

Updated and revised nomenclature for description of early pregnancy events

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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' and 'blighted ovum', which have persisted since their introduction many years ago (Robinson, 1975) 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. We hope that this paper will facilitate the introduction of a revised terminology in an attempt to provide clarity and to enhance uptake and use in the literature as well as clinical assessment and documentation.

Key words: early pregnancy/nomenclature

Introduction: recognizing the changes

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 (Everett, 1997). The great majority occurs early, before 12 weeks gestational age and fewer than 5% occur after identification of fetal heart activity (Brigham *et al.*, 1999). Second trimester loss, between 12 and 24 weeks, occurs less frequently and constitutes <4% of pregnancy outcomes (Ugwumadu *et al.*, 2003). The clinical assessment of every pregnancy loss history requires clarification of pregnancy loss type and accurate classification, whenever possible.

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. She may not realize that (spontaneous) abortion is not a termination of pregnancy because 'medical abortion' or 'legal abortion' is used in the same way.

Increasing knowledge about early pregnancy development, with the more widespread availability of serum β HCG measurement, the advent of high-resolution ultrasound and a clearer description of gestational age at pregnancy loss make for a more sophisticated assessment of miscarriage history but also help the couple's awareness from as early as 5 weeks of gestation. The advent of these important information milestones has not

been fully realized or incorporated into clinical event description for article publication.

The emergence of early pregnancy units (EPUs) in many hospitals has addressed the need for a dedicated clinical area for the diagnosis of miscarriage and patient support at a distressing time (Twigg *et al.*, 2002). 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 conclusively demonstrates that mortality from ectopic pregnancy has not declined and is still increasing over and above rates described 10 years ago (CEMACH Report, 2004). 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 (Kirk *et al.*, 2004).

Duration of pregnancy

Just as postnatal age begins at birth, prenatal age begins at fertilization. The embryonic period occupies the first 8 post-fertilization 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

(O’Rahilly and Muller, 2000). Clinicians, however, conventionally calculate from the first day of the last normal menstrual period (LMP). Confusion about the definition of pregnancy duration derives from the use in the published literature of terms such as ‘postovulatory age’ and ‘conceptual age’, and even misnomers like ‘menstrual age’.

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 by using a proper definition. The appropriate way to overcome this confusion is to choose GA based on a theoretical ovulation plus 2 weeks. As early ultrasound measurements of the fetus (crown–rump length, CRL) are reproducible (Pedersen, 1982) and more accurate than the use of the LMP, there is a need in publications to define GA based on LMP and/or ultrasound measurements.

The terms ‘egg’ and ‘ovum’, sometimes used in clinical publications, should be avoided because they have also been used incorrectly for both an oocyte and an embryo (O’Rahilly, 1986). This author suggested that the term ‘egg’ be reserved for a ‘nutritive object’ only. Similarly, the use of the term ‘embryo’ versus ‘fetus’ is confusing as infertility specialists use ‘embryo’ in the preimplantation period while anatomists use ‘embryo’ until 8 weeks after implantation.

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 (Jauniaux *et al.*, 1999). However, there are limits to ultrasound resolution of normal early pregnancy development. Recent advice concludes that a 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 (Royal College of Radiologists/Royal College of Obstetricians and Gynaecologists, 1995). 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 (Chittachoen *et al.*, 2004). 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’ (Hutchon and Cooper, 1997).

Gynaecologists and ultrasonographers acknowledge the ‘embryonic’ period by speaking about ‘fetal heart action’ and ‘fetal activity’ before the end of organogenesis. This evidence is vital to the patient, who sees them as clear signs of life. Embryologists, by contrast, may debate the meaning of ‘embryo’ in early pregnancy, but ‘embryo’ is more synonymous

with cells in an IVF laboratory than as the preclinical scientific description of anatomical 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, in which description has changed in the last two decades and is more patient-centred. The term ‘fetus’ receives an ultrasound definition that includes 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 and detail the event; for example, in the case of fetal demise at 8 weeks, to 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) (Stirrat, 1990). 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 (Stirrat, 1990), 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 placentation, as well as factors which may be embryopathic.

The absence of an identifiable pregnancy on ultrasound examination in combination with a positive urine or serum 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. ‘Hydatidiform mole pregnancy’ and ‘partial mole’ would be better replaced by ‘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 I). 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

Table I. Glossary of terms and early pregnancy events

| Avoid | Prefer | Ultrasound findings |
|---|--|--|
| Egg Embryo | Oocyte Fetus | Ultrasound-based definition to include fetal heart activity and/or crown–rump length >10 mm |
| Embryonic age Postovulatory age Conceptual age Menstrual age | Gestational age based on last menstrual period and/or ultrasound fetal measurement | |
| Threatened abortion Spontaneous abortion Medical abortion Legal abortion | Threatened miscarriage Spontaneous miscarriage Termination of pregnancy | |
| Recurrent abortion Habitual abortion Pregnancy test Preclinical embryo loss | Recurrent miscarriage consisting of 3 early consecutive losses or 2 late pregnancy losses Serum/urine level of HCG Biochemical pregnancy loss with description of falling low positive serum/urinary HCG | No definition of pregnancy location |
| Trophoblast regression Menstrual abortion/preclinical abortion Early embryonic demise Anembryonic pregnancy Embryonic death | Biochemical pregnancy loss Biochemical pregnancy loss Empty sac | Pregnancy not located on scan Gestation sac with absent structures or minimal embryonic debris without heart rate activity Previous identification of crown–rump length and fetal heart activity followed by loss of heart activity |
| 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. Same as for early pregnancy loss (see above) After 12 weeks gestational age where fetal measurement was followed by loss of fetal heart activity |
| Missed abortion Late abortion | Delayed miscarriage Late pregnancy loss | |
| Hydatidiform mole Partial mole Molar pregnancy | Gestational trophoblastic disease (complete or partial) Heterotopic pregnancy Pregnancy of unknown location (PUL) | Intrauterine plus ectopic pregnancy (e.g. tubal, ceryical, ovarian, abdominal) No identifiable pregnancy on ultrasound with positive blood/urine HCG |

Table II. Overview of commonest pregnancy loss events and ultrasound

| Type of loss | Typical gestation (range in weeks) | Fetal heart activity | Principal ultrasound finding | β 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 |

lethal trisomy karyotype or triploidy. This is because, irrespective of treatment intervention, pregnancy loss has occurred and may have been described as a ‘false’ treatment failure. Recent papers testify to the high rate of abnormal chromosome type when pregnancy loss has occurred (Bricker and Farquharson, 2002; Levine *et al.*, 2002; Stephenson *et al.*, 2002; Philip *et al.*, 2003; Morikawa *et al.*, 2004).

The authors understand that a modernized classification system is not able to address every clinical scenario, but the adoption of a revised terminology is a better way forward than persisting with an antiquated description that precedes the universal use of transvaginal ultrasound findings or serum HCG levels, (Table II).

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