Chapter 2
Fertility Management for Women with Cancer

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Cancer is now a disease with a variety of treatment options that are leading to longer and more productive lives in survivors. More than 200,000 men and women under the age of 45 years are diagnosed with cancer annually. However, challenges remain for cancer survivors striving to return to normalcy. Infertility can be a consequence of many of the more aggressive chemo- and radiation therapies that prolong and save lives. The ability to easily preserve sperm prior to cancer treatment provides hope at the time of diagnosis to have families later in life for male survivors. A notable example is Tour de France winner Lance Armstrong, who has three children conceived by using sperm collected and frozen days before he underwent the massive chemo- and radiation therapy that saved his life. When faced with a similar devastating diagnosis, women and girls have the same hope for recovery but lack the fertility preservation options that Mr. Armstrong was given. Unlike sperm, the female germ cell, the oocyte or egg, must be retrieved surgically. Moreover, the vast majority of collected oocytes will be immature at collection and cannot be used immediately by a woman who is ready to start a family.

Many of the principles and technologies discussed in this chapter in the context of cancer patients can equally well be applied to women with benign pelvic diseases that threaten their fertility. For example, some women with severe endometriosis or pelvic infection may need to have their ovaries removed as a part of radical surgical treatment for these diseases. In others, during the process of surgically removing ovarian cysts, germ cells can be damaged, thus reducing the woman’s fertility. Further, the treatment of benign diseases such as Bechet syndrome and glomerulonephropathies may require chemotherapy that could, just as with cancer patients, reduce ovarian reserve.

Ovarian Physiology

The process of germ cell (oocyte) loss from mid-pregnancy to menopause is a normal physiologic process (Fig. 2.1). At mid-pregnancy, a female fetus has about seven million germ cells that comprise the ovarian reserve. With atresia, this number is reduced to about one million per ovary at birth. The decline in germ cell...
number continues such that by puberty there is a total of about 300,000 germ cells, and by menopause, around 1,000 remain. Thus, prior to spontaneous ovulation, there is a degenerative process of oocyte attrition, the mechanism of which is not well understood. With the onset of menstruation and normal ovulatory function, it is estimated that dozens of oocytes are consumed monthly to achieve a single ovulation. At around age 35–38, there is acceleration in oocyte atresia until the ovarian reserve is exhausted and menopause ensues (Fig. 2.2).

It is evident that, in women, the complete loss of the germ cell population is a result of both spontaneous ovulation as well as an undefined atretic mechanism. While unknown environmental and epigenetic phenomena may be harmful to germ cells, several causative factors such as cancer treatment, including chemotherapy and radiation, as well as elective social activities such as smoking, may accelerate the rate of oocyte loss, thus decreasing fertility and bringing the age of menopause forward.

The decline in germ cell number is mirrored by a decline in female fertility. With increasing age, particularly after the age of 35 years, a woman’s natural fertility and chance of success with assisted reproduction declines. Since there can be quite substantial variations in fertility with age, the clinical assessment of a woman’s “ovarian reserve” typically involves not just age but also changes in the release of pituitary follicle-stimulating hormone (FSH) and corresponding production of estradiol and inhibin B by granulosa cells within ovarian follicles. As the germ cell pool declines and fewer ovarian follicles are present, there is a decrease in ovarian inhibin B production. Inhibin B provides negative feedback to FSH secretion and hence an increase in FSH can be detected as a result of declining inhibin B. Since FSH values vary during the menstrual cycle, it is standard practice to obtain a measurement of serum FSH on day 3 of the menstrual cycle. An estradiol

**Fig. 2.1** Photomicrographs illustrating the age-related decline of primordial follicle numbers in human ovaries (From Erickson GF. An analysis of follicle development and ovum maturation. Sem Reprod Endocrinol 1986; 4:233–254 by permission of Thieme Medical Publishers, Inc.)