

The vanishing twin: a review

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This article reviews the scientific literature discussing the vanishing twin phenomenon. Information pertaining to frequency, aetiology, and potential complications, as well as the impact of sonographic technology on our growing understanding of the events in early multiple pregnancy is provided.

Key words: first trimester/multiple gestation/pregnancy/resorption

Introduction

Stoeckel (1945) was the first to suggest that the conception rate of multiple gestations was greater than the birth rate: 'It thus appears that twins are more often conceived than born; not only in addition to the evidence of foeti papyracei, it may be that twin material is reabsorbed due to early death, without leaving any trace.'

Four decades later, the clinical application of ultrasound enabled visualization and confirmation of this event, now characterized as the 'vanishing twin' phenomenon. The continuing refinements and the broad use of sonography in early pregnancy have helped to confirm that what was once considered extraordinary is, in reality, a relatively frequent event.

In 1982, when we reviewed the world literature on the vanishing twin phenomenon (Landy *et al.*, 1982), only nine papers had been cited (Hellman *et al.*, 1973; Kohorn and Kaufman, 1974; Levi, 1976; Robinson and Caines, 1977;

Levi and Reimers, 1978; Finberg and Birnholz, 1979; Kurjak and Latin, 1979; Varma, 1979; Jeanty *et al.*, 1981). Since that time, the number of scientific papers about pregnancy loss in multifetal gestations in humans and animals has increased dramatically, assisted in no large part by steady developments in both sonographic and assisted reproductive technologies.

Diagnosis and frequency

Boklage (1995) recently put the vanishing twin phenomenon in perspective when he noted: 'The loss of one member of a twin pair can be understood quite simply as part of the highly imperfect biology of human reproduction. Most human conceptions fail before birth. It is no different and no more mysterious for twins ...' Although the precise mechanisms and pathophysiology are obscure, the process of early pregnancy disappearance appears to involve resorption and/or formation of a blighted ovum. When fetal death occurs beyond the first trimester, a fetus papyraceus may develop (Posner and Klein, 1954). The true incidence of vanishing concepti is difficult to assess. Reported frequencies range from 3.7 to 100%; however, these discrepant values reflect varying patient populations, sonographic criteria and methods, and outcome data (Figure 1). A better prognosis is seen in women under 30 years of age (Dickey *et al.*, 1990).

In the early years of sonography, interpretative and/or artefactual error may have exaggerated the true incidence of the vanishing twin phenomenon. Even with better technology, it is still important not to misinterpret as additional gestational sacs either normal early embryonic structures, such as the amniotic cavity, chorionic sac, yolk sac and extraembryonic coelom (Landy *et al.*, 1986), or other physiological conditions such as subchorionic haemorrhage or hydropic change in chorionic villi (Nakano *et al.*, 1981) or a decidual reaction in the second horn of a bicornuate uterus (Jeanty *et al.*, 1981). In some earlier reports, it is likely that subchorionic collections of fluid were misinterpreted as extra gestational sacs. Since

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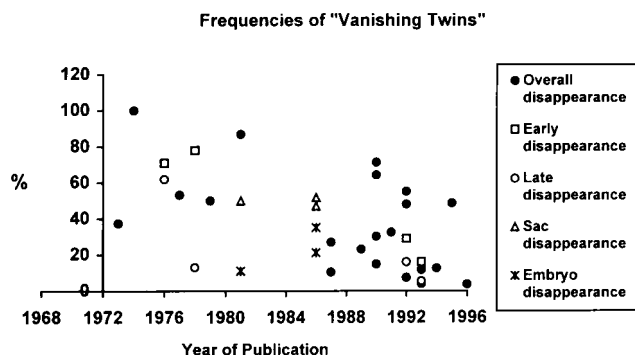


Figure 1. Disappearance of concepti; values are either published or calculated from citations (Hellman *et al.*, 1973; Kohorn and Kaufman, 1974; Levi, 1976; Robinson *et al.*, 1977; Levi *et al.*, 1978; Schneider *et al.*, 1979; Jeanty *et al.*, 1981; Nakano *et al.*, 1981; Landy *et al.*, 1986; Steptoe *et al.*, 1986; Belfrage, *et al.*, 1987; Meldrum *et al.*, 1987; Gerds, 1989; Bateman *et al.*, 1990; Dickey *et al.*, 1990; Hershlag *et al.*, 1990; Nakamura *et al.*, 1990; Kelly *et al.*, 1991; Blumenfeld *et al.*, 1992; Sampson and de Crespigny, 1992; Seoud *et al.*, 1992; Benson *et al.*, 1993, 1994; Botchan *et al.*, 1993; Kol *et al.*, 1993; Manzur *et al.*, 1995; Haning *et al.*, 1996).

subchorionic haemorrhage can be identified in up to 50% of frequently scanned patients in early pregnancy (Dickey *et al.*, 1992a), interpretive errors of this phenomenon may have been responsible for some reports of high rates of resorption (Dickey, *et al.*, 1992b).

Since 1987, transvaginal sonography has provided detailed information regarding early resorption in multiple gestations. The majority of pertinent studies published since 1990 involve predominant use of transvaginal sonography or a combination of both transvaginal and transabdominal approaches, and describe pregnancies usually conceived as a result of assisted reproductive techniques (Table I). Based on combined statistics from most studies outlined in Table I, frequencies of pregnancy resorption in the first trimester can be determined in assisted reproductive techniques versus spontaneous conceptions when early sonography demonstrates two sacs (Figure 2A) or two embryos (Figure 2B). Caution should be used in interpretation, given that (i) there are relatively low numbers of spontaneous conceptions from which these data are derived compared to study patients with pregnancies achieved after assisted reproductive treatment; and (ii) many patients with spontaneous conceptions underwent early sonography because of vaginal bleeding or other high risk conditions, which may not apply to the general population. Using these data on twin gestations, if two sacs are identified sonographically, loss of one twin can be expected in 27.1% of pregnancies achieved after assisted

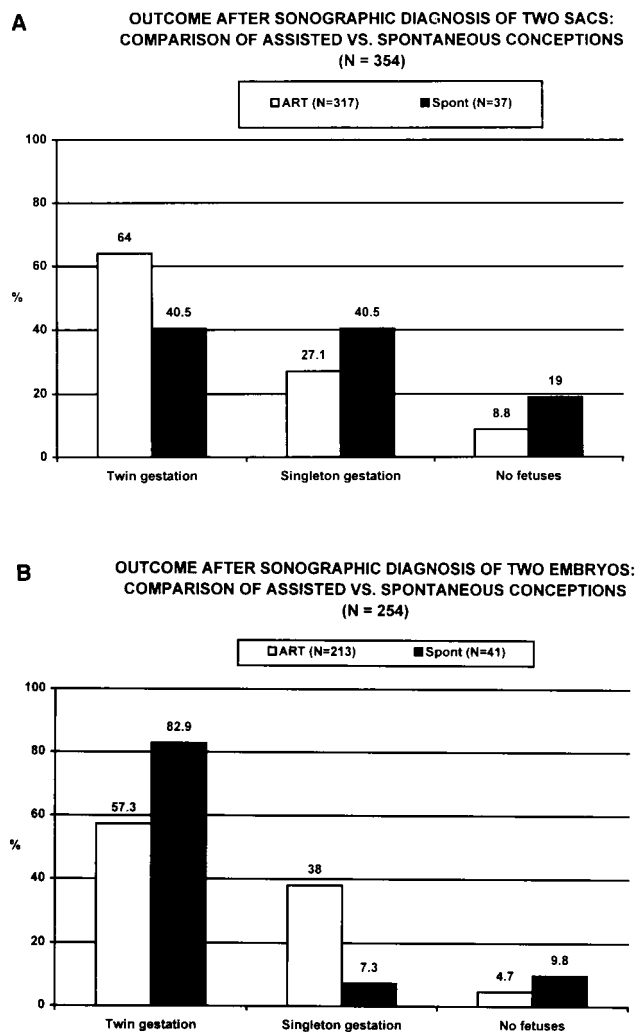


Figure 2. (A) Outcome beyond the first trimester in assisted versus spontaneous conceptions after the early sonographic diagnosis of two sacs. Data compiled from several studies (Dickey *et al.*, 1990; Kelly *et al.*, 1991; Blumenfeld *et al.*, 1992; Sampson and de Crespigny, 1992; Benson *et al.*, 1993; Botchan *et al.*, 1993; Kol *et al.*, 1993). (B) Outcome beyond the first trimester in assisted versus spontaneous conceptions after the early sonographic diagnosis of two embryos. Data compiled from several studies (Dickey *et al.*, 1990; Kelly *et al.*, 1991; Blumenfeld *et al.*, 1992; Benson *et al.*, 1993; Sampson and de Crespigny, 1992; Botchan *et al.*, 1993; Kol *et al.*, 1993). ART = assisted reproductive techniques; Spont = spontaneous conception.

reproduction and in 40.5% of spontaneous pregnancies; if two embryos are seen, the loss rate is 38% in pregnancies achieved after assisted reproduction and in 7.3% of spontaneous conceptions. The majority of pregnancies identified with twin sacs or embryos (~61%) continued as twin gestations whereas those with three sacs or embryos more frequently resulted in twin or singleton gestations.

Table I. Pertinent studies published since 1990 describing sonographic method, sonographic findings and patient population relative to spontaneous or assisted conceptions^a

Citation	Sonographic method (study period)	Sonographic findings	Patient population (n)
Bateman <i>et al.</i> , 1990	TV	2 or 3 sacs	ART (4) Spont (1)
Dickey <i>et al.</i> , 1990	TA (1976–87) TV (1987–90)	2, 3 or 4 sacs or embryos	ART (441) Spont (37)
Kelly <i>et al.</i> , 1991	TA (1985–86) TV (1987–89)	2 embryos	ART (40)
Blumenfeld <i>et al.</i> , 1992	TV	2, 3, 4 or 5 embryos	ART (88)
Sampson and de Crespigny, 1992	TV (<7 weeks) TA (≥7 weeks)	2 embryos	ART (67) Spont (59)
Kol <i>et al.</i> , 1993	TV	2, 3 or 4 embryos	ART (60)
Botchan <i>et al.</i> , 1993	TV	2, 3 or 4 sacs	ART (76)
Benson <i>et al.</i> , 1993	TA or TV (1987–90)	2 embryos	ART (27) Spont (41)
Benson <i>et al.</i> , 1994	TA or TV (1987–92)	2 embryos	ART (59) Spont (78)
Manzur <i>et al.</i> , 1995	TV	3 sacs or embryos	ART (38)

^aBateman *et al.*, 1990; Dickey *et al.*, 1990; Kelly *et al.*, 1991; Blumenfeld *et al.*, 1992; Sampson and de Crespigny, 1992; Benson *et al.*, 1993, 1994; Botchan *et al.*, 1993; Kol *et al.*, 1993; Manzur *et al.*, 1995.

TV = transvaginal; TA = transabdominal; ART = assisted reproductive techniques; Spont = spontaneous conception.

The data are more complete for twin gestations compared to pregnancies in which more than two sacs or embryos have been identified. Pregnancy outcome beyond the first trimester has been summarized for gestations with twins or triplets identified sonographically in Figures 3 and 4; there were too few patients with quadruplets or quintuplets to draw any meaningful conclusions. In compiling these data, late pregnancy information was not deemed to be pertinent given the high rates of preterm delivery for higher order multiples. As can be seen from these figures, overall data are similar for pregnancies in which either multiple sacs or embryos are identified sonographically.

Disappearance of sacs or embryos has been described throughout the first trimester, occurring more frequently earlier in time (Blumenfeld *et al.*, 1992; Sampson and de Crespigny, 1992; Benson *et al.*, 1993; Manzur *et al.*, 1995). Exact frequencies per given gestational week are not easy to extrapolate from the current literature. The study by Sampson and de Crespigny (1992) showed a 13% higher likelihood of live twin neonates resulting after a diagnosis of a viable twin gestation detected between 7 weeks and 8 weeks 6 days compared to before 7 weeks in in-vitro fertilization patients. Benson *et al.* (1993) found that the disappearance rate between 6 and 7.9 weeks of gestation was 21% for dichorionic and 50% for monochorionic twins compared to no spontaneous reductions from 8 to 13 weeks in both groups of patients. Similarly, in the report of triplet sacs and embryos by Manzur *et al.* (1995), almost 90% of resorptions occurred in the first 7 weeks of gestation. Spon-

taneous reduction has not been reported to occur beyond 13 weeks of gestation (Blumenfeld *et al.*, 1992; Manzur *et al.*, 1995).

Attempts to minimize interpretive error have led to the proposal that a true intrauterine gestational sac be identified using several sonographic characteristics. These include: (i) a double contour, (ii) identification of a yolk sac within the gestational sac, and (iii) recognition of an embryonic heart beat after 6 weeks of gestation (Blumenfeld *et al.*, 1992). Lack of adherence to such criteria may have contributed to the artefactual and erroneous overdiagnosis of multiple gestation in some early reports describing this condition (Defoort *et al.*, 1976); however, with today's sonographic improvements and the use of more strict diagnostic criteria, such errors should be minimal.

Complications and prognosis

Vaginal bleeding is a common obstetric complication in the first trimester, estimated to occur in 15–25% of all pregnancies and representing an increased risk of pregnancy loss (Stabile *et al.*, 1987; Falco *et al.*, 1996). It is not surprising, therefore, that vaginal bleeding or spotting is reported in association with disappearance of an embryo or a gestational sac. Although a wide range (7.8–76.5%) has been described in different populations (Varma, 1979; Jeanty *et al.*, 1981; Landy *et al.*, 1982, 1986; Gindoff *et al.*, 1986; Yoshida and Soma, 1986; Meldrum *et al.*, 1987; Stabile *et al.*, 1987; Saidi, 1988; Goldman *et al.*, 1989;

Jackson and Benirschke, 1989; Bateman *et al.*, 1990; Sampson and de Crespigny, 1992; Benson *et al.*, 1993, 1994; Gavril *et al.*, 1993; Yoshida, 1995), this is the only apparent complication described with disappearance. The clinical presentation of bleeding appears to coincide with the vanishing process. These data stress the importance of early sonography in the presence of first trimester bleeding.

The prognosis for continuing a pregnancy associated with the vanishing twin phenomenon is good, regardless of the chorionic status. Although some reports have linked twin death later in gestation with complications such as disseminated intravascular coagulation (Moore *et al.*, 1969) or brain damage in the surviving co-twin (Melnick, 1977; Rydhström and Ingemarsson, 1993; Okamura *et al.*, 1994), especially with monochorionic twins (Benirschke, 1961; Hoyme *et al.*, 1981; Szymonowicz *et al.*, 1986), such events have not been described in association with disappearance at this early stage in pregnancy. Benson *et al.* (1993) sought to differentiate between dichorionic and monochorionic gestations in both assisted and spontaneous conceptions. The relatively few monochorionic twin gestations (only nine) compared to 59 dichorionic twins makes accurate interpretation of the data difficult; this study, however, showed similar frequencies of spontaneous reduction to singleton gestations (12% of dichorionic and 11% of monochorionic twins) (Benson *et al.*, 1993).

Reliably predicting continued viability among twin gestations diagnosed early in pregnancy is difficult. A more accurate prognosis can be obtained, however, with later gestational ages and in the absence of abnormal sonographic findings, such as subchorionic haemorrhage, or with dichorionic rather than monochorionic twins (Benson *et al.*, 1993, 1994).

The sonographic identification of cardiac activity does not guarantee continuing fetal viability in multiple gestations. In one study, the rate of rise of serum human chorionic gonadotrophin concentrations was found to be a more reliable predictor of ongoing viability than fetal heart activity (Kelly *et al.*, 1991). Other data show that significant interfetal crown-rump length variability is associated with embryo disappearance (Kol *et al.*, 1993), aneuploidy or congenital anomalies (Weissman *et al.*, 1994). In an elaborate logistic regression analysis, Benson *et al.* (1994) found no prognostic effect of maternal age, spontaneous versus induced conception, or indication for sonographic evaluation. A bradycardic heart rate early in pregnancy, associated with impending embryonic death in singletons (Falco *et al.*, 1996), would be expected to have similar implications in multiple gestations.

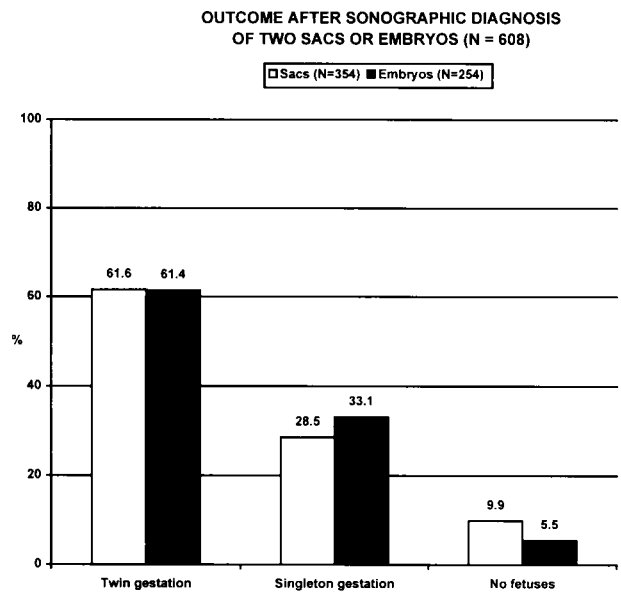


Figure 3. Outcome beyond the first trimester after the early sonographic diagnosis of two sacs or embryos. Data compiled from several studies (Dickey *et al.*, 1990; Kelly *et al.*, 1991; Sampson and de Crespigny, 1992; Blumenfeld *et al.*, 1992; Benson *et al.*, 1993; Botchan *et al.*, 1993; Kol *et al.*, 1993).

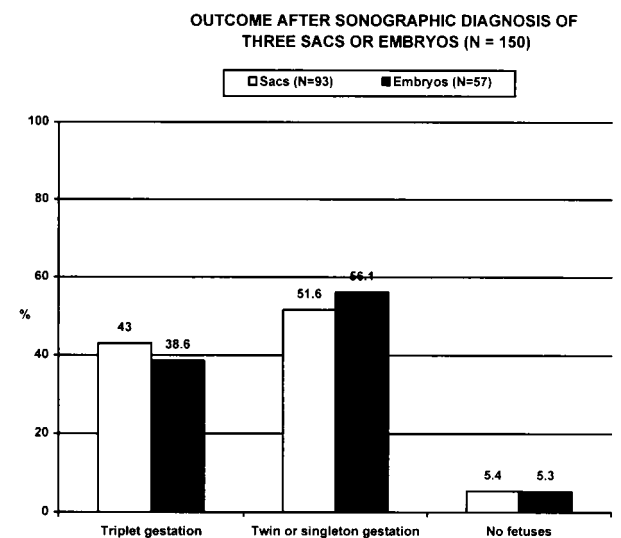


Figure 4. Outcome beyond the first trimester after the early sonographic diagnosis of three sacs or embryos. Data compiled from several studies (Dickey *et al.*, 1990; Blumenfeld *et al.*, 1992; Botchan *et al.*, 1993; Kol *et al.*, 1993; Manzur *et al.*, 1995).

Pathological considerations

Pathological confirmation of the vanishing twin has been well described. Finberg and Birnholz (1979) postulated

that a collection of old blood seen during pregnancy termination represented the sonographic finding of a second sac that had been adjacent to a viable gestation 6 weeks after the pathologically confirmed miscarriage of a 6 week fetus. Subsequent publications document more convincing histologic findings from the fetal surface of the placenta. These include reports of well-defined cysts or sacs (Levi and Reimers, 1978; Sulak and Dodson, 1986; Yoshida and Soma, 1986; Saidi, 1988; Callen *et al.*, 1991; Nerlich *et al.*, 1992), areas of degenerated chorionic villi (Sulak and Dodson, 1986; Rudnicki *et al.*, 1991), fibrin deposition or fibroid degeneration (Jauniaux *et al.*, 1988; Kapur *et al.*, 1991; Yoshida, 1995), placental nodules or plaques (Tharapel *et al.*, 1989; Falik-Borenstein *et al.*, 1994; Yoshida, 1995), embryonic remnants (Yoshida, 1995), and macerated or stunted embryos (Yoshida and Soma, 1986; Jauniaux *et al.*, 1988; Huter *et al.*, 1990; Blumenfeld *et al.*, 1992; Nerlich *et al.*, 1992).

The vanishing twin phenomenon has been used to explain discrepant chromosome results, first described by Tharapel *et al.* (1989). They postulated that trisomy 16 cells arose from residual villi belonging to a trisomic co-twin that never developed. Supportive evidence came from the cytogenetic analysis (46,XX/47,XX,+16 mosaicism) of a placental nodule identified at the time of delivery of a healthy infant. Since that report, in addition to trisomy 16 (Tharapel *et al.*, 1989; Post and Nijhuis, 1992), a similar aetiology has been suggested for other discordant karyotypic results, including trisomy 9 (Falik-Borenstein *et al.*, 1994), triploidy (Callen *et al.*, 1991), tetraploidy (Rudnicki *et al.*, 1991), and sex discrepancies (Reddy *et al.*, 1991; Association of Clinical Cytogeneticists, 1994).

It has also been proposed that the vanishing twin phenomenon may be responsible for some cases of isoimmunization developing during pregnancy in which a rhesus-positive fetus disappears in a previously unsensitized rhesus-negative mother (Landy *et al.*, 1986).

First trimester sonography of multifetal pregnancies

Routine sonographic assessment of early pregnancy has provided a clearer understanding of the complexities involved in the development of multifetal pregnancy. Thus, it is now understood that the frequency of human multiple pregnancy is far greater than suggested in reports published prior to 1970. Clinical frequencies range from 0.9 to 9.5% (Figure 5), with mathematical estimates that between 12 and 15% of all live births arise from twin embryogenesis: "[M]ore than one pregnancy in eight begins as twins, and

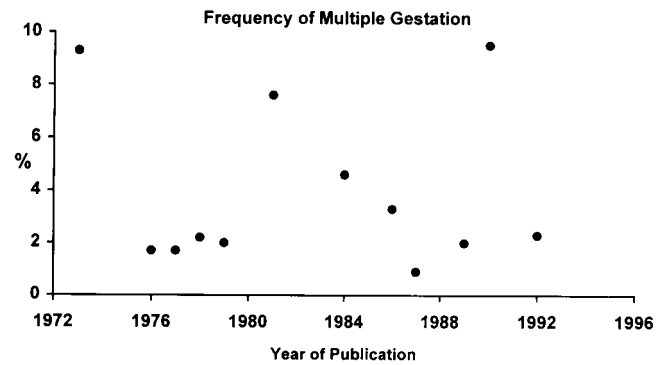


Figure 5. Range of frequency of human multiple gestation based on first trimester sonography; figures are either published or calculated from citations (Hellman *et al.*, 1973; Levi, 1976; Robinson and Caines, 1977; Levi and Reimers, 1978; Varma, 1979; Jeanty *et al.*, 1981; Kohorn and Kaufman, 1984; Landy *et al.*, 1986; Belfrage *et al.*, 1987; Gerds, 1989; Bateman *et al.*, 1990; Blumenfeld *et al.*, 1992).

that, for every liveborn twin pair, 10–12 twin pregnancies result in single births” (Boklage, 1995).

No discussion on the vanishing twin would be complete without commentary on the process of induced multifetal pregnancy reduction. During this procedure, the total number of fetuses in a multiple pregnancy, typically triplets or higher, is reduced by a transvaginal or transabdominal procedure in order to enhance potential survival of the remaining fetus(es). In a strict sense, this operation could be construed as an example of man attempting to imitate nature. Counselling patients about the difficult issues surrounding multifetal pregnancy reduction must also include appropriate data about the naturally occurring vanishing twin phenomenon, especially regarding proper timing of the procedure. Spontaneous resorption, more likely to occur earlier in gestation, may partially or totally obviate the need for the reduction in some cases (Berkowitz *et al.*, 1996). Given the low chance of spontaneous embryo disappearance later in the first trimester, however, most procedures are performed at 10–13 weeks (Berkowitz *et al.*, 1996).

Conclusions

The disappearance of gestational sacs or embryos after documented fetal heart activity in multiple pregnancies is not unusual. When it occurs, the process is known as the vanishing twin phenomenon. Among pregnancies with twin sacs or embryos, ~30% will ultimately result in singletons and <10% will result in no fetuses. Because of the potential association with vaginal bleeding at the time of disappearance, detailed sonography is recommended to follow progression of the vanishing process and to confirm

viability and continued growth in the remaining fetus(es). After delivery, careful evaluation of the placenta and membranes may confirm earlier sonographic findings.

As technology advances, the routine surveillance of early pregnancy will continue to provide a more complete understanding of fetal development and the relationship of early pregnancy wastage as it pertains to the evolutionary process and to human survival.

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