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Hormone Replacement Therapy after Prophylactic Adnexectomy

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In France, the National Collective Statement from the INSERM [1] recommends a prophylactic adnexectomy (PA) in women having an increased ovarian cancer risk due to mutations in *BRCA1* or *BRCA2* either at 40 years of age or at 35 years of age if the woman has decided she no longer wants children. PA can reduce the risks of ovarian cancer by more than 90% and breast cancer by more than 50%. However, the lack of oestrogen production caused by PA has numerous consequences. These are more pronounced in young women and include hot flushes, vaginal dryness, sexual troubles, joint stiffness and in the long term osteoporosis. Recent data from the large randomised American WHI Study [2, 3] have led the medical community to re-evaluate the benefits and risks of hormone replacement therapy (HRT) and to modify their prescription practices. As data on the HRT products used in France are not available, French agencies have recommended that in the general population HRT should be used at the lowest dose and for the shortest duration possible, and then only for menopausal problems [4]. Currently, many women in France are reluctant to use HRT because of the results of these studies. Gynaecologists also are reluctant to prescribe HRT due to the risk of legal proceedings in cases of cancer. This reluctance is much greater for women with increased risk of breast cancer. Although the Markov Model for predisposed women shows a favourable benefit/risk ratio for short-term HRT prescription, this analysis was carried out without precise data for the effect of HRT on predisposed women [5]. Moreover, breast cancer in women undergoing HRT may be falsely attributed to HRT due to the high incidence of breast cancer associated with *BRCA1/2* mutations. We have observed that PA is relatively well accepted in peri-menopausal women (for example after chemotherapy), although some young women still refuse or delay PA despite there being a high incidence of ovarian cancers in their family.

At the Curie Institute, we take into account the preferences of women after they have been thoroughly informed:

1. We recommend PA to women at 40 years of age if they have a *BRCA1* mutation, or a *BRCA2* mutation and a family history of ovarian cancer, and at 50 years of age if they have a *BRCA2* mutation without a family history of ovarian cancer.
2. In women unaffected by breast cancer, we give very complete information on the benefits and risks of HRT and alternatives, such as symptomatic treatments for hot flushes, vaginal oestrogens, and non-hormonal treatment for osteoporosis.
3. We always propose psychological support to allow each woman to estimate and anticipate the consequences of PA.
4. In case of uterine diseases such as fibroma, surgeons may propose a hysterectomy as well as PA, in which case oestrogens can be prescribed alone and progestins can be avoided (4).
5. After PA, a gynaecological consultation is offered: HRT is given only to thoroughly informed women who really want it and have accepted PA with the assurance that they would have HRT afterwards. HRT is also offered to women who have had a prophylactic bilateral mastectomy. For other cases,

clinical follow-up is proposed, and osteodensitometry is prescribed. If menopausal problems occur, alternative treatments are proposed first. For persistent problems, HRT is prescribed at the lowest dose for as long as the woman wishes. It is strongly recommended that treatment be stopped at the natural age of menopause, around 50 years of age.

We think that over-alarmist information on menopause and strongly held beliefs against HRT lead some young women to refuse or delay an intervention that may save their life. Therefore, we advocate clear information, honest dialogue, and shared decision making with each woman.

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