any vaginal discharge should be ascertained. Fetal movements may be reduced in strength or frequency after PPROM.
Examination

• pulse and temperature and a flushed appearance
• Abdominal examination may reveal a clinical suspicion of oligohydramnios or uterine tenderness if chorioamnionitis is present.
• The definitive diagnosis of PPROM can only be made by performing a sterile speculum examination, preferably after the patient has been resting supine for 20–30 minutes. A pool of amniotic fluid in the posterior vagina is diagnostic.
• Digital vaginal examinations should be avoided if possible in PPROM
Differential diagnosis

• Urine loss: incontinence and UTIs are both more common in pregnancy
• Vaginal infection
• Leukorrhoea: the cervical glands often become overactive during pregnancy
Investigations

Nitrazine testing

Amniotic fluid is alkaline, whereas the vaginal secretions are usually acidic. An elevated pH turns a nitrazine stick black. Unfortunately, false positives occur, with blood, semen and even urine limiting its usefulness. However, the predictive value of a negative test is very high.
Genital tract swabs

A high vaginal swab may help to guide antibiotic therapy, if subsequently required. Screening for group B streptococcus (GBS) can also be performed, as there is a substantial risk of labour in the next few days.

Maternal well-being

This should include regular assessment of the mother’s blood pressure, pulse and temperature. Some advise serial white cell counts and C-reactive proteins as early markers of infection, although this has not been shown to improve management.
Fetal well-being

Serial antepartum cardiotocography is important after PPROM, as a gradually increasing baseline heart rate or fetal tachycardia can be the first sign of intrauterine infection.

Ultrasound

Ultrasound can give valuable information about the amniotic fluid volume. The presence or absence of oligohydramnios provides further diagnostic support.
Amniocentesis

A sample of amniotic fluid can be sent for Gram stain, microscopy and culture, to establish whether there is an intrauterine infection (chorioamnionitis). There is, however, a risk of stimulating preterm labour by performing an invasive test.
Management of symptomatic women

Communication and support

A holistic approach to the situation is essential. Sympathy, explanations and reassurance are mandatory. Communication with the neonatal unit staff ensures that adequate and appropriate resources are available at the time of delivery.

While women in preterm labour need to be on an acute care unit, the ideal place for women experiencing a late miscarriage is a purpose-designed
Maternal steroids

Current evidence shows that a single course of maternal steroids (two injections 12–24 hours apart) given between 28 and 34 weeks gestation and received within 7 days of delivery results in markedly improved neonatal outcomes. This is primarily due to a reduction in neonatal respiratory distress syndrome (RDS). Maximum benefit from the injection is seen after 48 hours.
Tocolytics

Beta-agonists have significant maternal side effects, and maternal deaths from acute cardiopulmonary compromise are described. Smooth muscle relaxants used to treat preterm labour include nifedipine and glyceryl trinitrate. It is inexpensive, given orally and has a low side-effect profile.

The oxytocin antagonist atosiban now has a UK product licence. Although side effects are seen less frequently than with ritodrine,
non-steroidal anti-inflammatory drugs, such as indomethacin, have attracted considerable interest as tocolytics. They have been associated with significant fetal cardiovascular side effects, although these can be mitigated by limiting them to short-term use below 30 weeks gestation only.

Unfortunately, despite a multitude of pharmacological approaches, no tocolytic medication has yet been shown to have increased efficacy in comparison to ritodrine or to improve neonatal outcomes. At the time of writing, the role for tocolysis is to allow a course of steroids for fetal lung maturation to be completed and to facilitate transfer of the undelivered mother to a unit able to provide appropriate neonatal care, should delivery occur.
Antibiotics

Broad-spectrum antibiotics offering aerobic and anaerobic coverage are necessary in the presence of overt clinical infection, such as chorioamnionitis. The role of antibiotics in the absence of clinical signs of infection is much less clear. In PPROM, the same study concluded that a 10-day course of erythromycin led to improved short-term neonatal outcomes.

Most North American centres continue to give intrapartum antibiotics to women in preterm labour unless GBS status is known to be negative. For reasons that are unclear, the risk of early-onset neonatal disease appears much less in the UK and this approach has not been widely adopted.
Patient admitted with signs and symptoms of preterm labor

Obtain vaginal-rectal swab for GBS culture† and start GBS prophylaxis§

Patient entering true labor?†

Yes

Continue GBS prophylaxis until delivery**

No

Discontinue GBS prophylaxis

Obtain GBS culture results

Positive

GBS prophylaxis at onset of true labor

Not available prior to labor onset and patient still preterm

No GBS prophylaxis at onset of true labor;‡‡ repeat vaginal-rectal culture if patient reaches 35–37 weeks’ gestation and has not yet delivered§§
Emergency cervical cerclage

When a patient presents with an open cervical os and bulging membranes before viability, the idea of closing the cervix by passing a stitch around it seems logical. However, the results of emergency cervical cerclage are poor and are related to the cervical dilatation at insertion.

Bleeding, contractions and infection are all contraindications to cerclage. Depending on the initial dilatation of the cervix,
In some cases, it may be judged appropriate to hasten delivery, either because a late miscarriage appears inevitable or because the maternal or fetal risks of continuing the pregnancy are judged too high. Before 24 weeks, this would be carried out by inducing contractions with prostaglandins, such as Cervagem® or Cytotec®. Great care must be exercised if there is already clinical evidence of chorioamnionitis. In these cases, delay in ending the pregnancy may lead to worsening infection and consequent morbidity for both mother and baby.
Mode of delivery

With a late miscarriage, vaginal delivery will almost always occur, even if there is a transverse lie or fetal malformation. This is because of the relatively small size of the fetus.

As gestation advances, both neonatal outcomes and the ability to diagnose fetal compromise improve, and intervention for fetal reasons becomes appropriate. The safety of preterm breech vaginal delivery is often questioned and Caesarean section commonly performed.
Type of Caesarean section
At the earliest gestations and in the presence of oligohydramnios, the lower segment is often poorly formed. Vertical uterine incisions may be necessary. This ‘classical’ uterine incision carries an up to 5 per cent risk of uterine rupture in subsequent pregnancies, some of which will occur antenatally.
continuous fetal monitoring may be required, although there may be considerable difficulties interpreting the fetal heart rate pattern. Whenever possible, the presentation in preterm labour should be confirmed by ultrasound, as clinical palpation is notoriously unreliable. An estimated fetal weight, particularly below 28 weeks, can be helpful.
Management of high-risk asymptomatic women

Early dating scan

A first trimester dating scan ensures the precise assessment of gestational age in the current pregnancy.

Genital tract infection

Many vaginal pathogens, including bacterial vaginosis (BV), *Trichomonas vaginalis*, *ureaplasma* and *chlamydia*, have been associated with an increased risk of preterm birth in observational studies.
Asymptomatic bacteriuria

This also carries an increased risk of preterm birth. Short courses of antibiotics based on culture sensitivities reduce the risk of pyelonephritis and early delivery.

GBS genital colonization

Preterm infants are more susceptible to early-onset GBS infection, acquired during passage through the birth canal. In women known to be at increased risk of early delivery, testing for GBS antenatally with a combined low vaginal/rectal swab allows consideration of intrapartum prophylaxis.
Fetal fibronectin testing can only be undertaken after 23 weeks, as high levels may be physiological before then. In high-risk asymptomatic women with a positive fibronectin test at 24 weeks gestation, nearly half will deliver before 30 weeks gestation.

Progestational agents

Many studies, meta-analyses and reviews have shown no evidence of benefit from prophylactic or maintenance therapy with conventional oral or intravenous tocolytics.
Progesterone has long been recognized as a hormone involved in the support of pregnancy through uterine quiescence. However, it is also believed to affect cervical ripening and mucous production. It may also have anti-inflammatory properties. It appears to have a good safety profile when used in pregnancy. Initial trials using intramuscular or intravaginal progesterone have shown some promise, with reductions in the incidence of preterm birth. None have yet had the power to show an improvement in neonatal outcome,
Randomized trials of social support in the UK failed to improve pregnancy outcomes. In some studies, hospitalization for bed rest led to an increase in preterm birth. Roles for sexual abstinence and/or psychological support are no clearer.
Cervical ultrasound

Cervical length can be accurately and repeatedly measured by transvaginal ultrasound. In asymptomatic women with a short cervix at 23 weeks, the risk of very preterm delivery rises to 4 per cent with lengths of 11–20 mm. At 10 mm, the risk is 15 per cent, and it increases dramatically with further decreases in length.
Cerclage

Elective cerclage may be advised solely based on a woman’s past obstetric history. Randomized trials suggest benefit when a woman has had three or more late miscarriages or very preterm deliveries. In this situation, the procedure is usually performed at 12–14 weeks gestation. This is because the risk of first trimester miscarriage has passed and an initial assessment of fetal well-being can be performed with nuchal translucency.
Cervical cerclage can be done under general or regional anaesthesia. The commonest procedure, a McDonald cerclage, is also the simplest and quickest to perform. A Mersilene tape purse-string suture.

Although more invasive cerclage techniques can result in higher suture placement, they have not been definitively associated with better outcomes and are generally reserved for atypically high-risk cases. A further advantage of the McDonald technique is that removal later in pregnancy does not usually require anaesthetic.
Mersilene tape used for cerclage
McDonald-type cerclage as seen on ultrasound