



Early Menopause due to Chemotherapy

Chemotherapy is usually administered as part of cancer treatment but may also be given to women with severe connective tissue disorders such as systemic lupus erythematosus or kidney disease such as Wegener's granulomatosis. Survival rates for many cancers in women of reproductive age are increasing. However, many treatments used to combat the disease carry a substantial risk for future infertility. Chemotherapy is toxic to the ovaries causing loss of eggs and destruction of the supporting ovarian tissue. This may cause temporary cessation of menstrual periods or early menopause which can develop quickly or gradually.

Menopause in women younger than 40 years of age is called premature menopause or premature ovarian failure. Menopause occurring between 40-45 years of age is called early menopause. Diagnosis of ovarian failure due to a premature or early menopause has long term physical and psychological consequences, so women may need emotional support and long term medical follow-up. The following information does not apply to women who are having radiotherapy as part of their cancer treatment. The information here does not replace medical advice and may or may not be relevant to your own circumstances.

The impact of chemotherapy on the ovaries

- A woman is born with a limited number of eggs in her ovaries. As she ages, this supply of eggs naturally diminishes. Some chemotherapy can damage or destroy eggs, reducing the supply. The effects of chemotherapy on reproduction vary with the woman's age, the drugs used and the total dosages.
- The frequency of early menopause after chemotherapy is difficult to determine, because there are many possible influences, and the rate varies with the age of the woman and the type of chemotherapy. Depending on the type of chemotherapy, the age of the woman and her number of eggs, the incidence of early menopause ranges from 0 to 100%. Rates of early menopause range from 21 to 71% in younger women, and 49 to 100% in older women.
- There are many chemotherapy drugs that can affect reproductive function. A group of drugs called alkylating agents is the most likely to affect eggs and ovarian function. Cyclophosphamide, one of the most common drugs used in breast cancer treatment, is an alkylating agent. Taxol, also used in the treatment of breast cancer, may also affect ovarian function. The risk of menopause increases with age, most likely because older women have fewer eggs than younger women. For example, chemotherapy with cyclophosphamide, methotrexate and 5 fluorouracil (CMF – commonly used for the treatment of breast cancer) will usually result in loss of ovarian function in 33% of women under age 30, 50% of women aged 30-35, 75% of women aged 35-40 and 95% of women over age 40. Chemotherapy combined with radiotherapy affecting the ovaries is also associated with an increased risk compared to chemotherapy alone.

What are the consequences of loss of ovarian function?

When the ovaries stop functioning, they not only stop producing eggs but also stop producing female hormones – oestrogen and progesterone. This leads to:

- Loss of fertility, which for many women may be devastating.
- Loss of menstrual periods. This may be the first indicator of ovarian failure. Sometimes in the lead-up, the time between periods becomes longer or erratic. However, there is no specific menstrual pattern which signals that early menopause is about to occur



- Symptoms of oestrogen deficiency. These include hot flushes, mood change, sleep disturbance, joint aches, dry vagina or poor lubrication during sexual arousal. These symptoms may occur even while the woman is still having menstrual periods. The onset of symptoms may occur gradually or suddenly.
- Emotional turmoil. Women often feel confused, sad, jealous of other women's pregnancies or old before their time. Psychological counseling can ease this distress. Support from the woman's partner, family and friends is important.
- Long-term consequences include osteoporosis and, possibly, accelerated hardening of the arteries.
- Women must also cope with the diagnosis of cancer or severe medical illness which has necessitated the use of chemotherapy and the related long term consequences.

Diagnosis of Early Menopause

- At present there is no specific predictor of early menopause although several biochemical markers are under investigation.
- The diagnosis of early menopause may take several months to confirm. Evaluation of symptoms and blood tests will be required before a diagnosis of early menopause can be certain.
- Diagnosis can be stressful and difficult decisions have to be made. A woman should feel comfortable talking with her doctor as several consultations may be needed to establish the best management of this condition and plan for the future.

Fertility issues:

- For many young women, childbearing is only a distant possibility some time in the future, so making such decisions can be overwhelming, especially after a recent diagnosis of cancer. It is important to seek help and support from doctors, family and friends, professional counselors and support groups when necessary.
- Protecting ovarian function and fertility potential should be considered prior to commencing chemotherapy. Giving chemotherapy at a particular stage of the menstrual cycle, administration of potentially "ovarian protective" drugs (such as the oral contraceptive pill or Gonadotrophin-releasing hormone agonists) to women before chemotherapy have been tried but at present there is no established method of protecting the ovaries from the toxic effects of chemotherapy.
- The option of freezing embryos/eggs or ovarian tissue for future fertility should be considered. The best outcomes for future fertility are obtained when a woman goes through an IVF cycle in which mature eggs are removed, fertilised with sperm and embryos are, frozen and stored. Success rates for pregnancy in the future depend most on the age of the woman at the time her eggs are collected, whether or not she has a male partner and any prior chemotherapy. The advantage of freezing eggs or ovarian tissue is that, unlike making embryos, no sperm are required. The disadvantage is that these procedures are still experimental. Pregnancy rates from egg freezing are reported to be less than 3%. To date, there has been one pregnancy from frozen ovarian tissue world-wide.
- The desirability of becoming pregnant where a woman has cancer or severe medical illness is a decision she needs to consider after consultation with her treating doctors.
- Spontaneous pregnancy after chemotherapy is not common but to date no increase in fetal abnormalities has been reported.



- For those women who have developed early menopause, some women decide to opt for a childfree life, others may want to adopt or foster children. Some women try IVF or drugs to stimulate egg production but these have a low chance of success. Most women with early ovarian failure who achieve pregnancy use eggs from another woman donated either anonymously or by a friend or relative. All donors are screened for transmissible diseases which reduces the risk but does not take it away completely. Another option is achieving pregnancy using embryos donated by another couple.
- Some women who have chemotherapy remain fertile, but if a pregnancy is not desired or is inadvisable contraception should be used.

Hormone (replacement) therapy:

- After breast or endometrial cancer most women are advised to avoid medication containing hormones.
- Young women with early menopause may elect to take hormone (replacement) therapy (HT/HRT) to relieve the symptoms of oestrogen deficiency, and often higher doses may be required compared with older women. (See AMS information sheet: Menopause – Combined Hormone Replacement Therapy). The decision to use HT/HRT should be undertaken following discussion with her doctors as the presence of certain illnesses or cancers prevents the use of oestrogen therapy. For example, oestrogen therapy should usually be avoided after breast cancer. In this setting, non-hormonal treatments of hot flushes or vaginal dryness may be useful (see AMS Information Sheet: Non Hormonal Treatments for Menopause). Where HT/HRT is used then current advice is to continue this until the age of average menopause at 50 years.
- Options include patches, creams or implants of oestrogen. Oestrogen combined with a progestogen is required if a woman has not had a hysterectomy (See Menopause – Combined Hormone Replacement Therapy). In addition, regular vaginal oestrogen can be used to improve comfort during sexual activity.
- The combined oral contraceptive pill (OCP) can be used as a replacement hormone up to the age of 50 if the woman has no significant risk factors (such as a clotting tendency, past clots or is a current smoker and older than 34 years) The decision to use the OCP should be undertaken following discussion with her doctors as the presence of certain illnesses or cancers prevents the use of oestrogen therapy. For example, the OCP should usually be avoided after breast cancer. In this setting, non-hormonal treatments of hot flushes or vaginal dryness may be useful (see AMS Information Sheet: Non Hormonal Treatments for Menopause)

Prevention of bone loss:

- Osteoporosis (thin bones which fracture easily) is common in women who have had oestrogen deficiency at a young age. Certain drugs used in chemotherapy (such as high dose corticosteroids) and breast cancer treatment (such as aromatase inhibitors) can cause bone loss. Measurement of bone density is an important part of managing premature menopause. It is important to check bone mineral density every two to four years, particularly if the woman is not taking HT/HRT.
- A healthy lifestyle is important to maintain bone health. Women with early menopause should avoid smoking, engage in regular weight-bearing exercise, and ensure adequate dietary intake of calcium and vitamin D.
- If a woman suffers a bone fracture from osteoporosis, there are several proven therapies available to reduce her risk of further fractures.



Prevention of cardiovascular disease:

- Years of oestrogen deficiency may accelerate a young woman's chance of developing hardening of the arteries, which may lead to a heart attack or stroke; however this is still controversial.
- Women with early menopause should avoid risk factors for vascular disease by not becoming overweight, by exercising regularly, avoiding smoking, controlling diabetes and high blood pressure, and preventing high levels of cholesterol and triglycerides (fats in the blood).

Cognitive function

- Memory disturbance associated with chemotherapy is well recognised; however, the effect of long term oestrogen deficiency on memory and brain function is unclear at present.

Further information:

- ACCESS: Australia's National Infertility Network: www.access.org.au
- National Breast Cancer Centre: www.nbcc.org.au
- The Cancer Council of Australia: <http://www.cancer.org.au>
- The International Premature Ovarian Failure Association (IPOFA) website: www.pofsupport.org;
- American Cancer Society: <http://www.cancer.org>
- The Daisy Network Premature Menopause Support Group: www.daisynetwork.org.uk;
- www.endocrineonline.org.uk
- Fertile Hope website: <http://www.fertilehope.org>
- American Society of Clinical Oncology: <http://www.peoplelivingwithcancer.org>
- Resolve: The National Infertility Association website: www.resolve.org

February 2008