

Perspectives and Editorials:

Letter to the Editor

Innovative Mouse Model for Postchemotherapy Fertility Evaluation

To the Editor:

Fertility is an important issue in testis cancer patients, many of whom express a wish to father a child after completing treatment. Although cisplatin-containing chemotherapy has revolutionized the treatment of germ cell tumors (GCT), this drug is the most dominant cause of infertility.

Up to 50% of GCT patients are subfertile even prior to chemotherapy, and only few patients show recovery of impaired pretreatment spermatogenesis (Fossa et al, 1990). The rate of conception per unit time is the best measure of fertility in couples seeking parenthood (Berthelsen, 1987). Evaluation of fertility in these patients therefore is only feasible by comparison of patients after chemotherapy with GCT patients on surveillance (Pont et al, 1996).

Cumulative cisplatin doses of less than 400 mg/m² are unlikely to produce persistent infertility (Pont et al, 1996). Higher doses, by contrast, should be expected to cause long-term loss of exocrine and endocrine gonadal function. Therefore, investigations on the toxicity of different schedules for higher doses are of great interest. Because it is not feasible to perform routine testis biopsies in men, animal models could be helpful in demonstrating the intratesticular effects of different chemotherapy schedules.

Sawhney et al (2005) used a mouse model with excellent methodology to demonstrate the intratesticular changes caused by cisplatin at different cumulative doses and different schedules of administration. Human doses were calculated for the mice used and were given on 5 consecutive days, every 22 days. Exceeding the human dose of 400 mg/m², irreversible damage to the seminiferous epithelium could be demonstrated by evaluation of testicular weight, histopathology, and histochemistry. Moreover the authors provide evidence of a cisplatin toxicity threshold for recovery of spermatogenesis for up to 2 rounds of cisplatin, thus ensuring the safety of risk-

adapted treatment of stage IB nonseminomatous testis cancer. Additionally they describe the possible role of Sertoli cell damage in the development of infertility.

In the case of a partial response to chemotherapy, the aim of additional chemotherapy courses is to prevent a patient's death. In this situation, fertility has to be of minor interest. Therefore sperm banking should be offered prior to chemotherapy exceeding the critical dose for long-term impairment of spermatogenesis, although it is known that only 5% to 8% of patients will use their cryosperm for further reproduction (Fossa et al, 1989).

Mouse exposure models like that described in Sawhney et al (2005) could be extremely helpful toward simulating different schedules of cisplatin administration by measuring seminiferous tubule damage without exposing patients to a less effective treatment or to extended toxicity within large clinical trials.

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