

Chapter

Early pregnancy – models of healthcare

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Introduction

Early pregnancy problems form a major part of all gynecological emergencies. In the past, patients were admitted to the emergency receiving ward and waited for a considerable length of time before undergoing ultrasound scan and clinical assessment. With the appearance of early pregnancy assessment units (EPU), an increasing number of women are being assessed and managed as outpatient or office attenders. The advent of high-resolution transvaginal ultrasound coupled with the improved access to hCG measurements has allowed the development of models of care and improved delivery of care.

Within the UK the growth of EPU numbers has increased to the extent that over 200 active units are registered with the Association of Early Pregnancy Units (AEPU). The AEPU has set out, since its inception in 2001, to improve the standards of early pregnancy care and to provide a clearer pathway for the patient's journey (earlypregnancy.org.uk).

In recent years ultrasound diagnosis and improved understanding of problems related to early pregnancy have led to the introduction of medical and expectant management of miscarriage and selected cases of ectopic pregnancy. Randomized controlled trials have provided evidence-based practice (rcog.org.uk/guidelines). Patient choice has emerged as a powerful selector for treatment. The mission statement from the Association of Early Pregnancy Units has the patient at the center of all activity and the multidisciplinary care structure reflects the multitasking approach of care providers.

All women with early pregnancy problems will have prompt access to a dedicated Early Pregnancy Assessment Unit (EPU) that provides efficient evidence based care with access to appropriate information and counseling. At all times women will be

supported in making informed choices about their care and management.

Evolution

Early pregnancy loss before 12 weeks' gestation is a common event that causes a great deal of distress to women and their partners alike. Approximately 1 in 5 pregnancies will end in pregnancy loss which represents a considerable burden on individuals as well as the health-care providers.

As miscarriage causes such strong emotional reaction it is apparent that the great majority of sufferers clearly remember the event process leading up to the pregnancy loss. Most early pregnancy complications will have undergone ultrasound scan assessment. Many women recall precise details of ultrasound findings before or at the time of diagnosis. As a consequence there is a need to improve our description of early pregnancy events so that care providers and patients understand each other and use the same language to describe these findings. Upon this basis and using a pragmatic ultrasound-based approach, an attempt to replace old and misunderstood terms like blighted ovum has been made.

The nomenclature used to describe clinical events in early pregnancy has been criticized for lack of clarity and promoting confusion. There is no agreed glossary of terms or consensus regarding important gestational milestones. In particular there are old and poorly descriptive terms such as missed abortion or blighted ovum which have persisted since their introduction many years ago [1] and have not undergone revision despite the widespread application of ultrasound for accurate clinical assessment and diagnosis.

The authors are aware of these shortcomings in terminology and are keen to provide an updated glossary. The attached summary hopes to facilitate the introduction of a revised terminology in an attempt

Chapter 1 Early pregnancy – models of healthcare

to provide clarity and to enhance uptake and use in the literature, especially patient information leaflets, as well as clinical assessment and documentation (Table 1.1).

Recognizing the event

The commonest early pregnancy complication of spontaneous miscarriage occurs in approximately 15–20% of all pregnancies, as recorded by hospital episode statistics. The actual figure, from community-based assessment, may be up to 30%, as many cases remain unreported to hospital [2]. The great majority occurs early before 12 weeks gestational age and less than 5% occur after identification of fetal heart activity [3]. Second trimester loss, between 12 and 24 weeks, occurs less frequently and constitutes <4% of pregnancy outcomes [4]. The clinical assessment of every pregnancy loss history requires clarification of pregnancy loss type and accurate classification, whenever possible [5].

The traditional grouping of all pregnancy losses prior to 24 weeks as “abortion” may have had pragmatic origins, but it is poor in terms of definition and makes little sense. The term abortion is also confusing for the patient and its use should be abandoned. She may not realize that (spontaneous) abortion is not a termination of pregnancy because the terms medical abortion or legal abortion are used in the same way.

Increasing knowledge about early pregnancy development, with the more widespread availability of serum beta hCG measurement, the advent of high-resolution transvaginal ultrasound (TVU) and a clearer description of gestational age at pregnancy loss make for a more sophisticated assessment of previous miscarriage history. The advent of these important information milestones has not been fully realized nor incorporated into clinical event description for article publication.

The emergence of early pregnancy units (EPU) in many hospitals has addressed the need for a dedicated clinical area for the diagnosis of miscarriage and patient support at a distressing time (Box 1.1) [6,7]. With the establishment of an EPU network, it becomes more important that a standardized diagnostic classification system be employed for accurate and reproducible reporting of ultrasound findings and clinical outcomes so that direct comparisons between units can be readily understandable for both research and audit purposes.

The most recent Confidential Enquiry into Maternal Deaths (2007) conclusively demonstrates that mortality from ectopic pregnancy has not declined and is

still on the increase on rates described 10 years ago [8]. As the EPU represents the most likely point of ectopic pregnancy diagnosis, the importance of standardized reporting of very early pregnancy changes requires a robust approach following recent recommendations [9].

Length of pregnancy

Just as postnatal age begins at birth, prenatal age begins at fertilization. The embryonic period occupies the first 8 postfertilization weeks, during which organogenesis takes place. Thereafter, the fetal period is characterized by growth. Embryologists prefer the term embryonic age and assess this by using 23 internationally recognized morphological stages [10]. Clinicians, however, conventionally calculate from the first day of the last normal menstrual period (LMP). Confusion about the definition of pregnancy duration derives from use of terms such as postovulatory age, conceptual age or even misnomers like menstrual age within the published literature.

Clinicians do have to acknowledge that a woman does not become pregnant during the LMP, or during ovulation but exclusively after conception. Gestation is the condition of being carried in the womb during the interval between conception and birth. The term “gestational age” (GA) is therefore confusing, although generally accepted, and its widespread use can only be legitimized using a clear definition. The appropriate way to overcome this confusion is to choose GA based on a theoretical ovulation plus 2 weeks. As early ultrasound (US) measurements of the fetus (crown–rump length, CRL) are reproducible [11] and more accurate than the use of the LMP there is a need in publications to define GA as based on LMP and/or US. The continuing refinement of early pregnancy dating and growth studies will clearly help the patient’s experience and clarify uncertainty in the clinician’s mind [12].

Ultrasound criteria

With the introduction of transvaginal ultrasound, longitudinal assessment of early pregnancy development can be made, in terms of viability and growth. Ultrasound plays a major role in maternal reassurance, where fetal cardiac activity is seen and is pivotal in the assessment of early pregnancy complications, such as vaginal bleeding [13]. However, there are limits to ultrasound resolution of normal early pregnancy development. Recent advice concludes that a

Chapter 1 Early pregnancy – models of healthcare

Table 1.1 Revised nomenclature 2005 [5].

| Avoid | Prefer | Ultrasound findings |
|--|---|--|
| 1. Egg | Oocyte | |
| 2. Embryo | Fetus | Ultrasound-based definition to include fetal heart activity and/or crown–rump length >10 mm |
| 3. Embryonic age Postovulatory age Conceptual age Menstrual age | Gestational age based on last menstrual period and/or ultrasound fetal measurement | |
| 4. Threatened abortion | Threatened miscarriage | |
| 5. Spontaneous abortion | Spontaneous miscarriage | |
| 6. Medical abortion Legal abortion | Termination of pregnancy | |
| 7. Recurrent abortion Habitual abortion | Recurrent miscarriage consisting of 3 early consecutive losses or 2 late pregnancy losses | |
| 8. Pregnancy test | Serum/urine level of human chorionic gonadotrophin (hCG) | |
| 9. Pre-clinical embryo loss | Biochemical pregnancy loss with description of falling low positive serum/urinary hCG | No definition of pregnancy location |
| 10. Trophoblast regression | Biochemical pregnancy loss | |
| 11. Menstrual abortion Pre-clinical abortion | Biochemical pregnancy loss | Pregnancy not located on scan |
| 12. Early embryonic demise Anembryonic pregnancy | Empty sac | Gestation sac with absent structures or minimal embryonic debris without heart rate activity |
| 13. Embryonic death | Fetal loss | Previous identification of crown–rump length and fetal heart activity followed by loss of heart activity |
| 14. Early abortion | Early pregnancy loss | Ultrasound definition of intrauterine pregnancy with reproducible evidence of lost fetal heart activity and/or failure of increased crown–rump length over one week, or persisting presence of empty sac, at less than 12 weeks' gestation |
| 15. Missed abortion | Delayed miscarriage | Same as for early pregnancy loss (vide supra) |
| 16. Late abortion | Late pregnancy loss | After 12 weeks gestational age where fetal measurement was followed by loss of fetal heart activity |
| 17. Hydatidiform mole Partial mole Molar pregnancy | Gestational trophoblastic disease (complete or partial) | |
| 18. Heterotopic pregnancy | Intrauterine plus ectopic pregnancy (e.g. tubal, cervical, ovarian, abdominal) | |
| 19. | Pregnancy of unknown location (PUL) | No identifiable pregnancy on ultrasound with positive blood/urine hCG |

Chapter 1 Early pregnancy – models of healthcare

| Standard | Core pregnancy care | Aspirational |
|---------------------------------------|--|--|
| Patient information | Designated reception area. Universal use of clear, understandable terminology by all staff. | Dedicated staff constantly at reception desk to provide greeting, obtain patient details and explain structure and triage function of EPU. |
| Patient choice of management | Education of patient relevant to diagnosis and management. Open explanation of expectant, medical and surgical options. | Dedicated phone line for patient queries and electronic access to protocols from outside unit. |
| Dedicated quiet room | Room for breaking bad news away from work area. | Single-use room only with soft furnishing and absence of medical equipment. |
| Availability of service | 5 day opening during office hours. | 7/24 opening and service provision with full staffing and daily scan support. |
| Competence of scanning | Recognized ultrasound training and RCOG/BMUS preceptor assessment and validation. Register of staff competent at scanning. | Lead clinician. Presence of RCOG/BMUS trainer in EPU. Annual assessment of audited activity. |
| Blood hCG level measurement | Laboratory access to blood hCG measurement and result within 48 hours of sampling. | Same-day sampling and result with electronic result link to laboratory. |
| Written information leaflets | Visible open access to written information leaflets in EPU. | Online external access to PIL. |
| Acknowledgment of privacy and dignity | To provide individualized patient support and acknowledge confidentiality. | Place one to one care as best practice at all times. |
| Bereavement counseling | All staff trained in emotional aspects of early pregnancy loss. To enable access to counseling and provide immediate support. | To provide all emotional and psychological counseling requirements within EPU and supported by dedicated staff and related agencies. |
| Site of EPU | Geographically separate from all maternity areas. | Own EPU entrance/exit. |

diagnosis of an empty sac (previously named: anembryonic pregnancy, early embryonic demise or embryo loss) should not be made if the visible crown–rump length is less than 6 mm, as only 65% of normal embryos will display cardiac activity [14]. Repeat transvaginal ultrasound examination after at least a week showing identical features and/or the presence of fetal bradycardia is strongly suggestive of impending miscarriage [15]. The possibility of incorrect dates should always be remembered by the alert clinician. In addition, it should be remembered that when the fetus has clearly developed and the fetal heart is absent, the term “missed abortion” should be replaced by “delayed miscarriage” [16].

Gynecologists and ultrasonographers acknowledge the “embryonic” period by speaking about fetal heart action and fetal activity before the end of organogenesis. This evidence of heart action is vital to the

patient who sees clear signs of life. Embryologists, by contrast, may debate the meaning of embryo in early pregnancy but embryo is more synonymous with cells and gametes in an IVF laboratory than as the pre-clinical scientific description of anatomic organogenesis. Although a clear distinction between embryonic and fetal periods is significant in teratology, we have to accept that modern terminology should reflect daily clinical practice whose description has changed in the last two decades and is more patient-centered. The term fetus receives an ultrasound definition to include fetal heart activity and/or a crown–rump length >10 mm.

Classification of events

There has been a plea to classify pregnancy losses according to the gestational age at which they occur

Table 1.2 Commonest pregnancy loss types based on ultrasound features.

| Type of loss | Typical gestation (range in weeks) | Pregnancy loss classification | | |
|-----------------------------|------------------------------------|-------------------------------|---|--------------------------|
| | | Fetal heart activity | Principal ultrasound finding | Beta hCG level |
| Biochemical loss | <6 (0–6) | Never | Pregnancy not located on ultrasound | Low then fall |
| Early Pregnancy loss | 6–8 (4–10) | Never | Empty sac or large sac with minimal structures without fetal heart activity | Initial rise then fall |
| Late Pregnancy loss | >12 (10–20) | Lost | Crown–rump length and fetal heart activity previously identified | Rise then static or fall |

and detail the event; for example, in case of fetal demise at 8 weeks, define it as fetal death at 8 weeks gestational age. In this way, possible pathophysiological mechanisms may be postulated and studied. Historically, clinicians have grouped all pregnancy losses that occur at a gestational age prior to theoretical viability under the umbrella of “abortion.”

Between 1% and 2% of fertile women will experience recurring miscarriage (RM) [17]. Recently, among researchers in the field of RM, it has been recognized that the classification of pregnancy loss is more complex as the developing pregnancy undergoes various important stages, and different pathology at the time of pregnancy loss is exhibited at these different stages. As the majority of RM cases following investigation are classified as idiopathic [17], it is generally accepted that within the idiopathic group there is considerable heterogeneity and it is unlikely that one single pathological mechanism can be attributed to their RM history. Furthermore, there is considerable debate about cause and association as the exact pathophysiological mechanisms have not been elucidated. Current research is directed at theories related to implantation, trophoblast invasion and placenta-tion, as well as factors which may be embryopathic.

No identifiable pregnancy on ultrasound examination in combination with a positive urine or serum beta hCG pregnancy test is named a pregnancy of unknown location (PUL). Biochemical pregnancy loss is a better description than trophoblast in regression or preclinical embryo loss. After ultrasound identification of pregnancy a miscarriage can be classified as early, before 12 weeks or late, after 12 weeks.

Heterotopic pregnancy is a combination of an intrauterine pregnancy and an ectopic pregnancy.

Table 1.3 Pregnancy success prediction matrix [3]. Following idiopathic recurring miscarriage, the predicted probability (%) of successful pregnancy is determined by maternal age and previous miscarriage history (95% confidence interval <20% in bold).

| Age (years) | Number of previous miscarriages | | | |
|-------------|---------------------------------|----|----|----|
| | 2 | 3 | 4 | 5 |
| 20 | 92 | 90 | 88 | 85 |
| 25 | 89 | 86 | 82 | 79 |
| 30 | 84 | 80 | 76 | 71 |
| 35 | 77 | 73 | 68 | 62 |
| 40 | 69 | 64 | 58 | 52 |
| 45 | 60 | 54 | 48 | 42 |

Hydatidiform mole pregnancies and partial mole would better replaced by the term gestational trophoblastic disease, complete or partial.

Future direction

The revision of early pregnancy nomenclature is both desirable and essential in raising the standard of reporting (Table 1.2). To improve the accuracy of observational studies it is desirable to present a clear and consistent description of the pregnancy event that can be universally understood by the reader. For randomized controlled trials of treatments, it is essential to have a clear classification of pregnancy loss type for both fetal and very early loss events. In addition, there is a strong argument for mandatory karyotyping of all pregnancy losses to exclude a lethal trisomy karyotype or triploidy. This is because, irrespective of treatment intervention, pregnancy loss has

Chapter 1 Early pregnancy – models of healthcare

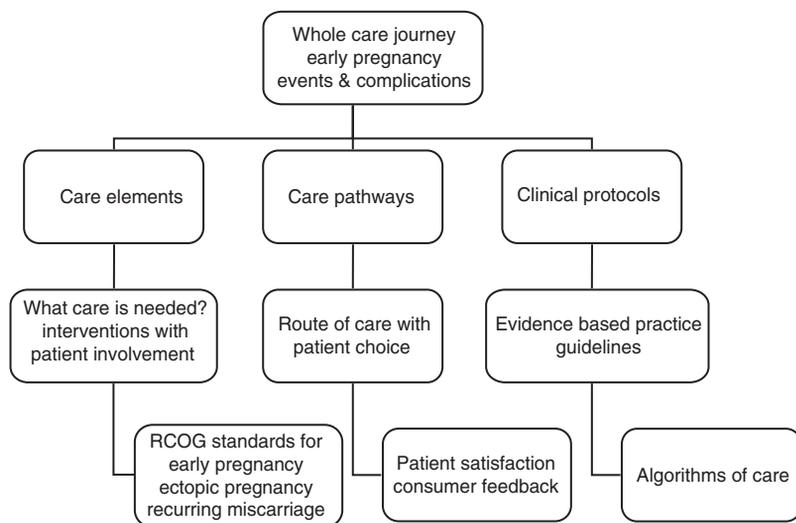


Figure 1.1 Overview of clinical model for early pregnancy.

occurred and may have been ascribed as a “false” treatment failure. Recent papers testify to the high rate of abnormal chromosome type when pregnancy loss has occurred [16,18,19]. By actuarial analysis, the success rate for the next pregnancy can be reasonably predicted based on maternal age and number of losses (Table 1.3) [3].

The authors understand that a modernized classification system is not able to address every clinical scenario but the adoption of a revised terminology [19] is a better way forward than persisting with an antiquated description that precedes the universal use of transvaginal ultrasound findings or hCG levels. High-resolution transvaginal ultrasound provides surveillance and reassurance for the majority of women.

Conclusions

- All women with early pregnancy complications should be evaluated in a dedicated early pregnancy unit (EPU).
- Management of patients should be conducted by trained and competent staff (Figure 1.1).
- Adequate facilities should exist to perform scans and for the measurement of hCG levels.
- Algorithms should be in place to guide management of spontaneous and recurrent miscarriage and ectopic pregnancy.
- Patients should be offered informed choice of management options.
- Patients should be furnished with written information in non-medical language.

- A quiet room conducive to breaking bad news should be located away from the work area.
- Bereavement counseling should be offered to all patients who suffer a pregnancy loss.
- Adherence to local and national standards should be audited regularly.

References

1. Robinson HP. The diagnosis of early pregnancy failure by sonar. *Br J Obst Gynaecol* 1975; **82**: 849–57.
2. Everett C. Incidence and outcome of bleeding before the 20th week of pregnancy: prospective study from general practice. *Br Med J* 1997; **315**: 32–4.
3. Brigham S, Conlon C, Farquharson RG. A longitudinal study of pregnancy outcome following idiopathic recurring miscarriage. *Hum Reprod* 1999; **14**: 2868–71.
4. Ugwumadu A, Manyonda I, Reid F, Hay P. Effect of early oral clindamycin on late miscarriage and preterm delivery in asymptomatic women with abnormal vaginal flora and bacterial vaginosis: a randomized controlled trial. *Lancet* 2003; **361**: 983–8.
5. Farquharson RG, Jauniaux E, Exalto N, ESHRE Special Interest Group for Early Pregnancy (SIGEP). Updated and revised nomenclature for description of early pregnancy events :consensus statement. *Hum Reprod* 2005; **20**: 3008–11.
6. Royal College of Obstetricians and Gynaecologists. The Management of Early Pregnancy Loss. 2006, Greentop Guideline No 25.

Chapter 1 Early pregnancy – models of healthcare

7. Twigg J, Moshy R, Walker JJ, Evans J. Early pregnancy assessment units in the United Kingdom: an audit of current clinical practice. *J Clin Excell* 2002; **4**: 391–402.
8. Lewis G (ed.). *The Confidential Enquiry into Maternal and Child Health (CEMACH). Saving Mother's Lives: Reviewing Maternal Deaths to make Motherhood Safer – 2003–2005. The Seventh Report on Confidential Enquiries into Maternal Deaths in the UK*. London: CEMACH, 2007.
9. Kirk E, Condous G, Bourne T. Ectopic pregnancy deaths: what should we be doing? *Hosp Med* 2004; **65**: 657–60.
10. O'Rahilly R, Muller F. Developmental stages in human embryos: revised and new measurements. *Cells Tissues Organs* 2010; Feb 26 [Epub ahead of print].
11. Pedersen JF. Fetal crown rump length measurement by ultrasound in normal pregnancy. *BJOG* 1982; **89**: 926–30.
12. Bottomley C, Bourne T. Dating and growth in the first trimester, best practice & research. *Clin Obst Gynaecol* 2009; doi: 10.1016/j.bpobgyn.2009.01.011.
13. Jauniaux E, Kaminopetros P, El-Rafaey H. Early pregnancy loss. In CH Rodeck, MJ Whittle (eds.), *Fetal Medicine*. Churchill Livingstone, 1999; 835–47.
14. Royal College of Radiologists/ Royal College of Obstetricians and Gynaecologists. *Guidance and Ultrasound Procedures in Early Pregnancy*. London: RCOG Press, 1995.
15. Chittacharoen A, Herabutya Y. Slow fetal heart rate may predict pregnancy outcome in first-trimester threatened abortion. *Fertil Steril* 2004; **82**: 227–9.
16. Hutchon DJ, Cooper S. Missed abortion versus delayed miscarriage. *Br J Obstet Gynaecol* 1997; **104**: 73.
17. Stirrat GM. Recurrent miscarriage: definition and epidemiology. *Lancet* 1990; **336**: 673–5.
18. Philipp T, Philipp K, Reiner A, Beer F, Kalousek DK. Embryoscopic and cytogenetic analysis of 233 missed abortions: factors involved in the pathogenesis of developmental defects of early failed pregnancies. *Hum Reprod* 2003; **18**: 1724–32.
19. Bricker L, Farquharson RG. Types of pregnancy loss in recurrent miscarriage: implications for research and clinical practice. *Hum Reprod* 2002; **17**: 1345–50.

Chapter

2

Risk factors for miscarriage

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What is a miscarriage and how common is it?

Miscarriage is the most common complication of early pregnancy. It is defined as the spontaneous end of a pregnancy at a time before fetal viability. In the UK the cut-off gestation defining a miscarriage is 24 weeks since the start of the last menstrual period (LMP). The death of a fetus at later gestations is referred to as a stillbirth.

Human reproduction is remarkably inefficient and only 30–50% of conceptions survive to a live birth (see Figure 2.1). Relatively little is known about embryo loss before the implantation stage (which happens around 20–23 days since LMP), but it is estimated from prospective studies of women attempting to conceive that around 1 in 3 pregnancies reaching the implantation stage will end in miscarriage [1–3]. The risk is strongly related to time since LMP, with around 25% of pregnancies ending in miscarriage between implantation and the 6th week since LMP [1–5]. Many of these early miscarriages go unnoticed because the woman may not know she is pregnant. After 6 weeks since LMP, the usual cut-off for defining a clinical pregnancy, recent epidemiological studies relying on self-report or linkage to clinical records find prevalences of 12–20% [6,7]. The vast majority of these occur between the 6th and 10th week since LMP, and in the second trimester of pregnancy (12–24 weeks since LMP) the likelihood of a pregnancy ending in miscarriage is only between 1 and 2%. Figure 2.1 illustrates how the risk of fetal loss varies by gestation.

The figures presented above describe the overall picture, and it is important to note that risk of miscarriage varies by individual maternal, paternal and fetal factors, which we summarize below. In this chapter we concentrate on risk factors for first-trimester miscarriage.

Why does miscarriage happen?

The causes of miscarriage are still not wholly understood. This is surprising given how common, and distressing, the event is. The main explanation for this is that miscarriage is very difficult to study: there are few clinical registers of miscarriage, and miscarriages are often not even recorded in medical notes. Large prospective cohort studies of pregnancy are theoretically the ideal epidemiological design [8], but these take a lot of organization, take time and are expensive. A practical approach, used in many studies, is to use self-reported information, not only on the event itself but also on the suspected risk factors. Population-based surveys which ask the women themselves for their full reproductive history, including fetal losses at all gestations and relevant information on behaviors and exposures, are useful and informative if conducted with care and with attention to limiting potential biases.

In this chapter we summarize the current literature on risk factors for first-trimester miscarriage. We will concentrate on biological, social and lifestyle factors and will include findings from the National Women's Health Study (NWHS), a large UK population-based study of early miscarriage which was planned and initiated by the authors [7,9].

Chromosomal abnormality in the fetus

There is good evidence that around a half of all miscarriages have some form of fetal chromosomal abnormality, with those ending at earlier gestations more likely to be affected than those ending later [10,11]. The largest single category of anomalies is autosomal trisomies, and molecular studies have shown that around 90% of these have their origin in maternal meiotic errors. Errors in paternal meiosis do occur and, for example, are responsible for 100% of monosomy X (Turner's syndrome) and around 50% of XXY

Chapter 2 Risk factors for miscarriage

(Klinefelter’s syndrome) cases, but these conditions are rarer and possibly also less likely to end in miscarriage than other conditions [11].

Maternal and paternal age

There is clear evidence that the risk of miscarriage increases with maternal age. Evidence from a large Danish study of over 1.2 million pregnancies, and from our UK study, shows a dramatic four-fold increase in risk between ages 20 and 40 [6,9] (see Figure 2.2). The risk of chromosomal anomaly is known to increase with maternal age, and this may explain much of the increase risk of miscarriage with advancing age. But it probably does not explain it all because there is some

evidence that miscarriages with normal karyotype also show a trend of increasing risk with maternal age [10]. Father’s age has also been shown to be related to increased risk of miscarriage, albeit less dramatically than for mother’s age [9,12,13].

Previous reproductive history of the mother

A previous history of miscarriage has been shown to be associated with an increased risk of miscarriage in the next pregnancy [14]. We looked at this in some detail in our own study [9], and found that having a miscarriage almost doubled the risk of miscarriage in

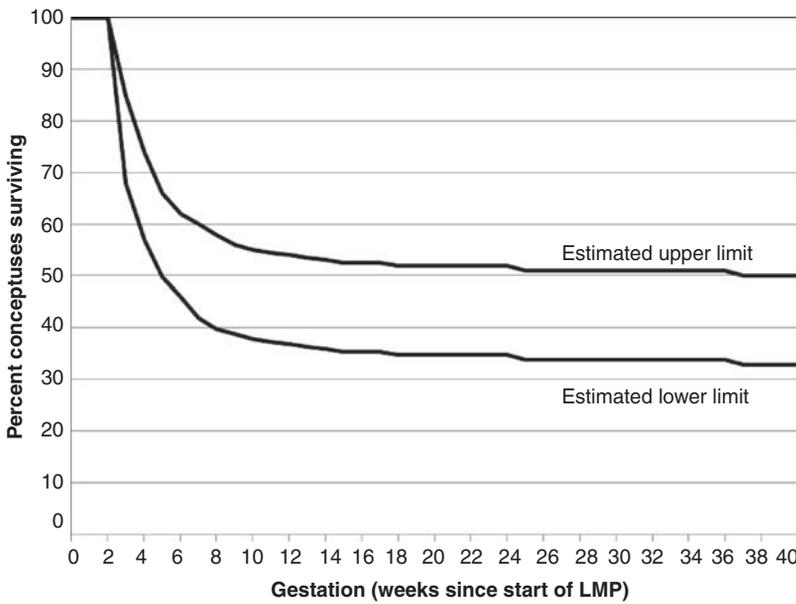


Figure 2.1 Estimated survival of human conceptions by gestation.

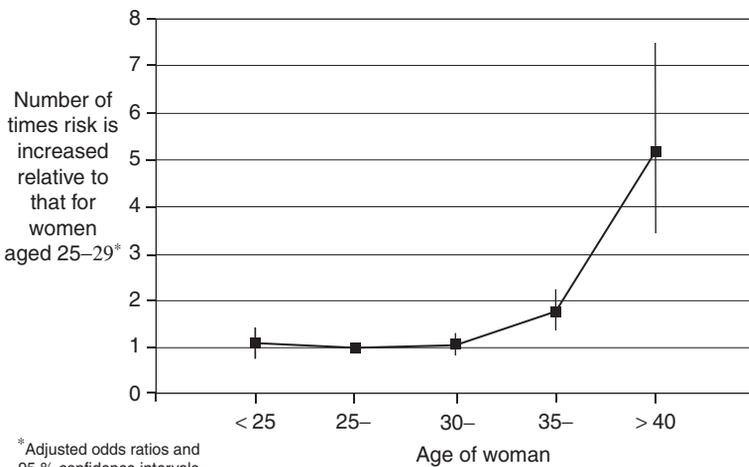


Figure 2.2 Association between miscarriage and maternal age within National Womens Health Study [9].

* Adjusted odds ratios and 95 % confidence intervals

Table 2.1 Summary of main findings from the National Women's Health Study [7].

| Factors associated with <i>increased risk of first-trimester miscarriage</i> | Factors associated with <i>decreased risk of first-trimester miscarriage</i> | <i>No evidence of association with risk of first-trimester miscarriage</i> |
|--|---|--|
| Socio-demographic factors Maternal age over 35 years Not living with the father of the baby Pre-pregnancy BMI Being underweight Obstetric factors Previous miscarriage Previous termination of pregnancy Longer time to conception Infertility problems, particularly tubal infertility Assisted conception Indicators of stress Being stressed or anxious Experiencing one or more stressful/traumatic events Having a stressful job Alcohol Regularly drinking alcohol High alcohol consumption Paternal factors Changing partners Paternal age over 45 years Other factors Bleeding during sexual intercourse | Obstetric factors Previous birth Nausea Vitamins and diet Taking vitamins (in particular folic acid, iron and multivitamins) Eating fresh fruit and vegetables daily Eating dairy products daily Eating chocolate daily (Possibly eating white meat and fish twice weekly or more) Indicators of wellbeing Feeling happy and relaxed Planned pregnancy Air travel Sexual intercourse (no bleeding) | Socio-demographic factors Social class Education Obstetric factors Pregnancy order (after accounting for previous pregnancy outcome) Short pregnancy interval Pre-eclampsia in previous pregnancies Work Full-time work Sitting or standing for 6 hours or more per day at work Lifting heavy objects or people at work Diet Eating red meat, eggs, soya products and sugar substitutes Caffeine consumption (after accounting for nausea) Smoking and alcohol Smoking Moderate and occasional alcohol consumption (after accounting for nausea) Exercise Strenuous exercise Paternal smoking and alcohol Paternal pre-conceptual alcohol Paternal pre-conceptual smoking (and during the first 12 weeks) |

subsequent pregnancies, with the risk increasing with each additional miscarriage. By contrast, having a live birth reduced the risk of miscarriage in subsequent pregnancies by around 40% (see Table 2.1).

Although these findings may seem alarming, it is important to consider them in the context of the overall experience of women. Of the women aged 35 and over in this survey, one in six had experienced one miscarriage, one in 25 had experienced two miscarriages, and only one in 70 had experienced three or more miscarriages over their lives [9]. These data indicate that recurrent miscarriage, although a devastating outcome for women, is rare. The topic of recurrent miscarriage will be covered in more detail in a separate chapter.

There is some evidence that having a previous termination for non-medical reasons appears to increase the risk of subsequent miscarriage [9,15], although the evidence strongly suggests that this is only for surgical procedures, and not for medical procedures [16,17].

There is a strong relationship between infertility and miscarriage. The loss of an embryo before or just after implantation is probably very common, and the effect will be an apparent inability to become pregnant [18]. In our study, the risk of miscarriage was

strongly associated with indicators of subfertility, such as time taken to conceive or having a fertility problem diagnosed. For example, those who had taken over a year to conceive had more than double the risk of those who took less than 3 months to conceive. We also found an increased risk of miscarriage if the pregnancy had been conceived following treatment for infertility [9] (see Table 2.1).

Socio-economic status

Studies have shown that risk of miscarriage varies by socio-economic position, but the trends are unclear [19] and most probably relate to exposure to environmental, occupational or behavioral risk factors [20] which we explore further in the sections below. In the NWHS we did not find any clear evidence of an effect of social class on risk, either when measured by the husband/partner's occupation or by the woman's own. There was, however, some suggestion of a shallow increasing trend in risk with increasing educational attainment, the opposite trend to that predicted. Interestingly, the risk of miscarriage was increased by around 73% if the couple were not married or living together, compared with those who were married or living together [9].