1. Are women with primary amenorrhea from premature ovarian failure equally likely to ovulate as are women with secondary amenorrhea from premature ovarian failure?

Response from Dr. Robert W. Rebar:

Because women with primary amenorrhea and premature ovarian failure are more likely to have forms of gonadal dysgenesis, with an abnormality in the X chromosome, they are probably less likely to ovulate as a group than those with secondary amenorrhea and premature ovarian failure. However, no direct comparisons have ever been reported.
2. Regarding spontaneous pregnancies in patients with premature ovarian failure: are many of these pregnancies achieved without exogenous hormones? Can exogenous estrogen alone reduce follicle resistance to gonadotropins, thereby allowing for follicle development and ovulation? What is the strength of the evidence that oral contraceptives, commonly used for hormone therapy in young women, are ineffective in providing contraception for these patients?

Response from Dr. Robert W. Rebar:

It is important to state at the outset that there really have been no trials of any magnitude with women with premature ovarian failure. Almost all of the studies are retrospective or observational. There seem to be about as many pregnancies reported while women are taking exogenous hormones, either in the form of oral contraceptives or replacement therapy, as there are while women are not taking any hormones. Why that is remains unknown.

3. Are rates of follicle activity and pregnancy the same among women with premature ovarian failure due to radiation therapy or chemotherapy compared with rates in women with spontaneous premature ovarian failure?

Response from Dr. Robert W. Rebar:

There are no good studies comparing rates of follicle activity and pregnancy among women with premature ovarian failure who underwent radiation or chemotherapy with rates in women with spontaneous premature ovarian failure. Because the rate of premature ovarian failure in women undergoing radiation therapy or chemotherapy is dependent on the dosage and upon the age of the woman at time of therapy, we might expect that some of these treated groups might have higher rates of subsequent pregnancy than those women with spontaneous premature ovarian failure. In general, the younger the woman at the time of radiation therapy
and/or chemotherapy, the less likely is permanent premature ovarian failure. There is increasing interest and research in attempting to develop appropriate means of preserving fertility in women who will undergo radiation therapy and/or chemotherapy for cancer. Except for the freezing of embryos derived from oocytes collected prior to beginning therapy, all such approaches must be considered experimental, with low success rates, at this time.

4. Is there any role for ovulation induction in women with premature ovarian failure who show signs of spontaneous follicular activity? Is it reasonable to consider clomiphene therapy in a woman with progestin-withdrawal bleeding or increased serum luteinizing hormone levels?

Response from Dr. Robert W. Rebar:

The few small trials with clomiphene citrate and exogenous gonadotropins that have been conducted do not indicate any higher rates of ovulation than those that occur spontaneously. It is not reasonable to use these agents in women diagnosed with this disorder. The real enigma here is the need to counsel women with premature ovarian failure who do not desire pregnancy and who are sexually active about the small but real possibility of pregnancy without the use of barrier contraception.
5. Although serum luteinizing hormone levels and pelvic ultrasonograms may indicate current follicular activity in women with hypergonadotropic hypogonadism, do they have any predictive value for future follicular development or pregnancy?

Response from Robert W. Rebar:

There is insufficient information to adequately answer this question. There seem to be reports of cases with women who have no evidence of follicular activity for years who unexpectantly conceive. Clearly pregnancy is impossible in the absence of follicular activity. That is probably the best that we can say.

6. How helpful is bone densitometry in patients under 25 years old? How would the results influence treatment choices?

Response from Dr. Robert W. Rebar:

There is little information about what is normal regarding bone density in younger women. Data are accumulating. In the absence of data, it is best to remember that maximal bone density is unlikely to be achieved in the absence of estrogen and to provide exogenous estrogen to all women in whom the diagnosis of premature ovarian failure is established. It is also important to ensure adequate intake of vitamin D and calcium. There is no indication for the use of other anti-resorptive agents in affected young women, regardless of the bone density.
7. Describe how your treatment of hypoestrogenic symptoms in young women with premature ovarian failure differs from treatment in women more than 50 years of age.

**Response from Robert W. Rebar:**

*Generally speaking, young women require about twice as much exogenous estrogen as do postmenopausal women. As is true for all women, the correct dose is determined by using the woman as her own bioassay. Breast tenderness is commonly experienced by hypoestrogenic women when first provided estrogen but typically disappears in a few weeks. Persistence usually indicates that the dose is too high for the individual woman. Dose is also determined by effectiveness in alleviating the other symptoms commonly associated with estrogen deficiency, including hot flashes, night sweats, and dyspareunia. Either 1.25 mg of conjugated estrogen or 100 microgram patches of 17β-estradiol is usually sufficient for young women with premature ovarian failure. There is no reason to measure circulating estrogen levels in a woman after initiation of treatment with exogenous estrogen.*