

## REVIEW

# Managing twins discordant for fetal anomaly

M. A. Rustico, M. G. Baietti, D. Coviello, E. Orlandi and U. Nicolini\*

*University of Milano, Department of Obstetrics and Gynaecology, Ospedale V. Buzzi, Milano, Italy*

An excess of structural anomalies is observed in twins compared to singletons. Approximately 1–2% of twin pregnancies may face the dilemma of expectant management versus selective termination following diagnosis of an anomaly affecting only one fetus. If the option of selective fetocide is considered, the main variable determining the technique to achieve this aim is chorionicity. In a dichorionic pregnancy, passage of substances from one twin into the circulation of the co-twin is unlikely due to the lack of placental anastomoses, hence KCl can be injected safely into the circulation of the affected twin to produce fetal asystole. In monochorionic twin pregnancies, selective termination needs to be performed by ensuring complete and permanent occlusion of both the arterial and venous flows in the umbilical cord of the affected twin, in order to avoid acute haemorrhage from the co-twin into the dying fetus, which may lead to death or organ damage. Bipolar cord coagulation under ultrasound guidance is associated with approximately 70–80% survival rates. Copyright © 2005 John Wiley & Sons, Ltd.

KEY WORDS: twins; fetocide; fetal malformations

## BACKGROUND

Without interference of assisted reproduction techniques, two thirds of spontaneous twin pregnancies are dizygotic (DZ), resulting from the fertilization of two eggs by different spermatozoa, and are therefore dichorionic (DC). The other third are monozygotic (MZ), occurring when one single fertilized egg gives rise to two separate embryos. Of these MZ pregnancies, a third are DC, with separate or fused placentas in which vascular communications are almost totally absent. The other two thirds of MZ twin pregnancies are monochorionic (MC). Here, division takes place later, after the chorion has formed. Hence there is only one placenta serving both embryos, with vascular communications connecting the twins (Benirschke and Kaufmann, 2000).

Many aspects of multiple pregnancies are influenced by chorionicity, and especially in the management of discordant anomaly, this is a crucial element.

## FETAL ANOMALIES IN TWINS

An excess of structural anomalies is observed in twins compared to singletons (Mastroiacovo *et al.*, 1999). However, the frequency of malformations in dizygotic (DZ) twins is thought to be similar to that of singletons (2–3%), while it has been reported to be two to three times higher in monozygotic (MZ) pairs, although the true incidence is difficult to assess since most studies failed to determine zygosity, and some assumed dizygosity in the presence of a discordant anomaly. These anomalies include malformations of the midline (conjoined twins, acardiac twin) that are part of the twinning process, neural tube defects, facial clefts, cloacal and abdominal wall anomalies,

and limb reduction defects (Hall, 2003; Mohammed *et al.*, 2004). Structural heart malformations in MZ twins without twin–twin transfusion syndrome are four times more common than in the general population (Karatzas *et al.*, 2002).

Structural malformations that are not genetically determined may obviously occur in only one of MZ twin pairs. Overall, it has been estimated that in approximately 15% of cases both twins are affected by one structural anomaly, whilst in the majority of cases only one twin is affected (Bryan *et al.*, 1987).

It would seem that a critical mass of cells is necessary for normal development and differentiation and that unequal allocation of blastomeres to the two embryos may be responsible for the mechanism of discordance and the excess of malformations in MZ twins (Machin, 1996). Some forms of discordance may also be explained by the single monochorionic (MC) placenta with the potential for unequal sharing of venous return from the placenta parenchyma (Gringas and Chen, 2001; Singh *et al.*, 2002).

Although MZ twins are thought to be genetically identical, more recent observations have found that this is not the rule and a number of discordances have been noted in MZ twins for chromosomal anomalies (Nieuwint *et al.*, 1999), single gene disorders (Shotelersuk *et al.*, 1999), mitochondrial diseases, and genomic imprinting defects (Gringas and Chen, 2001). The most frequently reported heterokaryotypia is the discordance for Turner syndrome (Gilbert *et al.*, 2002), which may be a consequence of an early postzygotic error, whereas MZ discordancy for trisomy 21 (Rogers *et al.*, 1982) and Klinefelter syndrome have been described but are probably uncommon. Discordance in phenotypic expression of X-linked diseases (examples reported include fragile-X syndrome, Aicardi's syndrome, Duchenne muscular dystrophy) in female MZ twins has been suggested as resulting from skewed X-chromosome inactivation (Goodship *et al.*, 1996).

\*Correspondence to: U. Nicolini, U. O. Ostetricia e Ginecologia, Ospedale V. Buzzi, via Castelvetro 32, 20154 Milano, Italy.  
E-mail: umberto.nicolini@unimi.it

Heterokaryotypic MZ twins, although extremely rare, should be considered in the presence of an associated discordant structural anomaly that would mandate the sampling of both fetuses (Jenkins and Wapner, 2000). Since all MC twins are MZ, most often they have the same karyotype, and the risk of chromosomal abnormalities approximates to the maternal age risk of a singleton. In a DZ pregnancy, each fetus presents an independent risk of aneuploidy, thus the pregnancy has approximately twice the risk of an affected fetus compared to singletons (Rodis *et al.*, 1990).

## TECHNIQUES FOR SELECTIVE FETOCIDE

### Dichorionic twins

In a dichorionic (DC) pregnancy, the passage of substances from one twin into the circulation of the co-twin is unlikely to be due to the lack of placental anastomoses; hence any drug that is able to produce fetal asystole can be injected safely into the circulation of the affected twin.

Selective fetocide was initially performed by fetoscopy and the injection of filtered air into an umbilical vessel of the affected twin (Rodeck *et al.*, 1982). Ultrasonic guided injection of potassium chloride (KCl) into the fetal heart, or, less frequently, into the umbilical cord, is now a well-established procedure, technically successful in almost 100% of reported cases.

The first step is to identify precisely the anomalous fetus by ultrasound detection of the structural anomaly, by discordant gender, or by previously documented placental location at the time of prenatal diagnosis. A description of which fetus is abnormal may be difficult in the presence of a chromosomal anomaly in like-sex twins with minor anatomical anomalies. This underlines the importance of the rigorous documentation of fetal and placental position when prenatal procedures are first performed. The procedure involves a transabdominal injection of KCl (usually at the concentration of 2 N) into the fetal heart, under ultrasound control. The left ventricle or atrium is the ideal target, since KCl immediately enters the coronary arteries. The needle is left in place until fetal asystole is observed for at least 2 min. The patient should be scanned again half an hour later to confirm fetal death. In the study conducted by Evans *et al.* (1994), 2 mL of KCl was needed for cases treated before 16 weeks' gestation, and 3–5 mL later in pregnancy. Evans *et al.* (1994) first published a multicenter study that included 183 cases of selective fetocide in DC pregnancies: fetal loss rate before 24 weeks was 8.3% with KCl, and 41.7% with air embolization; hence injection of KCl has become the standard technique. A subsequent collaborative study of 402 cases reported a 7.5% fetal loss rate before 24 weeks' gestation in twins (Evans *et al.*, 1999; see also Evans *et al.* this issue).

Since the fetus is thought to perceive pain from 26 weeks onwards (Smith *et al.*, 2000), adequate intra-operative fetal pain management could be considered. Senat *et al.* (2002) studied 10 women undergoing termination of pregnancy (between 32 and 38 weeks'

gestation) by umbilical vein injection of 5 µg sufentanil followed by 2 g KCl, avoiding the cardiac route. They did not observe any maternal electrocardiographic modifications, and maternal potassium levels did not vary following the procedure, supporting the view that fetal analgesia and fetocide via the umbilical vein is a safe procedure.

A comparative study including 106 women undergoing fetocide by administration of 15% KCl into the fetal heart or into the umbilical cord demonstrated that both routes can be used to achieve fetal asystole without compromising maternal safety (Bhide *et al.*, 2002).

### Monochorionic twins

The presence of placental anastomoses does not allow the injection of any lethal agent to achieve selective fetocide in MC twin pregnancies. In fact, the injected drug may leak into the unaffected twin's circulation causing death directly, or acute hemorrhage from the co-twin into the dying fetus may lead to death or organ damage (Nicolini and Poblete, 1999). The angio-architecture of the MC placenta thus needs a technique that is able to occlude completely and permanently both the arterial and venous flows in the umbilical cord of the affected twin.

There is still considerable debate over which method is the best for achieving this aim. All the techniques adopted so far have been used more frequently in the management of those disorders that commonly complicate MC pregnancies, such as twin-to-twin transfusion syndrome (TTTS) and twin reversed arterial perfusion sequence (TRAP), but less frequently in cases of a discordant anomaly.

One of the first techniques reported was the embolization of the umbilical cord using sclerosant agents (absolute alcohol, coils, embucilate gel), which can be easily injected via a standard 20-gauge needle. This technique is indeed effective for vascular occlusion in other branches of medicine. Now these are only of historical interest since the failure rate exceeds 70% because of the incomplete occlusion of the cord, or migration of the sclerosant agent to the co-twin (Denbow *et al.*, 1999).

Umbilical cord ligation by fetoscopy has the potential advantage of allowing simultaneous occlusion of all cord vessels. In the initial 23 published individual cases, only two technical failures occurred because of hemorrhage and poor visualization of the cord, and the survival rate was 71% (Challis *et al.*, 1999; Deprest *et al.*, 1998). However, 40% of women experienced premature rupture of membranes, the majority of which occurred before 32 weeks' gestation, probably resulting from the complexity of the procedure and the long operative time.

Alternatively, laser coagulation of the umbilical cord has been carried out as early as 16 weeks' gestation using a similar approach as for laser ablation of anastomoses in TTTS patients, but using a 1 mm fetoscope. After the cord of the affected fetus is visualized, the vessels are coagulated by a 400 µm laser fibre (Hecher *et al.*, 1997) (Figure 1). This procedure has some limitations, since it is ineffective in oedematous cords or at advanced gestational ages because these variables

reduce the optimal laser performance. Preterm labor and rupture of the membranes, along with vessel perforation are possible risks of the procedure.

Although probably not applicable in discordant MC twin pregnancies, interstitial laser has been used in selected cases complicated by TRAP sequence early on in pregnancy. Under ultrasound surveillance, a 17-gauge needle is inserted close to the vascular structures into the fetal abdomen, avoiding the risk of perforation of the umbilical cord, and a laser fibre is passed down with the aim of coagulating the tissue until the blood flow stops (Jolly *et al.*, 2001).

Monopolar thermocoagulation is very similar, involving insertion of the needle into the fetus (or into the umbilical cord later in pregnancy), and has been adopted in cases complicated by TRAP sequence early in gestation (Holmes *et al.*, 2001; Rodeck *et al.*, 1998). The survival rate is over 70%, but some failures have been described, particularly in cases complicated by TTTS.

A new technique, recently reported in 13 acardiac twins (Tsao *et al.*, 2002) and in one case of MC twins discordant for fetal anomalies (Shevell *et al.*, 2004), uses high-energy radio waves to induce coagulation. The radiofrequency device, first used in medicine to treat liver lesions, is inserted through a 14-gauge needle under ultrasound control, in direct contact with the umbilical cord or intrafetal vessels, avoiding injuring the co-twin.

A review of the literature analyzing pregnancy outcome using different modalities of occlusion of vascular supply in 74 acardiac twins reported that the intrafetal approach (performed in 31 cases by various techniques including interstitial laser) seems to be simpler, safer, and more effective when compared with occlusion cord techniques (Tan and Sepulveda, 2003).

Bipolar coagulation of the umbilical cord is probably the commonest technique used to perform selective fetocide in MC twin pregnancies complicated by disorders other than the TRAP sequence. The procedure can be carried out under ultrasound control, without direct fetoscopic visualization of the cord, using 2–3 mm bipolar forceps, which is inserted through an adapted cannula. It takes less time, can be carried out through a single port, and can also be performed successfully late

in pregnancy. Coagulation is done at power settings of 50 W applied for 10 to 30 s, and is repeated until the color Doppler confirms the absence of flow (Nicolini *et al.*, 2001) (Figure 2). Our experience comprises a series of 66 consecutive cases treated by this technique (61 twin pregnancies and 5 sets of triplets). In 34 cases (30 twin pregnancies, 4 sets of triplets) the procedure was carried out for TTTS, in six cases for TRAP sequence, in five cases for severe growth discordance, and in 21 cases for discordant chromosomal or structural anomaly (one of which was a triplet pregnancy).

Table 1 shows the characteristics of the pregnancies with discordant anomaly. Mean gestational age at the time of the procedure was 21 weeks (range 18–24 weeks), and mean gestational age at delivery was 32 weeks (range 19–41). The incidence of PROM within 3 weeks of the procedure was 14.3% (3/21), while in a further case PROM occurred 5 weeks after the procedure; another case was complicated by preterm delivery 4 weeks after cord coagulation. There were two fetal deaths within 24 h; one fetus of MC monoamniotic pregnancy died after 1 week. One newborn died in the neonatal period of sepsis. The median interval from procedure to delivery was 11 weeks (range 0–19 weeks). In twin pregnancies, the survival rate was 70% (14/20). Lewi *et al.* (2003) reported a survival rate of 78% in a series of 50 consecutive cord occlusions performed by laser or bipolar cord coagulation for various indications.

A multicenter study was conducted to test the feasibility of the fetoscopic approach in triplet pregnancies by cord occlusion or laser coagulation in five cases of complicated MC pregnancies (one with discordant anomaly) and seven cases of DC pregnancies (Van Schoubroeck *et al.*, 2004). In this study, the complication rate (25% of PROM before 32 weeks, long term problems in 13% of cases) was similar to those found in twin series, with 83% of survivors.

The current literature does not allow conclusions regarding what is the best method for selective fetocide in MC twins due to the wide range of techniques proposed and supported, mainly through small series, for different indications and at different gestational ages. All procedures described are associated with some risk of complications, and death of the co-twin. In the absence

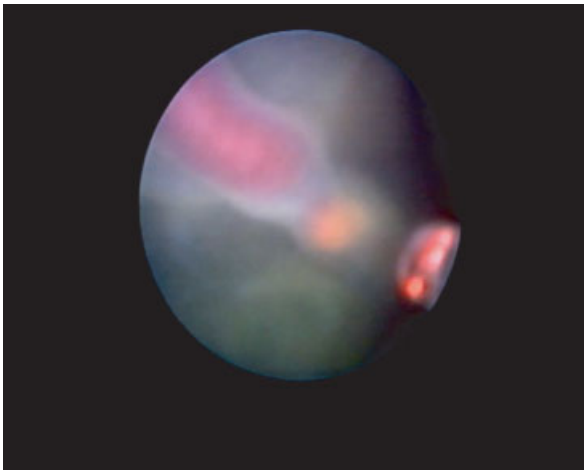


Figure 1—Fetoscopic image of laser coagulation of the umbilical cord



Figure 2—Ultrasound guided bipolar cord coagulation

Table 1—Bipolar cord coagulation in MC twins discordant for fetal anomaly

Case	GA at procedure (weeks)	Indication for cord occlusion	Complications	GA at delivery (weeks)	Weight (g)	Outcome
1	22	Trisomy 21	—	37	2550	A/W
2	19	45XO,HLV	PROM 24 weeks	24	—	IUD
3	20	45X0	PROM 23 weeks	30	1440	A/W
4	22	Spina bifida	—	31	1150	A/W
5	22	Spina bifida	—	41	3600	A/W
6	18	Encephalocele	—	37	2550	A/W
7	23	Ventriculomegaly	IUD	23	—	IUD
8	23	Ventriculomegaly	—	38	2900	A/W
9	23	Ventriculomegaly	—	38	2700	A/W
10	21	Dandy–Walker cyst	—	25	750	A/W <sup>c</sup>
11	24	Dandy–Walker cyst	—	39	3400	A/W
12	22	Dandy–Walker cyst	—	38	3340	A/W
13	24	ACC	—	37	2660	A/W <sup>d</sup>
14	19	Megacystis	—	34	3345	A/W
15	23	Bladder extrophy	—	38	3430	A/W
16	23	Omphalocele	—	39	3530	A/W
17	18	Multiple anomalies	PROM 19 wks	19	—	IUD
18	24	PAIVS	PROM 27 wks	31	1200	NND <sup>e</sup>
19	19	Arthrogyposis	IUD	19	—	IUD
20	21 <sup>a</sup>	LBWC	IUD	22	—	IUD
21	20 <sup>b</sup>	Omphalocele	—	33	1300/1700	A/W

PROM, premature rupture of membranes; HLV, hypoplastic left heart; ACC, agenesis of corpus callosum; PAIVS, pulmonary atresia intact ventricular septum; LBWC, limb body wall complex; A/W, alive and well; IUD, intrauterine death; NND, neonatal death. <sup>a</sup> monochorionic monoamniotic twins. <sup>b</sup> trichorionic diamniotic twins. <sup>c</sup> intraventricular hemorrhage grade I. <sup>d</sup> operated on at 7 days of ileal atresia. <sup>e</sup> neonatal death of sepsis.

of specific criteria for selecting patients and the optimal timing for the procedure, the choice is based on parental wishes and local experience. On the basis of published data, it could be reasonable to consider fetoscopically guided laser coagulation of the cord early in pregnancy for TRAP sequence, while later in gestation, bipolar cord coagulation is more effective for MC twins with normal haemodynamics, like those discordant for fetal anomaly.

#### CRITICAL ISSUES IN THE MANAGEMENT OF TWIN PREGNANCIES WITH DISCORDANT ANOMALY

Although selective fetocide is the obvious option in cases of discordant anomalies in twin pregnancies, expectant management might be considered an alternate strategy in selected cases.

Selective termination may in fact increase the risk of miscarriage and lead to damage of the co-twin, particularly in MC pregnancies, and the need to perform selective fetocide is questionable in cases of lethal malformations. On the other hand, some anomalies may jeopardize the outcome of the whole pregnancy, or increase the chances of intrauterine death, which in turn can cause demise or hypoxic–ischemic organ lesions in the co-twin of MC pairs.

This issue is best exemplified by anencephaly. A retrospective study of 14 DC pregnancies discordant for anencephaly (Lipitz *et al.*, 1995) found that expectant management was associated with a favorable outcome for the unaffected twin, with a mean gestational age at delivery of 35 weeks (range 29–39); mild polyhydramnios complicated six pregnancies but none needed

amnioreduction. In another study of 24 twin pregnancies (11 MC, 13 DC) discordant for anencephaly, Sebire *et al.* (1997a) reported that in the MC group, expectant management produced a high intrauterine death rate of the healthy twin (3/11), with a mean gestational age at delivery in the other eight cases of 34 weeks, but four of these pregnancies developed polyhydramnios. Five pregnancies in the DC group underwent selective termination at 17–21 weeks, and one had a spontaneous abortion. The other eight DC pregnancies were managed expectantly, but three developed polyhydramnios at 26–30 weeks, needing amniodrainage in one case, and selective fetocide in another. In this group, median gestational age at delivery was 35 weeks. Therefore, expectant management of anencephalic discordant DC twin pregnancies appears to be a reasonable option.

The natural history and outcome of pregnancies complicated by a variety of discordant anomalies in twins have been addressed by a number of studies, which mainly support the view that the presence of a major anomaly of one twin increases the likelihood of premature delivery. Heydanus *et al.* (1993) reported 23 twin pregnancies with one structurally abnormal fetus managed expectantly. The comparison group consisted of 23 normal twin pairs; in both groups there was a high, albeit not significantly different, rate of prematurity (57% vs 48%). However, later observations showed different results. A study of 14 twin pregnancies (11 DC, 3 MC) with one affected fetus compared with 78 normal twin pregnancies (chorionicity not specified) found that gestational age and birth weight at delivery were significantly lower in the anomalous group compared with the normal group ( $P = 0.008$  and  $P = 0.001$ , respectively). The risk of delivering at 36 weeks or less was 78.6% for

the anomalous group versus 59.0% for controls, resulting in a 19.6% attributable risk of preterm delivery based on the presence of an anomalous fetus (Malone *et al.*, 1996). A larger series (Alexander *et al.*, 1997) of 970 twin pregnancies comprising (1) 18 twins discordant for major anomalies (defined as anomalies with a significant impact on neonatal morbidity and mortality), (2) 38 twins discordant for minor anomalies, and (3) 914 with both fetuses free of anomalies, found differences between the major anomaly group and the non-anomaly group in gestational age at delivery (32 weeks vs 35 weeks,  $P < 0.05$ ), and birth weight at delivery (1759 vs 2291 g,  $P < 0.05$ ), but there was no difference in neonatal mortality and morbidity for the normal co-twin when compared with the minor and free of anomaly groups. In a retrospective review of 25 twin pregnancies with one structurally abnormal fetus and 547 normal twin gestations (Nassar *et al.*, 2000), there was a trend for pregnancies with one anomalous fetus to deliver earlier (34 vs 35 weeks,  $P = 0.02$ ), with an increased delivery rate before 37 weeks (76% vs 55%,  $P = 0.04$ ).

In a retrospective study exploring the management options in DC twin pregnancies discordant for trisomies (14 trisomy 21, 5 trisomy 18) (Sebire *et al.*, 1997), the main determinant in deciding whether to perform selective fetocide or expectant management was the type of chromosomal anomaly, since fetuses with trisomy 18 are unlikely to survive the perinatal period. In the four cases discordant for trisomy 18 managed expectantly, the trisomic fetus died in utero or early after birth, and the normal twin delivered at 33 to 40 weeks (median 37 weeks), whereas in the 14 cases of selective termination (13 trisomy 21, 1 trisomy 18) the normal co-twin delivered at 24 to 41 weeks (median 38 weeks). Lynch *et al.* (1996) studied 69 DC twin pregnancies that underwent selective fetocide for structural, chromosomal anomaly, or Mendelian disorders at a mean gestational age of 19 weeks (range 12–23). The comparison groups consisted of 42 362 singletons and 825 twins delivered over the same period. There were only two women who miscarried after selective termination and the remaining delivered at a mean gestational age of 36 weeks. Selectively terminated gestations had a lower rate of preterm delivery than control twin pregnancies (40% vs 58%,  $P < 0.005$ ), but a higher one than singletons (40% vs 10%,  $P < 0.001$ ).

The same study addressed the issue of which variables are relevant in determining outcome following selective fetocide (Lynch *et al.*, 1996). Termination of the presenting twin increased the risk of delivery before 37 weeks (adjusted OR 4.1, 95% CI 1.4–12.3) and low birth weight (adjusted OR 3.8, 95% CI 1.3–11.4). Preterm delivery and preterm premature rupture of membranes were more frequent when selective termination was performed at 20 weeks or later (adjusted OR 3.5; 95% CI 1.2–11.5). In contrast, Shalev *et al.* (1999) reported in a smaller series of 23 DC twins, that when selective fetocide was postponed to 28–33 weeks' gestation, after treatment for lung maturity, the procedure was as effective and delivery occurred at least 4 weeks later (range 4–11), with a favorable outcome for the normal fetus. Yaron *et al.* (1998) reported a single center experience

with 82 twin pregnancies undergoing selective termination. Procedures performed during the first trimester had a pregnancy loss rate of 9.7%, compared to 7.8% for terminations done later in gestation. This difference might be related to the different background risk of miscarriage as suggested by shorter procedure to pregnancy loss intervals for terminations done in the second trimester. In an international collaborative study, (Evans *et al.*, 1999) involving 402 DC pregnancies managed by selective termination for structural, chromosomal, and Mendelian anomalies (345 twins, 39 triplets, and 18 multiples), miscarriage before 24 weeks occurred in 30/402 cases (7.5%). Indication for termination had no influence on the loss rate, and there was no statistically significant correlation between loss rate and the timing of procedure (8.7% at 13–18 weeks, 6.8% at 19–24 weeks, 9.1% after 25 weeks).

The largest single center experience with selective termination of anomalous fetus in multifetal pregnancies was performed at a median gestational age of 19.6 weeks, and included 200 DC pregnancies (164 twins, 32 triplets, 4 quadruplets). The overall loss rate at less than 24 weeks was 4% (2.4% in twins and 12.5% in triplets). The median gestational age at delivery was 37.1 weeks. There was no significant difference in the incidence of delivery before 28 weeks in pregnancies managed by early selective termination (before 20 weeks) and those undergoing the procedure later on in pregnancy (Eddleman *et al.*, 2002).

## CONCLUSIONS

The frequency of malformations in DZ twins is similar to that of singletons, while it has been reported to be two to three times higher in MZ pairs. MZ twins are thought to be genetically identical, but a number of discordances have been reported for chromosomal anomalies, single gene disorders, mitochondrial diseases, and genomic imprinting defects. Therefore, approximately 1–2% of twin pregnancies may face the dilemma of expectant management versus selective termination following diagnosis of an anomaly affecting only one fetus.

Although expectant management of DC twin pregnancies discordant for nonviable anomalies such as anencephaly and trisomy 18 appears to be a reasonable option, a number of studies suggest that the presence of a major anomaly of one twin increases the likelihood of premature delivery.

If the option of selective fetocide is considered, the main variable that determines the technique to achieve this aim is chorionicity. In fact, the passage of substances from one twin into the circulation of the co-twin is unlikely in DC pregnancies due to the lack of placental anastomoses, and any drug able to produce fetal asystole can be injected safely into the circulation of the affected twin. Selective fetocide by injection of KCl into the heart or the umbilical cord of the affected twin is an effective and reasonably safe procedure. However, the optimum gestational age at which to perform the termination is still unresolved. In MC twin pregnancies, selective termination needs to be performed

by ensuring complete and permanent occlusion of both the arterial and venous flows in the umbilical cord of the affected twin, in order to avoid acute hemorrhage from the co-twin into the dying fetus which may lead to death or organ damage. A wide range of techniques have been proposed to obtain this. Fetoscopically guided laser coagulation of the cord early in pregnancy for TRAP sequence, and bipolar cord coagulation under ultrasound guidance in later gestation are associated with approximately 70–80% survival rates.

## REFERENCES

- Alexander JM, Ramus R, Cox SM, Gilstrap LC. 1997. Outcome of twin gestations with a single anomalous fetus. *Am J Obstet Gynecol* **177**: 849–852.
- Benirschke K, Kaufmann P (eds). 2000. *Pathology of the Human Placenta*, (4th edn). Springer-Verlag: New York.
- Bhide A, Sairam S, Hollis B, Thilaganathan B. 2002. Comparison of fetocide carried out by cordocentesis versus cardiac puncture. *Ultrasound Obstet Gynecol* **20**: 230–232.
- Bryan E, Little J, Burn J. 1987. Congenital anomalies in twins. *Baillieres Clin Obstet Gynaecol* **1**: 697–721.
- Challis D, Gratacos E, Deprest JA. 1999. Cord occlusion techniques for selective termination in monozygotic twins. *J Perinat Med* **27**: 327–338.
- Denbow ML, Overton TG, Duncan KR, Cox PM, Fisk NM. 1999. High failure rate of umbilical vessel occlusion by ultrasound-guided injection of absolute alcohol or enbucrilate gel. *Prenat Diagn* **19**: 527–532.
- Deprest JA, Van Ballaer PP, Evrard VA, et al. 1998. Experience with fetoscopic cord ligation. *Eur J Obstet Gynecol Reprod Biol* **81**: 157–164.
- Eddleman KA, Stone JI, Lynch L, Berkowitz RL. 2002. Selective termination of anomalous fetuses in multifetal pregnancies: two hundred cases at a single centre. *Am J Obstet Gynecol* **187**: 1168–1172.
- Evans MI, Goldberg JD, Dommergues M, et al. 1994. Efficacy of second trimester selective termination for fetal abnormalities: international collaborative experience among the world's largest centers. *Am J Obstet Gynecol* **171**: 90–94.
- Evans MI, Goldberg JD, Horenstein J, et al. 1999. Selective termination for structural, chromosomal, and Mendelian anomalies: international experience. *Am J Obstet Gynecol* **181**: 893–897.
- Gilbert B, Yardin C, Briault S, et al. 2002. Prenatal diagnosis of female monozygotic twins discordant for Turner syndrome: implication for prenatal genetic counselling. *Prenat Diagn* **22**: 697–702.
- Gringas P, Chen W. 2001. Mechanism for differences in monozygotic twins. *Early Hum Dev* **64**: 105–117.
- Goodship J, Carter J, Burn J. 1996. X-inactivation patterns in monozygotic and dizygotic female twins. *Am J Med Genet* **61**: 205–208.
- Hall JG. 2003. Twinning. *Lancet* **362**: 735–743.
- Hecher K, Hackeloer J, Ville Y. 1997. Umbilical cord coagulation by operative microendoscopy at 16 weeks' gestation in an acardiac twin. *Ultrasound Obstet Gynecol* **10**: 130–132.
- Heydanus R, Santema JG, Stewart PA, Mulder PG, Wladimiroff JW. 1993. Preterm delivery rate and fetal outcome in structurally affected twin pregnancies: a retrospective matched control study. *Prenat Diagn* **13**: 155–162.
- Holmes A, Jauniaux E, Rodeck C. 2001. Mopolar thermocoagulation in acardiac twinning. *Br J Obstet Gynaecol* **108**: 1000–1002.
- Jenkins TM, Wapner RJ. 2000. The challenge of prenatal diagnosis in twin pregnancies. *Curr Opin Obstet Gynecol* **12**: 87–92.
- Jolly M, Taylor M, Rose G, Govender L, Fisk NM. 2001. Interstitial laser: a new surgical technique for twin reversed arterial perfusion sequence in early pregnancy. *Br J Obstet Gynaecol* **108**: 1098–1102.
- Karatzas AA, Wolfenden JL, Taylor MJ, Wee L, Fisk NM, Gardiner HM. 2002. Influence of twin-twin transfusion syndrome on fetal cardiovascular structure and function: prospective case-control study of 136 monozygotic twin pregnancies. *Heart* **88**: 271–277.
- Lewi I, Jani J, Gratacos E, et al. 2003. Fifty consecutive cord coagulations in monozygotic twins. *Ultrasound Obstet Gynecol* **22**(Suppl. 1): 163.
- Lipitz A, Meizner I, Yagel S, Shapiro I, Achiron R, Schiff E. 1995. Expectant management of twin pregnancies discordant for anencephaly. *Obstet Gynecol* **86**: 969–972.
- Lynch L, Berkowitz RL, Stone J, Alvarez M, Lapinski R. 1996. Preterm delivery after selective termination in twin pregnancies. *Obstet Gynecol* **87**: 366–369.
- Machin GA. 1996. Some causes of genotypic and phenotypic discordance in monozygotic twin pairs. *Am J Med Genet* **61**: 216–228.
- Malone FD, Craigo SD, Chelmow D, D'Alton E. 1996. Outcome of twin gestation complicated by a single anomalous fetus. *Obstet Gynecol* **88**: 1–5.
- Mastroiacovo P, Castilla EE, Arpino C, et al. 1999. Congenital malformations in twins: an international study. *Am J Med Genet* **83**: 117–124.
- Mohammed SN, Swan MC, Wall SA, Wilkie AOM. 2004. Monozygotic twins discordant for frontonasal malformation. *Am J Med Genet* **130**: 384–388.
- Nassar AH, Adra AM, Gomez-Marin O, O'Sullivan M. 2000. Perinatal outcome of twin pregnancies with one structurally affected fetus: a case-control study. *J Perinatol* **2**: 82–86.
- Nicolini U, Poblete A. 1999. Single intrauterine death in monozygotic twin pregnancies. *Ultrasound Obstet Gynecol* **14**: 297–301.
- Nicolini U, Poblete A, Boschetto C, Bonati F, Roberts A. 2001. Complicated monozygotic twin pregnancies: experience with bipolar cord coagulation. *Am J Obstet Gynecol* **185**: 703–707.
- Nieuwint A, Van Zalen-Sprock R, Hummel P, et al. 1999. Identical twins with discordant karyotypes. *Prenat Diagn* **19**: 72–76.
- Rodeck CH, Mibashan RS, Abramowicz J, Campbell S. 1982. Selective fetocide of the affected twin by fetoscopic air embolism. *Prenat Diagn* **2**: 189–194.
- Rodeck C, Deans A, Jauniaux E. 1998. Thermocoagulation for the early treatment of pregnancy with an acardiac twin. *N Engl J Med* **339**: 1293.
- Rodis JF, Egan JF, Craffey A, Ciarleglio L, Greenstein RM, Scorza WE. 1990. Calculated risk of chromosomal abnormalities in twin gestations. *Obstet Gynecol* **76**: 1037–1041.
- Rogers JG, Voullaire L, Gold H. 1982. Monozygotic twins discordant for trisomy 21. *J Med Genet* **11**: 143–146.
- Sebire NJ, Sepulveda W, Hughes KS, Noble P, Nicolaidis KH. 1997a. Management of twin pregnancies discordant for anencephaly. *Br J Obstet Gynaecol* **104**: 216–219.
- Sebire NJ, Snijders RJ, Santiago C, Papapanagiotou G, Nicolaidis KH. 1997b. Management of twin pregnancies with fetal trisomies. *Br J Obstet Gynaecol* **104**: 220–222.
- Senat MV, Fisher C, Ville Y. 2002. Funipuncture for fetocide in late termination of pregnancy. *Prenat Diagn* **22**: 354–356.
- Shalev J, Meizner I, Rabinerson D, et al. 1999. Improving pregnancy outcome in twin gestations with one malformed fetus by postponing selective fetocide in the third trimester. *Fertil Steril* **72**: 257–260.
- Shevell T, Malone FD, Weintraub J, Thaker HM, D'Alton ME. 2004. Radiofrequency ablation in a monozygotic twin discordant for fetal anomalies. *Am J Obstet Gynecol* **190**: 575–576.
- Shotelersuk V, Tiftt CJ, Vacha S, Peters KF, Biesecker LG. 1999. Discordance of oral-facial-digital syndrome type 1 in monozygotic twin girls. *Am J Med Genet* **86**: 269–273.
- Singh SM, Murphy B, O'Reilly R. 2002. Epigenetic contributors to the discordance of monozygotic twins. *Clin Genet* **62**: 97–103.
- Smith R, Gitau R, Glover V, Fisk NM. 2000. Pain and stress in the human fetus. *Eur J Obstet Gynecol Reprod Biol* **92**: 161–165.
- Tan TY, Sepulveda W. 2003. Acardiac twin: a systematic review of minimally invasive treatment modalities. *Ultrasound Obstet Gynecol* **22**: 409–419.
- Tsao K, Feldstein VA, Albanese CT, et al. 2002. Selective reduction of acardiac twin by radiofrequency ablation. *Am J Obstet Gynecol* **187**: 635–640.
- Van Schoubroeck D, Lewi L, Ryan G, et al. 2004. Fetoscopic surgery in triplets pregnancies: a multicenter case series. *Am J Obstet Gynecol* **191**: 1529–1532.
- Yaron Y, Johnson KD, Bryant-Greenwood PK, Kramer RL, Johnson MP, Evans MI. 1998. Selective termination and elective reduction in twin pregnancies: 10 years experience at a single centre. *Hum Reprod* **13**: 2301–2304.