

SPECIAL REPORT from Dr. Bruce R. Gilbert

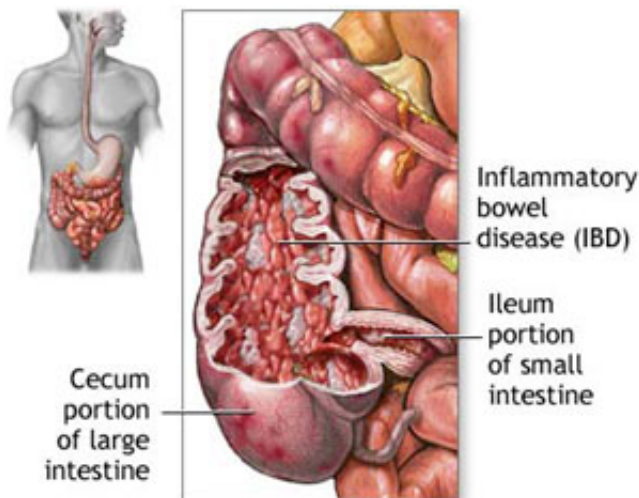
New Indication for Sperm Banking

Drug Treatment for Inflammatory Bowel Disease

Great Neck, New York Jul 12, 2004 It is well known that men treated for inflammatory bowel disease with Sulfazalazine have drug related impairment in sperm quality that often persists after cessation of the drug. This had prompted pharmaceutical companies to develop other "sperm friendly" treatment options.

The most frequent age of onset of the inflammatory bowel diseases including idiopathic chronic inflammatory bowel disease (IBD), Crohn's disease (CD) and Ulcerative Colitis (UC) is between 15 to 30 years of age. This range, of course, coincides with the peak reproductive years. Therefore, it makes good sense that the effect on male fertility, of any drug treatment, should be known. I am focusing on Azathioprine and 6-Mercaptopurine (6-MP) since they are effective immunosuppressive agents commonly used for the long term control of UC and CD in the steroid dependent patient.

Recently, several patients with inflammatory bowel disease have been referred to me for sperm banking prior to and after undergoing treatment with 6-Mercaptopurine or Azathioprine. Each presented with markedly impaired semen quality following treatment. Currently, there is no mandate for sperm banking when initiating therapy with these immunosuppressive agents. However, my review of the literature suggests a significant adverse effect of these drugs on sperm number, quality and function, as well as disturbing animal data on possible genetic damage to sperm.



The Data

Azathioprine is converted to 6-mercaptopurine which acts to decrease cell metabolism and DNA biosynthesis. A study by Russell and Hunsicker (Study of the base analog 6-mercaptopurine in the mouse specific-locus test., *Mutat Res.* 1987 Jan;176(1):47-52.) found that in mice 6-Mercaptopurine caused chromosomal damage (both structural and numerical) in all stages of development of the male germ-cell.

This data was again confirmed by Witt and Bishop (Mutagenicity of anticancer drugs in mammalian germ cells., *Mutat Res.* 1996 Aug 17;355(1-2):209-34). In a study in rats, a dose dependent decrease in sperm concentration, damage to the seminiferous tubules and a lowering of testosterone was found with Azathioprine therapy (Iwasaki M, Fuse H, Katayama T., The effects of cyclosporin azathioprine and mizoribine on male reproduction in rats, *Nippon Hinyokika Gakkai Zasshi.* 1996 Jan;87(1):42-9). Also, in a study in mice, spermatogenesis and fertility was also decreased (Sykora I. Dominant-lethal test of 6-mercaptopurine: dependence on dosage, duration and route of administration. *Neoplasma.* 1981;28(6):739-46).

There is some, but unfortunately not much data available on the effect of these agents on sperm production and sperm function in man. A study by Dejaco et al suggested that men treated with Azathioprine have no change in semen quality and implied that fertility was also unaffected (*Gastroenterology.* 2001 Nov;121(5):1048-53. Azathioprine treatment and male fertility in inflammatory bowel disease. *Comment in: Inflamm Bowel Dis.* 2002 May;8(3):234-5). Unfortunately in this study, paired data wasn't examined. In contrast, a case study by Sills and Tucker found markedly impaired semen parameters in a single patient who had conceived twice with his partner prior to three months of therapy with 6-MP (First experience with intracytoplasmic sperm injection for extreme oligozoospermia associated with Crohn's disease and 6-mercaptopurine chemotherapy. *Asian J Androl.* 2003 Mar;5(1):76-8).

This limited data presents a compelling case for sperm banking in reproductive-aged men prior to undergoing long term treatment with Azathioprine or 6-Mercaptopurine. I also believe we need more data in humans. Many questions remain unanswered, a few of which come to mind: Are the effects of these drugs in man similar to those found in rodents? Is it the medication used or the underlying disease that has a greater effect on sperm? Are the effects seen reversible, and if so over what time period? Additional research is needed to define the effect of these (and other) drugs used in the treatment of inflammatory bowel disease in reproductive-aged men.

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New York Cryo is Long Island's only NY State Licensed Sperm Bank for the long term storage of semen specimens which is also accredited by the American Association of Tissue Banks (AATB).

We are one of only ten accredited reproductive tissue banks in the country...and one of only two in New York State!

Our Great Neck facility is available 7 days a week for consultation, collection of specimens and cryopreservation. In addition, hospitalized patients can have semen specimens cryopreserved prior to urgent/emergent surgery, chemotherapy or radiation. We are available at all times to pick up specimens and consult with prospective patients...just call.

Website: <http://www.NewYorkCryo.com>

About Dr. Gilbert's Medical Practice

The practice is a multi-dimensional private Urology practice located in Great Neck on the North Shore of Long Island approximately 15 miles east of New York City.

The practice specializes in male fertility, male and female sexual function and medical acupuncture. On-site is a New York State licensed Andrology laboratory and Sperm Bank. We also have several ongoing Clinical Urology Research Studies.

Patient care is our primary concern. We are always available for questions or consultation. Our web site offers a wealth of information on many topics and is regularly updated with the latest medical data available.

Website: <http://www.brucegilbertmd.com>

New York Cryo and the Men's Fertility Laboratory

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