**Fertilization, introduction to embryology and pregnancy**

---Manuscript Draft---

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Kate Davies |
| Abstract:          | This continuing professional development article considers the period of development from fertilisation to birth. It has briefly reviewed the three stages of pregnancy (germinal, embryonic and foetal). It provided examples of when congenital defects may occur and considered the potential impact on the developing individual. The birth process of the normal term infant was also briefly described. |
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Fertilization, introduction to embryology and pregnancy
Doreen Crawford Amy Noakes and Kate Davies

Abstract
This continuing professional development article considers the period of development from fertilisation to birth. It has briefly reviewed the three stages of pregnancy (germinal, embryonic and foetal). It provided examples of when congenital defects may occur and considered the potential impact on the developing individual. The birth process of the normal term infant was also briefly described.

Introduction
This continuing professional development (CPD) article will focus on the early development of the individual and will consider the process of fertilisation. It will provide an introduction to embryological development and the usual foetal growth trajectories will be considered. Having a basic knowledge of these factors are important as an awareness of embryology can enhance the practitioner’s understanding of the deviations from normal that can occur during pregnancy. This knowledge can be used to educate parents and students on normal development and also on the pathology which may occur as a result of abnormal foetal development. Following completion of this CPD the reader should be able to:

- Discuss the stages of foetal development.
- Define congenital anomaly and provide examples of congenital defects which may occur during embryological development.
- Have some understanding of how an anomaly in the process of development can impact on the developing individual.

Understanding embryology and foetal development, including the sequence in which tissues and organs grow and develop, can provide a foundation for understanding human anatomy and physiology (Schoenwolf et al 2015). The term congenital anomaly can be defined as any defect which is present at delivery. Most originate well before birth, and can include structural, chromosomal, genetic, biochemical defects and a range of malformations (PHE 2017). Congenital defects are common, in one data set it was calculated to affect 1 in 49 births in England (PHE 2017). The most common congenital anomalies were chromosomal in origin (e.g. Down Syndrome, Edwards Syndrome, Patau Syndrome) with a prevalence of 50.2 per 10,000 total births. These syndromes are known to occur more commonly in the older mother > 35 years (NHS 2018). Owing to the complexity of embryological development congenital heart defects are also common affecting 49.9 per 10,000 total births. Limb anomalies affect 29.8 per 10,000 total births. Just over a quarter of congenital anomalies were known to be associated with genetic conditions (PHE 2017). Within the UK approximately 30,000 children are diagnosed with a genetic disorder each year (Genetic Disorders UK 2016).
Timeout 1
Make a list of any conditions that you have seen in practice which you think might have occurred as a result of deviations during the early developmental processes.

How a pregnancy progress
Gestation is identified as the time-span between conception until birth. Normal gestation is considered to last between 37 and 41 weeks. It is difficult to identify the exact point of conception therefore gestation is measured from the first day of the last menstrual cycle, although conception may not occur until week two. In respect of pre-natal development this may be divided into three main periods: germinal stage (first two weeks post conception), embryonic stage (third week from conception to the eighth week) and the foetal stage (week nine from conception until birth).

Another way of considering embryological development is by use of the Carnegie stage where the timings are based on the days or weeks from the conception. This is more accurate than gestational age (see link and Hill 2018), although there can be small individual variations in the general timings of events.

The process of fertilisation.

During ejaculation the male expels approximately 200 million spermatozoa into the vaginal canal. A fraction of the millions of sperm deposited actually reach the cervix and travel through to the uterus, due to the acidic nature of the vagina. At this point uterine contractions disperse the sperm throughout the uterus where phagocytes are present attempting to destroy them, meaning only about 10,000 spermatozoa will travel through to the fallopian tube with only 100 actually reaching the egg, known as an oocyte (Marieb and Hoehn 2016). Fertilisation occurs post capacitation whereby the spermatozoa membranes become fragile and motility increases caused by secretions from the cervical mucus, uterus and fallopian walls. The oocyte contains two outer layers known as the corona radiate and zona pellucida. Both must be crossed for a single sperm to penetrate the oocyte membrane. The spermatozoa that reach the oocyte work together, whereby the acrosome (tip of the sperm head) contain enzymes which on consistent contact with the follicles (corona radiate) surrounding the egg break this down. This creates gaps for further spermatozoa to weave their way through and combine with a sperm receptor in the zona pellucida (subsequent outer layer of the oocyte). This triggers the release of further enzymes and rupturing of the acrosomes, eventually enabling a path for a single sperm to reach the surface and combine with the oocyte (figure 1); when this occurs, the oocyte blocks further sperm from entering (Moini 2016).

**Figure 1: Fertilisation**

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The sperms’ inner content is released into the oocyte and there is combining of the male and female pro-nucleus from the sperm and egg. In normal circumstances this subsequently produces a diploid nucleus (containing 46 genes) also known as a zygote. This constitutes 23 pairs of chromosomes from the sperm and 23 from the
egg, containing 22 pairs of autosomes and one pair of sex chromosomes. As demonstrated in figure 2, women possess the sex chromosome XX and men have the sex chromosome XY. The Y chromosome triggers the development of male gonads (reproductive cells) and in the absence of this the zygote will develop as female (Scanlon and Sanders 2011). With the fusion of the genetic material from the mother and father a unique genetic blueprint is created, please see CPD on Genetics which was one of the earlier articles in this series.

Figure 2: Inheritance of gender

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Monosomy and trisomy

Monosomy (45 chromosomes) These conceptions are usually lethal; the most common monosomy is Turners Syndrome which occurs in about 1 in 2000 live female births. The defect is caused by a single x chromosome. The syndrome may be identified at birth and there are a number of associated defects and complications which can occur as a result of the condition. These include short stature, cardiac anomalies and an increased risk of hip dysplasia. The intellect is not usually affected although the life span can be shortened. Females with this condition do not go through puberty unassisted and are infertile (Daniel and Rohena 2018).

Trisomy 21 (47 chromosomes) The defect most commonly caused by a full additional chromosome on what should be the 21st pairing. This trisomy is the most common chromosomal condition in humans, it is associated with advancing maternal age and there are a wide range of characteristics associated with this syndrome (Mundakel and Descartes 2018). The condition is compatible with life and can affect 1 in 1000 infants in the UK. It occurs in people of all races, and males and females are equally affected. It was named after a British doctor who was credited as being the first person to describe the condition, it can be identified by the dating scan (NHS
Trisomy 18 (47 chromosomes) The defect being found on what should be the 18th pairing. Trisomy 18 was first described by Edwards et al and Smith et al in 1960. It is the second most common autosomal trisomy after trisomy 21. The disorder is usually lethal. Most affected infants are females and the condition is characterized by severe psychomotor and growth retardation, microcephaly, microphthalmia, malformed ears, micrognathia or retrognathia. The hands are distinctive, and the infants have clenched fingers, there are also a range of other congenital malformations associated with this syndrome (Lai and Rohena 2016). Screening for this syndrome can be offered (NHS Choices, 2018).

Trisomy 13 (47 chromosomes) The defect being found on what should be the 13th pairing. This trisomy is rarer and invariably lethal with the average survival being about 3 days. The infant can be affected by holoprosencephaly, polydactyly, flexion of the fingers, rocker-bottom feet, facial clefts, neural tube defects, and cardiac anomalies. The syndrome is usually identified at birth because of the extent of the structural birth defects (Best and Rohena 2017). Screening for this syndrome can be offered (NHS Choices, 2018).

The Germinal stage
Where the zygote will form a single individual, the zygote will begin to divide from approximately 24 hours post fertilisation, this is known as 'cleavage', whereby the cells divide without the size of the zygote changing; these cells will act as the foundation of embryonic construction (Marieb and Hoehn 2016). At the same time the zygote begins to move down the fallopian tube towards the uterus (figure 3). By approximately 36 hours two identical cells are produced, which continue to divide to four cells meaning that by 72 hours a solid sphere of approximately 16 cells is produced known as the morula. Approximately four days after fertilisation the morula reaches the uterus. During the next two days cells clump together at the top of the morula, called the inner cell mass, which will eventually form the embryo and cells also form on the outside called trophoblasts, leaving a cavity which is known as a blastocoele. At this stage, this is now termed a blastocyst and flows free in the uterus. The trophoblasts release enzymes which cause the zona pellucida to break down, this is known as 'hatching'. The blastocyst starts to enlarge, absorbing nutrients which have been secreted by the uterus. Approximately two to three days after floating in the uterus, implantation of the blastocyst occurs. The lining of the uterus wall will be optimally mature due to high levels of oestrogen and progesterone, this will include possessing carbohydrate molecules that fit the blastocyst. Once the trophoblast cells nearest to the inner cell mass adhere to the endometrial lining of the uterus these release hormones which make a crater, in which the blastocyst fits (Perry et al 2014). These trophoblast cells will become the chorion, which constitutes the foetal portion of the placenta; this process can take up to five days. At this point the woman may experience a light implantation bleed as the egg implants into the wall of the uterus. This is common and included in the causes as to why up to 25% of pregnant women bleed in the first trimester.

https://emedicine.medscape.com/article/262591-overview
Figure 3: Germinal stage

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Table 1 Deviations in development

<table>
<thead>
<tr>
<th>Type of twin/multiple birth</th>
<th>The biology behind the individuals.</th>
</tr>
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<tbody>
<tr>
<td>Monozygotic</td>
<td>Identical (monozygotic) twins happen when a single egg (zygote) is fertilised. The egg then divides in two, or more creating identical embryos who will all share the same genes. Identical twins, or multiples are always the same sex and as they have the same genetic blueprint they will look very alike. Monozygotic twins occur in 1 in 250 pregnancies. Every year there are around 200 triplet pregnancies in the UK and a handful of higher order births. Twins can be identified at the dating scan (NHS Choices 2017)</td>
</tr>
<tr>
<td></td>
<td>An extremely rare phenomena are the incomplete separation of the embryos this may be symmetrical or equal conjoined twins (i.e., two well-developed infants) or asymmetrical or unequal conjoined twins where a small part of the body may be duplicated, or an incomplete twin is attached to a fully</td>
</tr>
</tbody>
</table>
developed twin (Kamal and Minkes 2018)

| Dizygotic | Non-identical (dizygotic) twins happen when two separate eggs are fertilised and then implant into the uterus. These twins each have their own genetic blueprints and are no more alike than any other two siblings. Non-identical twins are more common, and some races have more twin pregnancies than others. |

Table collated from information from NHS Choices (2016 and 2017) see also resources developed by TAMBA in links.

The Embryonic stage

During implantation the blastocyst is converted into the gastrual whereby the inner cell mass separates from the trophoblast. This separation eventually gets greater generating the amniotic cavity. Within the inner cell mass each cell possesses Deoxyribonucleic acid (DNA) which has the potential to be switched on and off allowing for the specialisation of cells as they divide. By approximately 14 days the cells move towards a central line known as the primitive streak and eventually develop into three layers (germ layers) as demonstrated in figure 4. This is known as gastrulation. As the cells continue to divide the plate of cells begins to fold making the embryonic disc consisting of:

- Ectoderm- this will develop into the nervous system and skin;
- Endoderm- this will develop into the respiratory and digestive system;
- Mesoderm- this will develop into the skeletal and muscle system.

(Polin et al 2011)

Figure 4: The embryonic disc

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Within the germ layers four extraembryonic membranes develop to support growth and development (figure 5). By 20 days post fertilisation these can be clearly distinguished as:

- **Yolk sac** - This enables production of the first blood cells and sex cell formation, eventually this will dissipate into the umbilical cord;
- **Amnion** - This consists of both ectoderm and mesoderm cells. The amnion surrounds the embryo containing amniotic fluid protecting the embryo from physical injury and maintaining homeostatic temperature;
- **Allantois** - This constitutes both ectoderm and mesoderm cells which eventually creates the urinary bladder, during the embryonic stage this collects small amounts of urine produced by the kidneys. The allantois acts as a structural basis for the umbilical cord;
- **Chorion** - This is produced by mesodermal cells beneath the trophoblast. Initially when implantation occurs nutrients can reach the inner cell mass via diffusion, however as the embryo and trophoblast cells enlarge the distance between the two increases. Subsequently blood vessels develop to enable nutrients to reach the embryo, whereby projections from the chorion grow into the endometrial lining of the womb called chorionic villi. This also encourages hormonal stimulation of human chronic gonatropin (hCG) promoting placental production and generation of progesterone and oestrogen to sustain pregnancy (Marieb and Hoehn 2016)

Figure 5: Extraembryonic membranes

[Image of extraembryonic membranes]

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Neurulation is the process of developing a neural tube which will form the brain, spinal cord and nervous system. At week three the embryonic disk will have a cranial and cordial end (demonstrated in figure 6). The notochord induces the ectoderm and thickens to make a neural plate. The edges of the neural plate extend upwards to produce neural folds and these come together fusing at the midline, forming a hollow neural tube. Neural tube defects such as spina bifida occur when the neural tube does not close properly. The exact cause of this defect is unknown however zinc and folic acid deficiencies have been proposed as possible causes (World Health Organisation 2006). It is therefore recommended that women take a
folic acid supplement pre-conception and within the first trimester of pregnancy. There is also a risk of some medications causing neural tube defects or affecting normal neurological development. The drug Thalidomide, which was prescribed for morning sickness in the 1950s and 1960s became implicated in causing serious brain and limb deformities (Vargesson 2015). More recently the drug Epilim (Sodium Valporate) has been implicated in an increase in neurodevelopmental problems (Epilepsy Action 2013). This evidence highlights the need for women to be cautious regarding medication and other substance use in pregnancy.

Figure 6: Neurulation

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Timeout 2
Make a few notes on the medications, or substances, which you are aware may affect an unborn infant.

After gastrulation begins the body of the embryo separates from the rest of the embryonic disc whereby folding and differential growth of the embryonic disc produces a bulge (the head fold) into the amniotic cavity; comparable movements produce the tail fold (Martini and Bartholomew 2017). This lateral folding forms the primitive gut whereby the embryo transfers from a flat plate to a cylindrical body shape; by 24 days the embryo has a tadpole shape.

The heart is one of the first organs to be developed in the embryo, beginning from week three. This is derived from the mesoderm whereby the primitive heart consists of two tubes which merge into one, this subsequently swells to produce the various cardiac anatomical features. This will twist and turn in a rightward direction (dextral looping) producing the right and left ventricle. Abnormal looping in a leftward direction causes the ventricles to develop on opposite sides. The septum of the heart subsequently develops, and malformations such as an atrial septal defect, or the more common ventricular septal defect will occur when these do not correctly close (Alder and Subhi 2017, Ramaswamy and Weber 2015). Because of the complexity
of cardiac development, a heart defect is the most common congenital anomaly, they are many and varied some require no treatment, others require extensive and staged surgery (see links and also see a CPD which will appear later in this series).

**Foetal circulation**

As oxygen to the embryo is not provided via the foetal lungs, blood is oxygenated by the mother and her circulation conveys it to the placenta, this oxygen then crosses the placenta and combines with foetal haemoglobin. Oxygenated blood then travels to the right atrium of the heart. This circulatory path is facilitated by the presence of several shunts. The cardiac shunts are known as the forum ovale which connects the left and right atrium and the ductus arteriosus (a connection between the pulmonary artery and the aorta) see fig 7 and fig 9. These openings close soon after birth, if these closures do not occur the result is patent foramen ovale or patent ductus arteriosus (PDA). These may require surgery or other interventions to reduce pulmonary hypertension or the risk of congestive heart failure.

fig 7 The anatomical shunts which support foetal circulation

Taken from this website https://www.slideshare.net/AmbikaJawalkar/fetal-circulation-47393691 it would seem to be covered by the following agreement https://www.linkedin.com/legal/user-agreement Need to confirm that redrawn to use would not constitute any breaches

**Beginning to look human**

By week 5 the embryo has a definite and recognisable form and is approximately 22mm long from head to buttocks, consisting of a head, heart that is beating and small limb buds. Every embryo’s external genitalia is exactly the same until 8 weeks, all having a phallus, urogenital fold and labioscrotal fold. It is only in the presence of the Y chromosome, triggered by the sex determining gene, region Y (SRY gene), that testicular development begins. If this gene is missing or does not work, healthy testes will not develop. By week 12, the embryo is distinctively male or female. By week 8 organogenesis has occurred whereby organ systems are established. The eyes and ears start to take on human form, the limbs start to form and digits are separated, the neck is short but present and the head is as large as the rest of the
body. The initial weeks of development are the critical phases of development and the time in which any major abnormalities are most likely to occur, see figure 8.

Figure 8: Critical period where abnormalities may occur during pregnancy

<table>
<thead>
<tr>
<th>Conceptus</th>
<th>Embryonic development (weeks)</th>
<th>Fetal period (weeks)</th>
</tr>
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<tbody>
<tr>
<td>1 2</td>
<td>3 4 5 6 7 8</td>
<td>9 16 20-35 38</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>Description/definition</th>
<th>Stage of development</th>
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<tbody>
<tr>
<td>Monosomy/trisomy</td>
<td>Range of phenotypical characteristics and organ / structural defects. See text</td>
<td>Fertilisation</td>
</tr>
<tr>
<td>Diaphragmatic hernia</td>
<td>A serious and common malformation occurs in approximately 1 in 2200 births and usually as a posterolateral defect of the diaphragm. The defect is usually unilateral with a large opening in the left side of the foramen of Bochdalek. As the muscle is not fused the abdominal contents may pass into the thoracic cavity. The heart and mediastinum are often</td>
<td>From fertilisation week 4 to week 6 Carnegie stages 13-17 (Hill a 2018)</td>
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Table 2 Examples of the more common congenital defects and the critical time of development.
| Condition | Description | Timeframe
|-----------|-------------|-----------
| Exomphalos / omphalocele | An omphalocele is a midline abdominal wall defect of variable size, containing abdominal contents. The defect occurs at the base of the umbilical cord, with the cord/umbilical vessels inserting at the apex of the omphalocele sac (Glasser and Rosenkrantz 2017, Stephenson, Lockwood, Mac Kenzie, et al 2018). Incidence considered to be 1 in 4000 births and the condition is associated with syndromes. (Glasser and Rosenkrantz 2017). | Weeks 4 and 5 (Stephenson, Lockwood, MacKenzie, et al 2018, Hill b 2018) |
| Gastroschisis | A Gastroschisis is a herniation of the abdominal contents through an abdominal defect. The abdominal herniation is usually to the right of the umbilical cord. A gastroschisis usually contains small bowel and is not encased by a membrane. The defect can be identified before birth and affects 1 in 2000 births (Khan and Lin 2016). | Weeks 6-10 (Glasser and Rosenkrantz 2017, Hill b 2018) |
| Trachea oesophageal fistula | In infants a tracheoesophageal fistula (TOF) is a congenital communication between the trachea and oesophagus. The condition may lead to severe and potentially fatal pulmonary complications (Sharma and Kapoor 2016). The condition occurs in about 1 in 2000 births and the majority of these infants will have other anomalies. | Weeks 4- to 6 (Sharma and Kapoor 2016, Hill b 2018). |
| Spina Bifida / neural tube defects | Neural tube defects have a range of presentations, from lethal to incidental radiographic findings of an occult lesion. The higher the lesion the more serious the functional defect. For example myelomeningocele is very obvious at birth and involves lower limb paralysis and sensory | Neural tube defects occur early between the 17th and 30th days (Foster and Moberg-Wolff 2016, Hill c 2018) |
loss, bladder and bowel dysfunction, and often cognitive dysfunction because of associated hydrocephalus (Foster and Moberg-Wolff 2016).

The defect can be identified at the first antenatal scan (NHS Choices 2017).

| Ambiguous genitalia | A disorder of sex development. This can occur in approx. 1 in every 300 births, but true ambiguous genitalia occurs in 1 in every 5000. This is usually due to a gene regulation breakdown which is responsible for gonadal development. | Occurs during the developmental stage at 7 – 8 weeks (Davies 2019) |


The Foetal stage

By 12 weeks the placenta is fully formed consisting of both foetal and maternal tissues, including the chorion of the embryo and the endometrial lining of the uterus (Scanlon and Sanders 2011). The placenta acts as an exchange system between the foetal and maternal systems whereby the foetus is dependent on the mother for oxygen and nutrients whilst removing waste products. The placenta also produces hormones to sustain pregnancy. The umbilical cord connects the foetus to the placenta carrying oxygen to the foetus via the umbilical vein and returning waste products to the mother via the two umbilical arteries as shown in figure 8.

Figure 9: The placenta

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At 12 weeks the foetus continues to have a large head in comparison to the body, the retina is formed, and brain development continues. The external genitalia of males and females are fully developed. Blood cell formation commences in the spleen and bone marrow (Moore et al 2016). Urine formation begins and is expelled through the urethra into the amniotic fluid. The liver is seen as overly enlarged and the hard palate starts to fuse.

A routine dating scan is provided to women at approximately 12 weeks, this aims to confirm viability, establish gestational age, determine the number of foetuses and detect any major abnormalities. The Nuchal Translucency (thickness of the fluid build-up at the back of the head) is measured as this can be an indicator of such conditions as Down Syndrome or Trisomy 18.

At 16 weeks although the eyes are still fused closed, eye movement can be observed, and the foetus can make sucking motions. The body growth is enhanced, and the limbs appear to be a more proportionate size, with coordinated movement. The kidneys and bones appear more distinctive; however, the skin is so transparent that blood vessels can be seen beneath it.

At approximately 20 weeks the woman will have a routine anomaly ultrasound scan to review foetal development and identify any physical abnormalities. It is at this point the sonographer is able to inform the woman of the foetus’ gender, although this is dependent on the positioning of the baby at that time.

Additional aids to support a diagnosis of foetal anomaly include chorionic villus sampling and amniocentesis, the identification of an abnormality can incur several ethical and legal issues which differ depending on where the family are resident, however such news should always be imparted with sensitivity and the family provided with privacy and support (Springer and Grewal 2018).

The foetus will have lanugo present, which is fine, soft hair providing anchorage for vernix caseosa to stay on the skin, a waxy substance protecting the skin from the amniotic fluid and subsequently abrasions. This lanugo usually sheds by 36 weeks and is replaced by vellus hair. Hair on the head and eyebrows are present. The eyes are structurally complete, the ears are in position and the skin appears less transparent (London et al 2014).

At approximately 22 to 23 weeks surfactant starts to be produced in the lungs, this reduces surface tension in the lungs keeping the alveolae open. The most common lung condition of premature babies is respiratory distress syndrome caused by the lungs not producing adequate amounts of surfactant due to immaturity (Walsh et al 2010). By 26 to 28 weeks the foetus’ eyes can now open, the finger and toe nails are fully developed and the bone marrow solely produces red blood cells. Babies born prematurely at this point have greater chance of survival with intensive support because the lungs have developed sufficiently for gas exchange and the central nervous system has matured enough to enable rhythmic breathing and body temperature control (Perry et al 2014).

By 32 weeks the sucking reflex has developed and myelination within the brain commences (development of fatty insulating sheath around nerve fibres) in addition
the pupillary light reflex of the eyes is present. From 35 weeks of pregnancy rapid weight gain of the foetus occurs and maternal antibodies are transferred (London et al 2014). The baby will move further down the pelvis assuming the head down position in preparation for birth. A baby born from 37 weeks is considered to be term (Gittinger and Isaacs 2015), with developed organs ready for delivery although some organs will continue to mature into childhood such as the digestive tract, brain and lungs.

Timeout 3
A student you are working with asks you what abnormalities can be detected during the 12 week and 20-week scans, what are you going to include in your explanation?

The delivery of a normal term infant

Although only about 5% of deliveries arrive on their due date, nearly 80% of infants are delivered at full term (Gittinger and Isaacs 2015, NICE 2014). Birth can take place in a number of locations such as the family home, a midwifery facility or an obstetric unit depending on the woman’s choice and the degree of risk assessed to the mother and infant (NICE 2014).

The birth process is divided into 3 stages. During the first stage, the cervix dilates as a result of progressive rhythmic uterine contractions, this is usually the longest stage of labour (Gittinger and Isaacs 2015) This stage also involves cervical effacement, or thinning, the experience of pain during labour differs between mothers and pain should be sensitively managed (NICE 2014). Labour progresses best when the woman is relaxed and active.

The first stage of labour is divided into the latent and active phases. The latent phase can last for several hours as the cervix dilates slowly. The active phase lasts from the end of the latent phase until delivery and is characterized by rapid cervical dilation, it is faster when the woman has had previous vaginal deliveries (Gittinger and Isaacs 2015).

The second stage of labour is defined as the time between complete cervical dilation and complete delivery of the infant, this phase can last a few minutes or extend into hours (NICE 2014). The length of time is affected by the placement of an epidural and any previous deliveries.

During the second stage of labour the head becomes engaged into the lower pelvis and flexion of the head places the occiput of the infant’s skull into the presenting position. The infant will then descend through the pelvis. An internal rotation of the infant will help them to manoeuvre past the lateral ischial spines of the maternal pelvis. To pass beneath the maternal symphysis the infant head is extended and external rotation of the head after delivery will enable the shoulders to be delivered (Gittinger and Isaacs 2015).

The delivery is concluded following the expulsion of the placenta and is regarded as the third and final stage of labour. This normally occurs within 30 minutes of the delivery of the infant. It is a result of separation between the placenta-endometrium
interface and uterine contractions (Gittinger and Isaacs 2015). Worldwide between 1-5% of deliveries a post-partum haemorrhage occurs, and this is the largest contributor to maternal mortality, treatment depends on the cause of the haemorrhage and the level of skill the birth attendant has (Ayadi, Robinson, Geller et al 2013). Prophylactic oxytocin is common, the use of other uterotonic agents are emerging, occasionally surgery is required (Ayadi, Robinson, Geller et al 2013).

**Conclusion**

This CPD has considered the period from conception to birth and linked the developmental process to a range of anomalies. The embryological period is a brief period of development where the potential for a deviation from the norm can have serious and lifelong implications for the individual.

**Time out 4 complete the following Quiz**

1 – Which stage of neural development occurs within the first two weeks of embryological development?
A – Gastrulation
B – Neurulation
C – Cell proliferation
D – Neuronal migration

2 – From which week gestation does the neural tube begin to close?
A – 2 weeks
B – 3 weeks
C – 5 weeks
D – 6 weeks

3 – Around what day gestation does the heart start functioning?
A – 7 days
B – 21 days
C – 28 days
D – 36 days

4 - At which gestational age can a baby born prematurely breathe independently?
A - Week 20
B - Week 24
C - Week 28
D - Week 32

5 – What does the nuchal translucency test look at?
A – The thickness of a baby’s neck
B – Length of the baby’s femoral bone
C – Head circumference
D – Sex of the baby

6 – Up to what age gestation is all embryo’s external genitalia identical?
A – 4 weeks
B – 8 weeks
C - 12 weeks
D – 16 weeks

7 – What is the first organ to develop in the embryo?
A – The brain
B – The lungs
C – The heart
D – The spine

8 – What is not one of the primary germ layers?
A – Ectoderm
B – Neuroderm
C – Ectoderm
D – Mesoderm

9 – When should a woman begin to take folic acid?
A – As soon as she knows she is pregnant
B – When she has her 12 week scan
C – As soon as she begins to show
D – Before conception

10 – Within the germ layers, what is not one of the four extraembryonic membranes?
A – Yolk sac
B – Amnion
C – Allantois
D – Morula
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https://emedicine.medscape.com/article/186735-overview#a5 accessed August 2018


Resources and links

NHS Choices (2017) the pregnancy dating scan 
https://www.nhs.uk/conditions/pregnancy-and-baby/dating-scan-ultrasound-10-11-12-13-weeks-pregnant/ last accessed August 2018

TAMBA Resources for health professionals https://www.tamba.org.uk/health-professionals-welcome accessed August 2018. To use these resources you will have to register which is free. last accessed August 2018

Hill 2018 
https://embryology.med.unsw.edu.au/embryology/index.php/Timeline_human_development last accessed August 2018
Hill 2019 Carnegie Stages

Fetal Circulation  https://www.slideshare.net/AmbikaJawalkar/fetal-circulation-47393691  last accessed August 2018

Congenital Heart Defects  https://www.nhlbi.nih.gov/health-topics/congenital-heart-defects  Accessed August 2018