

Journal of Andrology, Vol. 26, No. 1, January/February 2005  
Copyright © [American Society of Andrology](#)

# Cisplatin-Induced Long-term Failure of Spermatogenesis in Adult C57/Bl/6J Mice

PRAGATI SAWHNEY<sup>\*</sup>, C. JOHN GIAMMONA<sup>\*</sup>, MARVIN L. MEISTRICH<sup>†</sup> AND JOHN H. RICHBURG<sup>\*</sup>

*From the <sup>\*</sup> Division of Pharmacology and Toxicology, College of Pharmacy, the University of Texas at Austin, Austin, Texas; and the <sup>†</sup> Department of Experimental Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas.*

Correspondence to: Dr John H. Richburg, the University of Texas at Austin, College of Pharmacy, PHR 5.218C, 1 University Station, A1915, Austin, TX 78712-0125 (e-mail: [john\\_richburg@mail.utexas.edu](mailto:john_richburg@mail.utexas.edu)).

Exposure to cisplatin results in impaired spermatogenesis, azoospermia, and, sometimes, permanent infertility in male patients. The mechanism(s) by which cisplatin induces damage to testicular cells is poorly understood. We previously reported that acute exposure to cisplatin results in elevated germ cell apoptotic rates and that this indicates long-term damage to the seminiferous epithelium. Here, we present data that implicate an injury to Sertoli cells as a possible mechanism to explain an elevated rate of germ cell apoptosis and consequent infertility. Normal adult C57/Bl/6J mice were exposed to 1, 2, or 4 rounds of 1, 2.5, or 5 mg/kg cisplatin in a regimen designed to resemble clinical chemotherapeutic exposure (1 injection daily for 5 days with a recovery phase of 16 days between cycles). A dose-dependent reduction in testicular weight due to germ cell loss was observed. While exposure to 1 mg/kg caused only temporary germ cell depletion, higher doses (2.5 and 5 mg/kg) revealed widespread testicular atrophy as evidenced by gaps in the epithelium due to cytoplasmic vacuolization and loss of differentiating germ cells. Although the acute loss of germ cells by apoptosis can result in temporary infertility, the testis has the ability to repopulate itself with mature cells, provided the stem germ cell population remains unharmed. Here, we demonstrate that a sustained disruption of spermatogenesis occurs despite the continued presence of stem spermatogonia in the seminiferous epithelium. These results suggest that cisplatin-induced germ cell loss may occur, in part, as a result of Sertoli cell injury-dependent alterations in germ cell microenvironment.

Key words: Apoptosis, testis, germ cell, Sertoli cell

This article has been cited by other articles:

## This Article

- ▶ [Full Text](#)
- ▶ [Full Text \(PDF\)](#)
- ▶ [Alert me when this article is cited](#)
- ▶ [Alert me if a correction is posted](#)

## Services

- ▶ [Similar articles in this journal](#)
- ▶ [Similar articles in PubMed](#)
- ▶ [Alert me to new issues of the journal](#)
- ▶ [Download to citation manager](#)

## Citing Articles

- ▶ [Citing Articles via HighWire](#)
- ▶ [Citing Articles via Google Scholar](#)

## Google Scholar

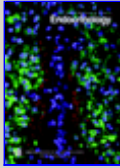
- ▶ [Articles by Sawhney, P.](#)
- ▶ [Articles by Richburg, J. H.](#)
- ▶ [Search for Related Content](#)

## PubMed

- ▶ [PubMed Citation](#)
- ▶ [Articles by Sawhney, P.](#)
- ▶ [Articles by Richburg, J. H.](#)



I. Fenic, H. M. Hossain, V. Sonnack, S. Tchatalbachev, F. Thierer, J. Trapp, K. Failing, K. S. Edler, M. Bergmann, M. Jung, *et al.*  
In Vivo Application of Histone Deacetylase Inhibitor Trichostatin-A Impairs Murine Male Meiosis  
J Androl, March 1, 2008; 29(2): 172 - 185.  
[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)



G. Shetty, C. C. Y. Weng, S. J. Meachem, O. U. Bolden-Tiller, Z. Zhang, P. Pakarinen, I. Huhtaniemi, and M. L. Meistrich  
Both Testosterone and Follicle-Stimulating Hormone Independently Inhibit Spermatogonial Differentiation in Irradiated Rats  
Endocrinology, January 1, 2006; 147(1): 472 - 482.  
[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)



W. Albrecht and M. De Santis  
Innovative Mouse Model for Postchemotherapy Fertility Evaluation  
J Androl, March 1, 2005; 26(2): 169 - 169.  
[\[Full Text\]](#) [\[PDF\]](#)