Mechanisms and management of normal labour

Jennifer M Thornton
Brendan Browne
Meenakshi Ramphul

Abstract
Normal labour is a complex process involving hormonal, biochemical and mechanical interdependence. There are four phases of parturition: quiescence, activation, stimulation and involution. These reflect the transition from the maintenance of myometrial acontractility and cervical structural integrity, to progressive uterine contractions, cervical effacement and dilatation, delivery of the fetus and placenta, and recovery to the non-pregnant state. Whilst parturition is chiefly controlled by the oestrogen:progesterone ratio, multiple hormones such as prostaglandins, corticotropin-releasing hormone, oxytocin and relaxin play a role in the initiation, maintenance and progression of normal labour. The mechanical challenge of labour is overcome when progressive, effective contractions occur in conjunction with satisfactory fetal and maternal pelvic dimensions. Clinically, there are three stages in the management of normal labour, reflecting cervical dilatation up to 4 cm, delivery of the fetus, and the placenta, respectively. Robust knowledge of the mechanisms and management of normal labour is key to our understanding of when to clinically intervene and recognize areas where maternal and fetal morbidity can be reduced.

Keywords birth; labour; management of labour

Introduction
Normal labour has different parameters according to the experiences of the clinical care provider. For some, normal labour might be synonymous with spontaneous labour, leading to the vaginal delivery of an infant without augmentation or intervention. In other settings, this term may extend to encompass induction and augmentation of labour, high risk labour such as TOLAC (trial of labour after caesarean), and interventions such as episiotomy and instrumental vaginal delivery.

For the purposes of this review, we will outline the biochemical, hormonal and mechanical phases of normal spontaneous labour and vaginal delivery, before describing how these may be influenced at different points by intervention, or by the risk status of the labouring woman.

Simply, normal labour aims to produce progressive effective uterine contractions, leading to:

- Cervical effacement and dilatation
- Expulsion of the fetus through the birth canal
- Separation and expulsion of the placenta

Labour is a complex process involving many preparatory steps prior to the more progressive active phase of labour as we know it. Throughout pregnancy, maternal and fetal paracrine and autocrine signalling work synergistically to achieve fetal maturity and initiate parturition appropriately. The importance of this cooperation is underscored by the fact that iatrogenic induction of labour is often required in its absence, for example due to fetal demise or anencephaly.

Phases of labour

Four phases of natural parturition have been described:

1. Quiescence — this phase involves not only the maintenance of myometrial acontractility but also that of cervical structural integrity.
   a. The myometrium increases in vascularity throughout pregnancy, affording essential nutrient and gaseous exchange, not only for the developing fetus, but also in anticipation of the extensive energy requirements of labour.
   b. This phase is controlled by progesterone, relaxin and prostacyclin. Progesterone inhibits contraction-associated proteins (CAPs) by increasing the transcription factor zinc finger e-box binding homeobox protein 1 (ZEB1) and connexin 43. ZEB1 and connexin 43 recruit other repressor proteins, such as pyrimidine tract binding protein-associated splicing factor (PSF) and yeast switch-dependent 3 homolog A/histone deacetylase corepressor complex (Sin3A/HDACs). The repressor proteins decrease the number of myometrial gap junctions, thereby maintaining acontractility. Hormonal control of labour will be discussed in further detail later.

2. Activation — the transition from quiescence to active labour.
   a. This phase is predominantly controlled by the relative increase in the oestrogen:progesterone ratio, occurring in a gradually accelerative manner throughout the last few weeks of the third trimester.
   b. The myometrium becomes more responsive to signalling, and as progesterone decreases, CAPs are no longer inhibited, therefore increasing uterine contractility. This in turn increases PSF and Sin3A/HDACs further.
   c. Cervical tissue compliance and distensibility increases.

3. Stimulation — including active labour.
   a. This phase is predominantly mediated by prostaglandins, oxytocin and relaxin.

Jennifer M Thornton MB BCH BAO Specialist Registrar in Obstetrics and Gynaecology, Cambridge University Hospitals NHS Trust, Addenbrooke’s Hospital, Cambridge, UK. Conflicts of interest: none declared.

Brendan Browne MB BCH BAO Specialist Registrar in Obstetrics and Gynaecology, Cambridge University Hospitals NHS Trust, Addenbrooke’s Hospital, Cambridge, UK. Conflicts of interest: none declared.

Meenakshi Ramphul MB BCH BAO MRCPG MRCPI PhD Consultant in Obstetrics and Gynaecology, Rotunda Hospital, Dublin, Ireland. Conflicts of interest: none declared.
b. Progressive uterine contractions with concurrent cervical effacement and dilatation aim to expel the fetus through the birth canal.

c. Placental separation and expulsion.

4. **Involution** — refers to the recovery of the mother throughout the puerpuerium

a. Oxytocin mediates uterine involution and milk letdown.

b. Initiation of inflammatory pathways expediting healing.

**Hormonal control of labour**

As already mentioned, parturition is chiefly controlled by the oestrogen:progesterone ratio. However, they do not act in isolation and it is the interplay of multiple hormones that leads to the maintenance of pregnancy and the achievement of successful labour (Figure 1).

**Corticotropin-releasing hormone (CRH)**

CRH is both a hypothalamic and placental peptide. It is produced in varying concentrations throughout pregnancy and labour, but is known to increase exponentially near term. It is thought that elevated CRH levels in mid-pregnancy might confer an increased risk of prematurity. CRH acts on targets within the fetal adrenal—pituitary axis, placenta and myometrial smooth muscle, and is thought to play a part in the initiation of labour.

**Progesterone**

Progesterone acts to inhibit myometrial contractility and to promote cervical competency. It suppresses oxytocin-induced prostaglandin production and the myometrial response to oxytocin. Progesterone withdrawal is a key component in the facilitation of parturition.

Progesterone formulations are often used as part of fertility treatment in an effort to prevent miscarriage. Progesterone antagonists, such as mifepristone (used in medical management of miscarriage and medical termination of pregnancy), soften the cervix and generate an inflammatory response, increasing the number of myometrial gap junctions, and thereby increasing susceptibility to prostaglandins and oxytocin.

**Oestrogen**

Early in pregnancy, oestrogen augments the effect of progesterone through gene regulation. This role shifts near term as the oestrogen:progesterone ratio increases. At this stage oestrogen enhances oxytocin receptor expression.

**Oxytocin**

Oxytocin plays a role in the activation of myometrial smooth muscle, and in cervical remodelling. Response to oxytocin depends on gestation and phase of parturition, reflective of the progesterone:oestrogen balance at the time. Oxytocin receptor concentration increases significantly as term approaches, and is at its highest in early labour. Oxytocin receptors are distributed in the highest concentration at the uterine fundus and in the decidua, followed by the lower segment, and finally by the cervix.

Oxytocin has both direct and indirect actions. It acts directly on the myometrium to produce regular, effective contractions, and indirectly on the decidua to increase production of prostaglandins.

**Relaxin**

Relaxin is produced by the corpus luteum, the placenta and decidua. Levels of relaxin peak at the end of the first trimester,
Mechanical processes of labour

Rosa stated that “delivery can occur only when the uterine contraction, the axis of engagement, the descending fetus and the pelvic diameters all fit together”. With this in mind, one thinks of the three Ps — Power, the Passenger and the Passage. The intimate relationship between these components is key to a competent understanding of the mechanical process of labour.

We will first explore the preparatory mechanical changes before looking at the three Ps in more detail.

Cervix

The cervix is composed of fibrous connective tissue, collagen (types I, III and IV), elastin, vasculature, fibroblasts and minimal smooth muscle. The proportion of collagen decreases with increasing gestation.

Cervical ripening is a product of increased vascularity, stromal and glandular hypertrophy, and changes in the cervical extracellular matrix by matrix metallo-proteases, proteases and collagenases. Cervical nerve density is sustained or increased at term, and alterations in this signalling pathway have been noted to delay cervical ripening and reduce immune cell infiltration in animal studies.

The structural integrity of the cervix is reduced following a progressive decrease in the number of crosslinks between collagen helices and a switch from straight to wavy fibres, which are further disorganized by the infiltration of macrophages and neutrophils and an increase in hyaluronic acid production. This effect is compounded by an influx of water, which occurs due to an increase in decorin expression. Concurrently, there is decreased expression of collagen synthesis enzymes and proteins, such as lysyl hydroxylase, lysyl oxidase, thrombospondin 2, and tenasin C. Genetic mutations in this synthetic pathway are thought to be associated with cervical insufficiency, itself a major player in miscarriage and pre-term birth. Infection, leading to premature cervical remodelling, is associated with 25–40% of preterm birth. Cervical length surveillance is another focus in an effort to identify those at increased risk of pre-term delivery.

Inflammatory processes continue throughout labour. Increased activity of mediators such as IL-1 and IL-6. IL-6 stimulates prostaglandin and leukotriene production, leading to cervical vessel dilatation and further inflammatory cell extravasation.

Calcitonin gene-related peptide (CGRP) acts as a vasodilator, and as sensitivity to CGRP rises during pregnancy, it is thought to contribute not only to vascular remodelling in early pregnancy, but also towards uterine quiescence, and eventually to vasodilation during cervical ripening. Substance P has a significant role in the promotion of processes required for cervical ripening, and can also induce uterine contractions.

The net result of the changes detailed above is increased cervical compliance and cervical response to an increase in uterine pressure, due to progressive uterine contractions. The cervix becomes progressively effaced and dilated to 10 cm, to allow delivery of the fetus and placenta.

The cervix may be manipulated both chemically and mechanically in induction of labour. Common methods include vaginal prostaglandins and cervical balloon catheters.

Uterus

The uterus is predominantly composed of smooth muscle and changes shape from the first few weeks of pregnancy to accommodate the growing fetus and prepare for its eventual expulsion.

As outlined in further detail below, processes within the myometrium generate electrical activity which leads to the contractile forces required for labour. These processes are controlled by hormonal, metabolic and mechanical factors.

Although the uterus receives both parasympathetic and sympathetic innervation, it is a myogenic organ, i.e. it can contract without nervous stimulation. Uterine myocytes are relatively large, in keeping with the powerful contractile forces required during labour. They are connected by gap junctions, which increase in number as pregnancy progresses and thereby increase the capacity of the uterus to contract. Uterine contractions occur due to the generation of action potential within the myocyte. When threshold potential has been reached, voltage-dependent channels are activated, increasing intracellular calcium (Ca2+) and therefore action potential. Opening of voltage-dependent potassium (K+) channels leads to outward K+ current, inactivating L-type Ca2+ channels, and leading to repolarization. It is thought that myocyte resting membrane potential becomes more depolarized as gestation advances, facilitating Ca2+ influx and increasing the frequency of myometrial contractions. Reductions in K+ channels near term also prolong myocyte action potentials and enhance contractility.

Intracellular Ca2+ forms a complex with calmodulin and activates myosin light-chain kinase (MLCK), leading to phosphorylation of myosin and cross-bridge cycling with actin myofilaments, generating a contraction. In this way, myometrial contractions may be suppressed by blocking voltage-dependent L-type Ca2+ channels (dihydropyridine receptors); this is the mechanism for current tocolytics, such as Nifedipine.

Myocytes are noted to have proportionately large sarcoplasmic reticula (SR). SR not only store Ca2+, but also affect smooth muscle excitability. Ca2+ released by SR augments cytosolic Ca2+, and contributes to the actions of oxytocin, vasopressin and PG, thereby strengthening uterine contractions. SR Ca2+ release is regulated by intracellular pH and metabolites. Interestingly, during spontaneous labour, Ca2+ entry and efflux across the plasma membrane is responsible for uterine contractions, and there the SR does not contribute.

Oxytocin binds to a receptor in the cell membrane, thereby inducing an increase in cytosolic Ca2+, depolarizing the mitochondrial membrane potential and enhancing contractility. Whilst the importance of Ca2+ is apparent, K+ conductance is the main determinant of resting membrane potential in myocytes. Manipulation of K+ channels affects the duration of the action potential and repolarization. K+ channel activity is associated with uterine
quiescence, and downregulation of $K_{ATP}$ occurs in preparation for labour. TREK-1 K channels respond to myometrial stretching by increasing outward $K^+$ current. However, their activity is limited until gene expression increases close to term, to allow for uterine distension and accommodation of fetal growth.

A subunit of $K^+$ voltage dependent channels is thought to be expressed in lower levels in obese women. This may be compounded by the fact that elevated cholesterol levels also increase outward $K^+$ current. Both pathways result in increased $K^+$ conductance and supposedly poorer myometrical activity, which may contribute to the fact that obese women are more likely to require delivery by caesarean section.

It has been suggested that uterine myocytes have inherent pacemaking activity, however, to date, no anatomical or histological pacemaking structure has been identified.

Contractions increase in amplitude and frequency as labour progresses. In the process myometrial vessels are compressed and occluded. The phasic nature of uterine contractions is therefore important, so as to prevent prolonged myometrial hypoxia, leading to fetal asphyxia. As contractions reach their peak, lactic acid builds up within the myocytes, affecting the $Ca^{2+}$ current and decreasing the intensity of the contraction to baseline. The following rest period is essential in order to reverse hypoxic metabolic changes and restore pH, before the action potential is generated again.

Short cycles of hypoxia are thought to maintain the progressive augmentation of contractions required for labour. This is often referred to as hypoxia-induced force increase (HIFI). Parturition requires significant preparation, not only with respect to myometrial hypertrophy and increases in contractile proteins, but also glycoprotein and free fatty acid storage ahead of the hypoxic challenges of labour. Strict control of $Ca^{2+}$ and pH is necessary for uterine function. Oxidative phosphorylation provides the energy required for contractions, while anaerobic metabolism supports ionic regulation.

Lactate is produced by the myometrium even in the presence of sufficient oxygen and despite transportation out of the myocyte, continues to have an inhibitory effect on contractility. Accumulation of extracellular lactate is thought to contribute towards dystocia, and a recent trial has proposed that ingestion of oral bicarbonate may have a therapeutic role in this regard.

The changes detailed above are rapidly reversed in involution, where progressive remodelling of the uterine collagen and elastin content occurs. The uterus is back to near pre-pregnancy size in about 6 weeks, due to changes in endocrine levels and removal of mechanical stretch.

### Perineum and vagina

Perineal and vaginal muscle vascularity increases throughout pregnancy. Perineal connective tissue softens and smooth muscle cells hypertrophy to enable distension during labour.

### Pelvis

The ischial spines are a landmark for assessing descent of the fetal presenting part. Table 1 and Figure 2 summarize the dimensions of the pelvis.

### Power

The mechanical principles behind contraction production on a cellular level have already been detailed. Contractions alter the intrauterine pressure, thereby exerting force on both the fetus and the more pliable soft tissues, leading initially to cervical dilation, and then combining with maternal effort to produce expulsive force.

### Passage

Primarily the cervix must ripen and dilate. Maintaining an upright position during the first stage of labour is thought to shorten this process, however, the mechanics of this have not been thoroughly elicited. Thereafter there are three bony landmarks (Table 1), which may present a challenge to the fetal presenting part. Maternal position may also assist in this regard, for example the use of McRobert’s position to drop the sacral promontory and thereby assist delivery in cases of shoulder dystocia.

Pelvic floor soft tissue must also adequately stretch to accommodate delivery. There are mixed opinions as to whether high pelvic tone aids the fetal passage, or obstructs it. It is thought that it may guide presentation, as well as passively stretching as required. Unsurprisingly, it has been demonstrated that the perineal muscle force on the fetus increases as it descends through the pelvis. Consequently, those who deliver vaginally have been observed to have lower levels of pelvic tone than those who were delivered by Caesarean Section due to failed induction.

### Passenger

The diameter of the fetal head poses the greatest mechanical challenge, and so a cephalic, fully-flexed presentation is optimal. If an infant’s head is successfully delivered, the healthcare

#### Dimensions of the pelvis (cm)

<table>
<thead>
<tr>
<th>Boundaries</th>
<th>Transverse</th>
<th>Oblique</th>
<th>Anteroposterior</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inlet</strong></td>
<td></td>
<td>12.7 (Longest distance between</td>
<td>10 (Obstetric conjugate: sacral</td>
</tr>
<tr>
<td>Sacral promontory, linea terminalis</td>
<td></td>
<td>the bilateral linea terminalis)</td>
<td>promontory -&gt; symphysis pubis)</td>
</tr>
<tr>
<td>Mid</td>
<td></td>
<td>11.5 (iliopectineal eminence -&gt;</td>
<td>11.5 (S3 -&gt; midpoint of pubic symphysis)</td>
</tr>
<tr>
<td>Ischial spines</td>
<td>11.5</td>
<td>sacroiliac joint)</td>
<td>11.5 (Pubis -&gt; sacrococcygeal joint)</td>
</tr>
<tr>
<td><strong>Outlet</strong></td>
<td>10</td>
<td>10 (between ischial tuberosities)</td>
<td></td>
</tr>
<tr>
<td>Base at level of line drawn</td>
<td>10</td>
<td>11.5 (lower sacroiliac joint -&gt;</td>
<td></td>
</tr>
<tr>
<td>between the ischial tuberosities,</td>
<td></td>
<td>midpoint of obturator membrane)</td>
<td></td>
</tr>
<tr>
<td>tip of sacrum, subpubic area</td>
<td></td>
<td>11.5</td>
<td></td>
</tr>
</tbody>
</table>

![Table 1](image-url)
provider has greater confidence that the rest of the infant will not pose a mechanical challenge, compared to vaginal breech deliveries. In this instance, especially in cases of pre-term delivery (due to greater disparity between the size of the fetal head relative to the rest of its body), there is a relative risk of head entrapment.

**Lie**

The lie describes the long axis of the fetus with respect to the long axis of the mother:
- Longitudinal
- Transverse
- Oblique

**Presentation**

Presentation refers to the fetal part that engages with the maternal pelvis. This has important mechanical implications in the second stage of labour (see Table 2).
- Cephalic: Vertex/Occiput, Face, Sinciput, Brow
- Breech: This is much less common than cephalic presentation, comprising only 3–4% of term deliveries. Whilst vaginal breech delivery is beyond the scope of this article, and indeed is much less common currently, presentation may be further described as frank, complete or footling.

**Position**

Position describes the relation of the fetal presenting part to the maternal pelvis, the cephalic variations of which are demonstrated in Figure 3.

Table 2 summarizes the diameter of presenting part and important landmarks of the fetal skull. Figure 3 illustrates variations of the fetal head position when the presenting part is cephalic. Figure 4 demonstrates the descent and delivery of the fetal head during labour.

**Management of normal labour**

For the purposes of clinical management, labour is divided into three stages:

**Stage 1:** commencing with preparatory mechanical and biochemical changes as aforementioned, up to the achievement of full cervical dilatation. This stage is further subdivided into:
- Latent phase: up to 4 cm of cervical dilatation.
- This phase of labour may often be distressing and prolonged, particularly for the nulliparous woman. It has been confirmed that support at this stage reduces maternal anxiety, increases confidence and may be associated with lower rates of epidural use and syntocinon augmentation.
- Active phase: from 4 cm to full cervical dilatation.
- In low risk women, a vaginal examination should be offered every 4 h to ensure adequate progress. Satisfactory progress is defined as cervical dilatation at a rate of 1 cm every 2 h, as per national guidelines. In the event of suspected slow progress, vaginal examination should be repeated in 2 h, and delay diagnosed as appropriate. Findings, including maternal and fetal observations, should be recorded on the partogram.
- Clinical assessment should be sought in the event of slow progress or dystocia. Women with confirmed delay should be transferred to an obstetric-led unit. At this stage, augmentation with amniotomy and/or oxytocin infusion may be offered if appropriate. Women should be informed that amniotomy may shorten labour by approximately 1 h, and may increase the intensity and pain associated with contractions. It should also be noted that whilst oxytocin infusion will shorten labour, it does not affect mode of birth or other outcomes. Women should be informed that they will require continuous fetal monitoring in the presence of an oxytocin infusion.
- At all stages, women should be made aware of all analgesic options available, and in particular, epidural analgesia should be offered prior to commencing an oxytocin infusion.
Stage 2: encompassing the time between full cervical dilatation and delivery of the fetus. Again, there is further subdivision of this stage.

- Propulsive phase: this refers to passive descent of the fetus, allowing for rotation. Often in the presence of epidural analgesia, and in the absence of fetal or maternal concerns, this phase is limited to 2 h in nulliparous women, and 1 h in multiparous women.
- Expulsive phase: This refers to active pushing, and should be limited to 3 h in the nullipara and 2 h in the multipara. The woman should be guided by her own urge to push, however, guided pushing may be sought if this is not adequately effective. A vaginal examination should be offered hourly to assess descent and fetal position.
- Of note, obstetric review should be sought in the absence of delivery following 2 h of active pushing in nulliparous women, and 1 h of active pushing in multiparous women. At this stage operative vaginal delivery should be considered.
- Perineal trauma is common following vaginal delivery. In order to mitigate this, the “hands on” (perineal guarding and flexion of the infant’s head) or “hands poised” technique may be used. Episiotomy should not be performed routinely, however, it may be indicated if there is suspected fetal distress, or if operative vaginal delivery is performed. A right mediolateral technique is preferred, at an angle between 45 and 60 degrees. Adequate analgesia should be confirmed prior to performing an episiotomy. Postnatally, assessment and repair of perineal trauma should be performed by appropriately trained clinical care providers.

Stage 3: from delivery of the infant to delivery of the placenta and membranes. Active management is recommended, due to the significantly decreased risk of postpartum haemorrhage, and requirement for blood transfusion. However, low risk women may choose to pursue physiological management of the third stage, and should be supported in making an informed decision.

- Active management: routine use of uterotonic drugs, delayed cord clamping and controlled cord traction following signs of placental separation. 10 IU of oxytocin is administered IM following delivery of the anterior shoulder. The cord may be clamped between 1 and 5 min postnatally in the absence of neonatal concern.
- Physiological management: no routine use of pharmacological agents, no cord clamping until the cessation of pulsation, placental delivery with maternal effort.
Following delivery, the infant should be dried and stimulated as appropriate, and transferred to the mother for skin-to-skin contact.

Obstetric review should be sought if the third stage is prolonged, at 30 min for active management, and at 1 h for physiological management.

Monitoring

NICE do not recommend continuous monitoring in low risk women, due to increased rates of intervention, without a reciprocal reduction in adverse outcome. For this reason, it is recommended that low risk women receive intermittent auscultation of the fetal heart, for at least 1 min following each contraction. Fetal concerns that indicate escalation to continuous monitoring include rising baseline or audible decelerations. Maternal concerns that indicate escalation of monitoring are varied, and include hypertension, proteinuria, vaginal bleeding, constant abdominal pain, pyrexia or suspected sepsis, contractions lasting longer than 60 s, or more than five contractions per minute, and dystocia.

Particular circumstances

Induction of labour

Induction of labour is indicated in certain cases where shortening the pregnancy has been shown to reduce maternal and fetal morbidity. Although not strictly considered ‘normal’, induction of labour may often be the most realistic means of achieving a ‘normal’ vaginal delivery. The process is commenced with exogenous prostaglandin pessaries, or mechanical dilatation devices, to encourage cervical ripening. Endogenous prostaglandin release is then stimulated by amniotomy, and once the cervix is sufficiently ‘ripe’, synthetic oxytocin infusion is commenced to stimulate regular, strong contractions. Concurrently, oxytocin also binds to PG receptors in the decidua and cervix to activate further prostaglandin release.

Vaginal birth after caesarean section

With increasing rates of caesarean section across the world, vaginal birth after caesarean section (VBAC, also known as TOLAC) is now considered a normal means of delivery in many centres. A review conducted in 2013 compared planned caesarean section to VBAC, and concluded the presence of risks and benefits with both options. During VBAC, there is a small risk of uterine rupture and thus this necessitates continuous monitoring throughout labour, which in turn increases the rate of intervention in labouring women.

Conclusion

Labour is a varied experience for women and there is often an overwhelming amount of information available from different, and sometimes contradicting sources. As the clinical care provider, it is important to respect and acknowledge an individual woman’s choices, whilst providing her with evidence-based information and advice. Robust knowledge of the mechanisms and management of normal labour is key to our understanding of when to clinically intervene, and recognize areas where maternal and fetal morbidity can be reduced.

FURTHER READING


Inducing labour: NICE Clinical Guideline 70. et. NICE, 2008.


Practice points

- Labour is dependent on the interplay between biochemical, hormonal and mechanical factors which prepare for parturition far in advance of established labour.

- Successful vaginal delivery requires cervical effacement and dilatation, progressive and effective uterine contractions and concordance between the diameters of the fetal presenting part and the maternal pelvis.

- Knowledge of the rate of progress expected during normal labour is essential for the correct diagnosis of dystocia, and as such, when escalation of care and intervention are required.