

Endometrial receptivity after oocyte donation in recipients with a history of chemotherapy and/or radiotherapy

Valérie Vernaève¹, Daniel Bodri, Marta Colodrón, Ricard Vidal, Mercé Durbán and Oriol Coll

Clinica Eugén, Calle Entenza 293-295, 08029 Barcelona, Spain

¹Correspondence address. Tel: +34-93-322-11-22; Fax: +34-6-66-82-17-99; E-mail: vernaeve@telefonica.net

INTRODUCTION: Information is scarce regarding the outcome of oocyte donation (OD) in patients with a history of cancer treatment. Therefore, we conducted a matched controlled analysis on the outcome of OD in these recipients. **METHODS:** Between January 2000 and November 2005, 33 patients with a history of chemotherapy and/or radiotherapy had an OD cycle. Matching was performed to the chronologically closest patient without a history of cancer therapy by number of days of hormonal stimulation before embryo replacement, number of replaced embryos, day of embryo transfer and origin of sperm. **RESULTS:** The primary diseases of the patients were Hodgkin's lymphoma ($n = 12$), non-Hodgkin's lymphoma ($n = 3$), leukaemia ($n = 7$), ovarian cancer ($n = 6$), Ewing's sarcoma ($n = 2$), breast cancer ($n = 1$), sympathoblastoma ($n = 1$) and histiocytosis X ($n = 1$). Twenty-three patients had undergone chemotherapy and radiotherapy, nine patients chemotherapy only and one radiotherapy only. The mean age of the recipients was 33.1 years [95% confidence interval (CI) 30.9–35.3] and 39.6 (95% CI 37.1–42.1) in the study and control groups, respectively. The average number of received oocytes and transferred embryos, was similar in both groups. Nineteen (57.6%) versus 13 (39.4%) pregnancies resulting in an ongoing pregnancy (i.e. viable at 12 weeks) in 15 (45.4%) versus 9 cycles (27.3%) (NS) were obtained in study and control groups, respectively. Implantation rate in study and control groups was 35.8 versus 17.9%, respectively ($P = 0.02$). **CONCLUSIONS:** The results suggest that patients with a history of cancer treatment have a pregnancy rate after OD similar to that in the general population of oocyte recipients.

Keywords: chemotherapy; oocyte donation; pregnancy; radiotherapy; ICSI

Introduction

Improvements in cancer therapy have contributed to the enhancement of survival of children and adolescents with a malignant neoplasm. It has been estimated that one per thousand young adults, aged between 17 and 35 years, have been treated for cancer during childhood (Critchley *et al.*, 2002). However, anticancer treatments can permanently impair reproductive functions as a result of chemotherapy and/or radiotherapy (Madsen *et al.*, 1995).

Preserving fertility in female patients is important because it has been shown that a high percentage of the women treated with chemotherapy will develop premature ovarian failure (POF) due to primordial follicle damage (Familiari *et al.*, 1993). About 50% of women over 25 years of age and 20% of women under 25 years treated with MOPP (Mustin, Oncovin, Procarbazine, Prednisone) will develop a premature menopause (Schilsky *et al.*, 1981). The results of pilot studies on the effects of a GnRH agonist depot in women receiving chemotherapy for the prevention of POF are promising but need to be further elucidated in randomized controlled

trials (Blumenfeld *et al.*, 2005; Franke *et al.*, 2005). Another preventive measure in the female is the transposition of the ovaries prior to pelvic irradiation (Williams *et al.*, 1999) and a third possibility is the cryopreservation of embryos if the patient has a male partner (Nugent *et al.*, 1997; Falcone *et al.*, 2004). However, this option presents several issues: the possible carcinogenic risk of ovarian stimulation on the disease, the risk of postponing the start of the anticancer therapy, and when the cancer is ovarian, the risk of tumour cell dissemination by follicle puncture. Oocyte freezing and ovarian tissue cryopreservation are also often proposed before anticancer treatment although remain experimental (Demeester *et al.*, 2006; Donnez *et al.*, 2006).

Because none of the above mentioned preventive options give consistently satisfactory results, the only possibility for the majority of patients with a history of cancer treatment who wish to have children is adoption or to receive oocytes by oocyte donation (OD). However, only very few data based on case reports are available in the literature on the outcome of OD cycles in this particular subgroup of oocyte

recipients. Most published reports show that OD is feasible but is associated with a lower pregnancy rate than that expected in the general population of oocyte recipients (Pados *et al.*, 1992; Sauer *et al.*, 1994; Remohi *et al.*, 1997; Anselmo *et al.*, 2001; Kavic *et al.*, 2001). However, two other reports, also based on a limited number of patients, showed no difference in pregnancy rate in cancer survivors (Paulson *et al.*, 1997; Moomjy *et al.*, 1999).

More information regarding the success rate of OD and the pregnancy outcome in patients with a history of cancer treatment by chemotherapy and/or radiotherapy is needed in order to counsel the patients adequately. We therefore conducted a retrospective, matched controlled analysis on the outcome of OD and pregnancy outcome in this particular subgroup of oocyte recipients.

Materials and Methods

Between January 2000 and November 2005, 33 patients with a history of chemotherapy and/or radiotherapy (study group) underwent a first OD cycle with fresh embryo transfer. Matching was performed to the chronologically closest patient without a history of cancer therapy (control group) according to the number of days of hormonal stimulation before embryo replacement (± 5 days), the number of replaced embryos, the day of embryo replacement (day 2 or day 3) and the origin of sperm (ejaculated or testicular).

A total of 50 OD cycles were performed in these patients during the study period, as some patients repeated the OD procedure. However, repeated cycles were not used for matching.

Before treatment, a standard evaluation for oocyte recipients was carried out. The patients were declared cured and disease-free by their oncologists before initiating OD treatment. Oral estradiol valerate (Progynova®, Schering Spain, Madrid, Spain) was used in a progressively increasing dose regimen for the endometrial preparation. Patients on standby received up to 6 mg estradiol valerate a day and the duration of the treatment varied in accordance with the availability of a phenotype-matched donor, ranging from 13 to 51 days. Endometrial thickness was not routinely measured before embryo replacement (Remohi *et al.*, 1997; Soares *et al.*, 2005). From the day of oocyte retrieval, 800 mg of micronized progesterone (Utrogestan®, Laboratorio Seid, Barcelona, Spain) was administered vaginally.

OD was performed according to the Spanish Act on Reproduction. Donation was anonymous and altruistic, with donors required to be aged between 18 and 35 years. A conventional clinical and psychological workup was performed, including karyotype.

The ovarian stimulation of the donors was performed using recombinant FSH or human menopausal gonadotrophin and hypophysary suppression was obtained using either GnRH agonists or antagonists in a short-stimulation protocol. The ICSI procedure was performed routinely in order to avoid immature oocytes being given to the recipients and to enhance the fertilization rate. The laboratory procedures have been described previously (Joris *et al.*, 1998). Frozen–thawed sperm, obtained during the first appointment, were used for reasons of convenience for those patients living abroad, enabling them to be absent on the day of oocyte retrieval. Cleaving embryos with <50% of their volume containing nucleate fragments were considered eligible for transfer. Cleaving embryos were transferred into the uterine cavity 2 or 3 days after the ICSI procedure.

A rise in serum β -HCG levels 14 days after transfer indicated pregnancy. Each pregnancy with at least one intrauterine sac revealed by ultrasonography ~ 5 weeks after transfer was considered as a clinical

pregnancy. The implantation rate was defined as the ratio of gestational sacs to the number of embryos transferred. Ongoing pregnancy was defined as a viable pregnancy confirmed on an ultrasound scan performed at the 12th week. Pregnancy rates were defined per embryo transfer.

Statistical analysis

Values are expressed as mean with 95% confidence intervals (95% CI). The Student’s *t*-test and chi-square test were used when appropriate. A *P*-value of <0.05 was considered statistically significant.

Results

The primary diseases of the patients were Hodgkin’s lymphoma (*n* = 12), non-Hodgkin’s lymphoma (*n* = 3), leukaemia (*n* = 7), ovarian cancer (*n* = 6; three borderline tumours, one dysgerminoma, one vitelline tumour and one ovarian seminoma), Ewing’s sarcoma (*n* = 2), breast cancer (*n* = 1), sympathoblastoma (*n* = 1) and histiocytosis X (*n* = 1). Twenty-three patients had undergone chemotherapy and radiotherapy, nine patients chemotherapy only and one radiotherapy only. The average age at diagnosis was 21.0 years (95% CI 17.3–24.7). All but four patients had a POF. The average age of onset of the menopause was 23.9 years (95% CI 19.7–28.0). The average time between onset of the menopause and the OD was 9.1 years (95% CI 5.7–12.2). The average remission time before the onset of the oocyte donation cycle was 11.7 years (95% CI 8.3–15.0).

Concerning the 24 patients (31 cycles) who received radiotherapy, the localization of the irradiation was pelvic in 8 (11 cycles), total body irradiation (TBI) in 7 (10 cycles) and supra-diaphragmatic in 9 patients (10 cycles).

The average age of recipients in the study and control groups was significantly different: 33.1 years (95% CI 30.9–35.3) and 39.6 years (95% CI 37.1–42.1), respectively. In 2 (6%) versus 8 patients (24.2%), the recipient had a previous delivery (*P* = 0.04) and in 6 (18.2%) versus 1 patient (3%), a previous donation had been performed (*P* = 0.05), in the study and control groups, respectively. The mean number of days of hormonal replacement before embryo transfer was 28.9 (95% CI 23.4–34.3) and 29.1 (95% CI 24.3–33.9) in the study and control groups, respectively.

Laboratory findings were similar in study and control groups (Table 1). Pregnancy and delivery rates were similar in both groups (Table 2). Only the implantation rate was significantly higher in the study group (35.8%) when compared with the control group (17.9%) (*P* = 0.02). Regarding perinatal results,

Table 1: Laboratory characteristics in patients with (Study group, *n* = 33) and without (Control group, *n* = 33) history of cancer treatment

	Study group average, <i>n</i> (95% CI)	Control group average, <i>n</i> (95% CI)
Number of received oocytes	7.7 (6.5–8.9)	8.4 (6.5–10.4)
Metaphase II oocytes	5.4 (4.7–6.2)	5.8 (5.0–6.6)
2 Pronuclei	4.1 (3.5–4.8)	4.0 (3.2–4.8)
Transferred embryos	2.0 (1.8–2.2)	2.0 (1.8–2.2)
Frozen embryos	0.4 (95% CI 0.0–0.8)	0.1 (95% CI –0.1 to 0.4)

Table 2: Pregnancy and delivery rates per cycle in patients with and without history of cancer treatment

	Study group	Control group	<i>P</i> -value
Number of embryo replacements	33	33	
Replaced embryos, <i>n</i>	67	67	
Pregnancies, <i>n</i> (% per ET)	19 (57.6)	13 (39.4)	<i>P</i> = 0.1
Ongoing pregnancies, <i>n</i> (% per ET)	15 (45.4)	9 (27.3)	<i>P</i> = 0.1
Implantation rate, %	35.8	17.9	<i>P</i> = 0.02
Delivery rate, <i>n</i> (%)	15 (45.4)	9 (27.3)	<i>P</i> = 0.1

ET, embryo transfer.

15 (45.4%) and 9 patients (27.3%) delivered at least one child (*P* = 0.1) in the study and control group, respectively. Three patients in the study group and one in the control group delivered a set of twins.

In the study group, one patient had a successful embryo reduction from triplets to a singleton. Vaginal delivery occurred in five patients (33%) in the study group and in three patients in the control group (33%). An emergency Caesarean section was performed for placental haemorrhage in one case at 37 weeks with the birth of a stillborn child in the study group, and this patient delivered a healthy child in a subsequent pregnancy.

The average gestational age at delivery was 36.9 weeks (95% CI 34.2–39.6) versus 38.4 weeks (95% CI 36.7–40.1) in study and control groups, respectively. The average birth weight of singletons was 2977 g (95% CI 2372–3583) versus 3566 g (95% CI 3245–3887) and that of the twins was 2070 g (95% CI 1418–2721) versus 2430 g (95% CI 2374–3486), in the study and control groups, respectively. Premature delivery (delivery <37 weeks) was observed in three pregnancies (20%) in the study group and in one (11%) in the control group. In the study group, other antenatal complications occurred in two pregnancies: pre-eclampsia in one and placental haemorrhage with the birth of a stillborn child at 37 weeks in the other patient.

Concerning the study population, the average age at diagnosis of the malignancy was 20.7 years (95% CI 14.5–26.9) and 21.1 years (95% CI 16.5–25.8) in the non-pregnant (*n* = 14) and pregnant (*n* = 19) patients, respectively.

Of the 12 patients with a history of Hodgkin's lymphoma, 7 became pregnant and 5 delivered, while of the 3 with a history of non-Hodgkin's lymphoma 2 women became pregnant and delivered. Of the seven women with a leukaemia history, five achieved a pregnancy, of whom four delivered. Two of the six patients with previous ovarian cancer became pregnant and delivered. One of the two patients with Ewing's sarcoma was pregnant and delivered. The only patient with a history of breast cancer was successful in becoming pregnant and delivered. The patient with sympathoblastoma did not become pregnant and the woman with histiocytosis X aborted her pregnancy.

Out of 15 patients that received either pelvic or TBI, 8 became pregnant (53.3%) and 7 had an ongoing pregnancy with an implantation rate of 31%. Four patients underwent a second cycle and one, a third cycle; all were pregnant in their last cycle, however, one was a biochemical pregnancy.

Details on the outcome of these pregnancies are given in Table 3.

Discussion

Only very few data are available in the literature about the success rate of oocyte donation in patients with a history of chemotherapy and/or radiotherapy. The largest available study on this subject evaluated the outcome of OD and pregnancy among 24 women (40 cycles) who had survived a malignancy and reported a clinical pregnancy rate of 42.5% with a spontaneous abortion rate of 11.8% (Kavic *et al.*, 2001). No comparison was made with their general population of oocyte recipients and no details were available on the type of radiotherapy the patients were exposed to. Anselmo *et al.* (2001) described the outcome of OD in six women (16 cycles) previously treated for Hodgkin's disease. They found a cycle success rate of 37% and an implantation rate of 17%. Larsen *et al.* (2000) reported three cases of OD in women cured of cancer by bone marrow transplantation, including TBI. One woman delivered a healthy child in the 37th week of gestation, another woman miscarried in the 17th week of gestation and the third had not yet conceived. Two studies reported impaired pregnancy rates after chemotherapy and/or radiotherapy. Sauer *et al.* (1994) reported greater pregnancy losses after prior exposure to chemotherapy (*n* = 8); Pados *et al.* (1992) reported the lowest pregnancy rate after chemotherapy and/or radiotherapy (*n* = 11) (9%). One study investigating pregnancy and birth rates after OD found no influence of the cause of entering the OD programme but only two patients enrolling had a history of cancer treatment (Remohi *et al.*, 1997).

Our data, based on a larger patient population (*n* = 33), did not show any difference in pregnancy rate among women with a history of chemotherapy or radiotherapy, compared with other recipients matched for the main confounding factors. These results are in accordance with the results published by Paulson *et al.* (1997) concerning 21 cycles of recipients who received chemotherapy and those published by Moomjy *et al.* (1999) based on 12 cycles in cancer survivors. The implantation rate in the current study is significantly lower in the control group, which could be due to the relatively small number of patients studied.

The general characteristics of the study and control group were similar in our series, except that the recipients with a history of cancer treatment were significantly younger and had fewer previous deliveries than the controls. No matching was performed on the basis of age of the recipients in this analysis, as in our centre we have found no correlation between recipient's age and OD outcome. The differences in age and presence of previous deliveries in the current study are easy to explain, as the women with prior cancer treatment would have been aware of the expected difficulty of having their own genetic child, as most had POF and therefore sought OD earlier. Anselmo *et al.* (2001) found that the age at cancer treatment was important and that women treated in adolescence seemed to have more substantial uterine damage than women treated in adulthood. In our study, we found that

Table 3: Details of 15 patients (21 cycles) having had infradiaphragmatic or TBI

Patient	Age (years)	Type of cancer	Type of irradiation	Dose of irradiation	Outcome	Pregnancy complications
1a	31	Hodgkin	Mantle + inverted Y	Information not available	Not pregnant	
1b	32				Caesarian section at 30 weeks in twin pregnancy	Premature delivery
2	31	NHL	TBI	Information not available	Delivery twin at 32 weeks	Premature delivery
3	34	Leucemia	TBI	Information not available	Not pregnant	
4a	31	Leucemia	TBI	12 Gy	Delivery singleton	Caesarian at 37 weeks for placental haemorrhage with the birth of a stillborn child
4b	33				Delivery singleton	Caesarian at 36 weeks
5	38	Ewing	Pelvic	55 Gy (left semi-pelvis) + 10 Gy (right semi-pelvis)	Delivery singleton by caesarian	none
6	24	Leucemia	TBI	12 Gy	Vaginal delivery singleton	Premature delivery at 26 weeks
7	43	NHL	TBI	12 Gy	Not pregnant	
8	30	Hodgkin	Inverted Y and Mantle	40 Gy and 40 Gy	Vaginal delivery at term	None
9a	27	Symphoblastoma	Abdominal	15 Gy	Not pregnant	
9b	28				Biochemical pregnancy	
10	29	Hodgkin	Mantle, Inverted Y	Information not available	Vaginal delivery at 38 weeks	Pre-eclampsia
11	37	Hodgkin	Mediastinum and retroperitoneal	39 and 34 Gy	Elective caesarian section at 38 weeks	None
12	34	Hodgkin	Inverted Y	Information not available	Not pregnant	
13	35	Leucemia	TBI	Information not available	Biochemical pregnancy	
14a	38	Ovarian tumour	Subdiaphragmatic and Supradiaphragmatic	36 Gy and information not available	Not pregnant	
14b	39				Delivery singleton by caesarian	Pre-eclampsia
15a	29	Leucemia	TBI	Information not available	Not pregnant	
15b	29				Not pregnant	
15c	30				Delivery twin by caesarian	Premature delivery at 35 weeks

NHL, non-Hodgkin's lymphoma.

treatment age was similar in the pregnant and non-pregnant recipients.

Potentially, radiotherapy, more than the chemotherapy, could lead to a lower success rate after OD as it causes not only ovarian but also uterine damage (Critchley *et al.*, 2005). The type of radiotherapy used is of paramount importance for the impact on the future fertility of the patients. There is little risk of premature menopause in women treated with radiation fields that exclude the pelvis (Madsen *et al.*, 1995). However, radiotherapy below the diaphragm includes the risk of ovarian failure and significantly impairs the development of the uterus. Uterine volume correlates with the age at which radiation was received and despite standard estrogen replacement, the uterus of these young girls is often reduced to 40% of normal adult size (Holm *et al.*, 1999). It has been suggested that radiation may result in damage to the myometrium and uterine vessels, inducing fibrosis with an increased

risk of subsequent defective implantation (Critchley *et al.*, 2002). Thus it seems that women treated for a childhood cancer, besides the problem with uterine size, also have to overcome endometrial structural and functional damage. However, the results of our study do not support this hypothesis, as the implantation rate in patients who received pelvic irradiation or TBI (which also carries a high risk for impaired uterine growth and blood flow) was 31%, comparable to our general population of oocyte recipients. It has been recommended to add a combined treatment of pentoxifylline and tocopherol in patients with previous pelvic irradiation or TBI in order to improve the pregnancy rate (Letur-Könirsch *et al.*, 2002). More studies, however, are needed in order to reach a definitive conclusion regarding this suggestion and these should be multicentric because of the low incidence of this problem. Investigation of uterine Doppler evaluation prior to and during pregnancy in such patients is also needed.

Besides the impact of radiotherapy on the fertility of the patient, exposure of the pelvis to radiation has been reported to be associated with an increased risk of miscarriage, mid-trimester pregnancy loss, preterm birth and low birth weight (Wallace *et al.*, 1989; Urbano and Tait, 2004; Signorello *et al.*, 2006). In this series, in the subgroup of patients having had a pelvic irradiation or TBI, we observed a miscarriage rate of 15% and pregnancy complications in eight patients (two pre-eclampsias, five premature deliveries and one placental haemorrhage with the birth of a stillborn child). This series is too small to give definitive conclusions about pregnancy complications in this subgroup of oocyte recipients, but our findings underscore the need for careful monitoring of pregnancies achieved in women with a previous pelvic irradiation or TBI.

The results of this study suggest that patients with a history of cancer treatment have a pregnancy rate after OD similar to that in the general population of oocyte recipients. As matching was performed according to the main confounding factors in OD, we can conclude that chemotherapy and/or radiotherapy does not seem to have a major impact on endometrial receptivity in these patients.

Acknowledgements

The authors thank the paramedical staff of our clinic that helped us collecting the data.

References

- Anselmo AP, Cavalieri E, Aragona C, Sbracia M, Funaro D, Maurizi Enrici R. Successful pregnancies following an egg donation program in women with previously treated Hodgkin's disease. *Haematologica* 2001;**86**:624–628.
- Blumenfeld Z, Eckman A. Preservation of fertility and ovarian function and minimization of chemotherapy-induced gonadotoxicity in young women by GnRH-a. *J Natl Cancer Inst Monogr* 2005;**34**:40–43.
- Critchley HO, Bath LE, Wallace WH. Radiation damage to the uterus – review of the effects of treatment of childhood cancer. *Hum Fertil (Camb)* 2002;**5**:61–66.
- Critchley HO, Wallace WH. Impact of cancer treatment on uterine function. *J Natl Cancer Inst Monogr* 2005;**34**:64–68.
- Demeestere I, Simon P, Buxant F, Robin V, Fernandez SA, Centner J, Delbaere A, Englert Y. Ovarian function and spontaneous pregnancy after combined heterotopic and orthotopic cryopreserved ovarian tissue transplantation in a patient previously treated with bone marrow transplantation: case report. *Hum Reprod* 2006;**21**:2010–2014.
- Donnez J, Martinez-Madrid B, Jadoul P, Van Langendonck A, Demylle D, Dolmans MM. Ovarian tissue cryopreservation and transplantation: a review. *Hum Reprod Update* 2006;**12**:519–535.
- Falcone T, Attaran M, Bedaiwy MA, Goldberg JM. Ovarian function preservation in the cancer patient. *Fertil Steril* 2004;**81**:243–257.
- Franke HR, Smit WM, Vermes I. Gonadal protection by a gonadotropin-releasing hormone agonist depot in young women with Hodgkin's disease undergoing chemotherapy. *Gynecol Endocrinol* 2005;**20**:274–278.
- Holm K, Nysom K, Brocks V, Hertz H, Jacobsen N, Muller J. Ultrasound B-mode changes in the uterus and ovaries and Doppler changes in the uterus after total body irradiation and allogeneic bone marrow transplantation in childhood. *Bone Marrow Transplant* 1999;**23**:259–263.
- Joris H, Nagy Z, Van de Velde H, De Vos A, Van Steirteghem A. Intracytoplasmic sperm injection: laboratory set-up and injection procedure. *Hum Reprod* 1998;**13**(Suppl 1):76–86.
- Kavic SM, Sauer MV. Oocyte donation treats infertility in survivors of malignancies: ten-year experience. *J Assist Reprod Genet* 2001;**18**:181–183.
- Larsen EC, Loft A, Holm K, Muller J, Brocks V, Andersen AN. Oocyte donation in women cured of cancer with bone marrow transplantation including total body irradiation in adolescence. *Hum Reprod* 2000;**15**:1505–1508.
- Letur-Konirsch H, Guis F, Delanian S. Uterine restoration by radiation sequelae regression with combined pentoxifylline-tocopherol: a phase II study. *Fertil Steril* 2002;**77**:1219–1226.
- Madsen BL, Giudice L, Donaldson SS. Radiation-induced premature menopause: a misconception. *Int J Radiat Oncol Biol Phys* 1995;**32**:1461–1464.
- Moomjy M, Cholist I, Mangieri R, Rosenwaks Z. Oocyte donation: insights into implantation. *Fertil Steril* 1999;**71**:15–21.
- Nugent D, Meirow D, Brook PF, Aubard Y, Gosden RG. Transplantation in reproductive medicine: previous experience, present knowledge and future prospects. *Hum Reprod Update* 1997;**3**:267–280.
- Pados G, Camus M, Van Waesberghe L, Liebaers I, Van Steirteghem A, Devroey P. Oocyte and embryo donation: evaluation of 412 consecutive trials. *Hum Reprod* 1992;**7**:1111–1117.
- Paulson RJ, Hatch IE, Lobo RA, Sauer MV. Cumulative conception and live birth rates after oocyte donation: implications regarding endometrial receptivity. *Hum Reprod* 1997;**12**:835–839.
- Remohi J, Gartner B, Gallardo E, Yalil S, Simon C, Pellicer A. Pregnancy and birth rates after oocyte donation. *Fertil Steril* 1997;**67**:717–723.
- Sauer MV, Paulson RJ, Ary BA, Lobo RA. Three hundred cycles of oocyte donation at the University of Southern California: assessing the effect of age and infertility diagnosis on pregnancy and implantation rates. *J Assist Reprod Genet* 1994;**11**:92–96.
- Schilsky RL, Sherins RJ, Hubbard SM, Wesley MN, Young RC, DeVita VT. Long-term follow up of ovarian function in women treated with MOPP chemotherapy for Hodgkin's disease. *Am J Med* 1981;**71**:552–556.
- Signorello LB, Cohen SS, Bosetti C, Stovall M, Kasper CE, Weathers RE, Whitton JA, Green DM, Donaldson SS, Mertens AC *et al.* Female survivors of childhood cancer: preterm birth and low birth weight among their children. *J Natl Cancer Inst* 2006;**98**:1453–1461.
- Soares SR, Troncoso C, Bosch E, Serra V, Simon C, Remohi J, Pellicer A. Age and uterine receptiveness: predicting the outcome of oocyte donation cycles. *J Clin Endocrinol Metab* 2005;**90**:4399–4404.
- Familiari G, Caggiati A, Nottola SA, Ermini M, Di Benedetto MR, Motta PM. Ultrastructure of human ovarian primordial follicles after combination chemotherapy for Hodgkin's disease. *Hum Reprod* 1993;**12**:2080–2087.
- Urbano MT, Tait DM. Can the irradiated uterus sustain a pregnancy? A literature review. *Clin Oncol* 2004;**16**:24–28.
- Wallace WH, Shalet SM, Crowne EC, Morris-Jones PH, Gattamaneni HR. Ovarian failure following abdominal irradiation in childhood: natural history and prognosis. *Clin Oncol* 1989;**1**:75–79.
- Williams RS, Littell RD, Mendenhall NP. Laparoscopic oophorectomy and ovarian function in the treatment of Hodgkin disease. *Cancer* 1999;**86**:2138–2142.

Submitted on October 22, 2006; resubmitted on May 27, 2007; accepted on June 6, 2007