



Gene Trek

Familial Cancer Unit Newsletter



November 2007



From the editor

Dear Readers,

Welcome to the second edition of Gene Trek for 2007. In this issue our feature article is "Non-hormonal therapies for menopausal symptoms" by Prof Alastair MacLennan and Dr Alice MacLennan. Our Counsellors' corner features information on equivocal genetic test results. We also have our usual Familial Cancer Unit data update, some great website and support group resources, and a healthy carrot, zucchini and date cake recipe.

My name is Kirsty Stallard. I am the new Cancer Genetics Education Project Officer at The Cancer Council SA. It is my pleasure to be the new editor of Gene Trek. I look forward to keeping you up to date with the latest developments in cancer genetics. If you have any feedback about this edition or any suggestions for future topics, I'd love to hear from you.

Kind regards,
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Non-hormonal therapies for menopausal symptoms

Oestrogen deficiency is the cause of most menopausal symptoms and tailored oestrogen therapy is the most efficient way to alleviate these symptoms. To tailor oestrogen therapy, the oestrogen dose for a particular woman is trialled until an optimal dose is achieved. An optimal dose is one in which the individual gets the best relief from their menopausal symptoms and any side effects of the treatment are manageable.

Hormone replacement therapy (HRT) has been used for many years for the treatment of menopausal symptoms. HRT contains a synthetic combination of the female hormones, progesterone and oestrogen. Although there are no adequate long term trials, preliminary evidence

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suggests that the use of HRT may increase the risk of breast cancer and it appears that the progestogen component of HRT causes the increase in risk.

Often women with a personal history of breast cancer or major genetic risk factors may have been told to avoid hormone replacement therapy (HRT) as it could further increase their risk of breast cancer. In these women it is highly appropriate that the effectiveness of non-hormonal therapies be explored in the first instance. However, it should be noted that if symptoms remain debilitating, oestrogen only therapy may still be a possible option if tailored to the individual by an expert in the menopause.

Alternative and complementary medicines

There is a vast array of both prescription and over-the-counter medications designed to target menopausal symptoms. Many over-the-counter medicines are known as alternative or complementary medicines.

'Registered' products are those that have been scrutinised by a federal authority for safety and efficacy. They are labelled with an 'AUST R' number on the pack. Products with an 'AUST L' number on the pack are 'Listed' products and they have not been tested in accordance with the appropriate guidelines.

There are many 'Listed' products that are sold over-the-counter for menopausal complaints. They often contain traditional herbal constituents and some are derived from plant oestrogens (phytoestrogens). To date, these products have not been shown to provide significant relief from menopausal symptoms in the majority of women and the long-term effect of phytoestrogens on breast cancer risk has not been adequately studied.

We caution the use of alternative, complementary or 'Listed' medicines for those at increased risk of breast cancer. This caution includes so called 'bioidentical' or natural HRT products compounded by chemists. These locally compounded preparations are not Registered, Listed or tested, and there are concerns about their safety. It is known that some alternative products eg Black Cohosh (Remifemin) have been associated, on rare occasions, with liver failure. We encourage people to seek medical advice before pursuing such therapies.

Non-medicinal alternatives

To date, there is little evidence from clinical trials to suggest that the use of non-medicinal alternative therapies such as yoga, acupuncture, exercise, meditation, homeopathy, naturopathy, iridology or Reiki provide significant relief from menopausal symptoms in the majority of women.

Common sense intervention

During menopause, the body's thermostat often functions poorly causing inappropriate sweating, flushing, shivering or palpitations. By avoiding triggers for hot flushes like cigarette smoke, alcohol, caffeine and extreme temperature changes, the symptoms can be minimised.

Prescription non-hormonal medications

There are some non-hormonal medications available by prescription that may be used to specifically target certain menopausal symptoms like hot flushes, depression, joint pain, urinary symptoms and sleeplessness.

An example is Venlafaxine (Efexor) which may help reduce hot flushes and some symptoms of depression. Although not as effective as oestrogen in clinical trials, some individuals have a better response than others. Side effects are common at the beginning of therapy and include dry mouth, dizziness, nausea and headache.

Other prescription drugs that may reduce hot flushes are Clonidine (used for high blood pressure) and Gabapentin (a neurological drug). These therapies have to be individualised and only reduce hot flushes.

Sexual function

A common menopausal symptom is vaginal dryness and discomfort during intercourse. Non-hormonal lubricants are a first option. However, if these are not effective, local low dose vaginal oestrogen therapy may be an alternative. There are no adequate clinical trials in the use of this type of therapy in women with high breast cancer risk, but since therapy does not raise blood oestrogen levels long-term, it is unlikely to increase the risk of breast cancer further in these women.

Research study

Tibolone (Livial) is a synthetic product which has an oestrogenic, progestogenic and androgenic action. It is not a true HRT and has different effects from HRT, especially in the breast where it does not increase breast density on mammography and is not associated with breast tenderness. The result of a 3 year trial of Tibolone in women with a previous history of breast cancer (LIBERATE) will be reported in mid-2008. Tibolone reduces fracture risk and may improve libido.

Non-hormonal treatment of other post-menopausal medical complaints

Other medical disorders that increase after menopause are osteoporosis, heart disease and memory loss.

To prevent osteoporosis, all women should ensure they have an adequate calcium and vitamin D intake. Osteoporosis can be successfully treated with non-hormonal therapies such as Raloxifene (EVISTA), which actually reduces some breast cancers, or bisphosphonates (eg FOSAMAX).

Cardiovascular disease is best treated with lifestyle intervention, for example smoking cessation, weight loss, exercise and the treatment of high blood pressure and cholesterol.

Loss of memory and the risk of dementia are currently not easily preventable with non-hormonal therapies.

Conclusions

Menopausal therapy should be individualised and in women at high risk of breast cancer, this may be best done at a menopause clinic. Some women experience more relief from non-hormonal therapies than others and therapy usually needs to be tailored over several visits.

New hormonal and non-hormonal therapies that target menopausal symptoms but do not increase the risk of breast cancer are currently being studied.

Authors:

Professor Alastair MacLennan – Head of the Discipline of Obstetrics and Gynaecology, The University of Adelaide.

Dr Alice MacLennan – President of the Australasian Menopause Society.

References:

Statement on the management of the menopause after breast cancer (C-Gyn 15, July 2007) by the Royal Australian and New Zealand College of Obstetricians and Gynaecologists in conjunction with the Breast Section of the Royal Australian College of Surgeons.

Editor's note: Article has been edited for publication purposes; a copy of the original transcript is available on request from genetics@cancersa.org.au

Your place

My name is Anne and in March 2004 I was diagnosed with breast cancer. I had decided not to have children as cancer was in my mum's side of the family. It was something I was aware of and thought about now and then, but at the age of 35 I thought I still had time. My mum had breast cancer at the age of 38, two of her sisters also had breast cancer and her brother had bowel cancer. My mum had hoped it would stop in her generation but unfortunately it didn't. My cousin was then diagnosed with breast cancer and now me.

I have a sister who has not had cancer, but had been to the Familial Cancer Unit because she was worried about our strong family history. She told me that now I had developed cancer, I could be tested to see if I have an abnormal gene that can cause cancer. Then if I have the gene, other members of the family could be tested to see if they have it too. My sister wanted me to be tested because it could help her daughter in the future. I agreed and thought with all the history of cancer in my family that I would be told that I had the abnormal gene.

After a few months the test results came back. I got a phone call to say that they had found an abnormality in my genes but they could not say for sure if it had caused my cancer. This meant that my results were equivocal and that other family members could not be tested.

At first I was surprised because I was so sure that I would have the gene. I thought the test results would

be as simple as black and white, you either had it or you didn't. My surprise then turned to disappointment and frustration. I was disappointed that I could not help my niece by helping her find out if she had the gene and what her choices were. I was frustrated because there was an abnormality there and they could not give me a *yes* or *no* answer.

Maybe if they could tell me that I didn't have the gene there would be less chance of my children having breast cancer and I would consider having children. It is the not knowing that is so hard. When you are tested for something, you hope to get an answer one way or the other. When you don't, you feel left in limbo. All you can do is hope that one day they will come up with other ways of testing, so I can get the answer I am waiting for.

Editor's note:

Client's name has been changed for publication purposes. If you wish to share your story please let your genetic counsellor know.

Counsellors' corner



The genetic counsellors from the Familial Cancer Unit
From left: Jacquie Armstrong, Debbie Trott, Sally Russell
and Vanessa Huntley

Equivocal genetic test results

Anne's story is a common experience in Australia and internationally. We share her frustration and disappointment at not being able to provide her family with a useful answer to help them better manage their risk of developing breast cancer in the future.

About 10% of all the families that we initiate genetic testing in receive an equivocal result. An equivocal result means that in the course of screening the known cancer genes, the laboratory finds a change or variation in the gene, but is unable to interpret whether that change is the underlying cause of the family's experience of cancer. In some families, new information over time will tell us that the change is likely to be the cause of cancer, while in others, new information may tell us that the change

found in the gene is likely to represent the normal genetic variation that makes us all unique individuals.

This is a new and evolving field of medicine and there is good cause to be cautious before giving families a definitive answer for their experience. We are conscious that family members may be basing decisions about surveillance, preventative surgery or reproductive decisions on the test results that we provide. This means that we need to be confident in the accuracy of the information we give.

For families who receive an equivocal result, it is very important that relatives still undertake cancer screening. The clear message for these families is that a genetic test can only confirm the presence of an underlying genetic cause of the family's cancer experience; it can never take away the family history of cancer. This is the same for families who receive a normal result. Relatives still remain at increased risk of developing cancer, and as such should still undergo the appropriate cancer screening. This advice does not apply in families where an abnormal gene is found and at-risk relatives are able to have pre-symptomatic testing to determine if they have inherited the abnormal gene.

Jacquie Armstrong

Counsellors' update

- In May we held a successful information evening for clients living with bowel cancer risk. Professor Graeme Young concentrated on the medical issues and management, while Professor Lynne Cobiac addressed the nutritional aspects.
- Jacquie flew to Auckland in May to attend the annual Human Genetics Society Association conference. This was a particularly special event for her, as she was awarded her Part II certification in Genetic Counselling – congratulations Jacquie.
- In August Sally and Vanessa attended the Familial cancer: research and practice conference at Couran Cove in Queensland. Sally presented the SA experience of the support groups for carriers of a BRCA mutation, which generated a great deal of interest and discussion from other cancer genetics services in Australia.
- Since our initial pilot of the BRCA carriers support group, we have had three groups of women through the program, with positive feedback after each group. We now plan to run this once a year, with the next group to be held in 2008.

It can take time to adjust to living with an increased risk of cancer and the important people in your life can also be affected. Issues can arise weeks, months or even years later. If there are any issues that you would like to discuss in more detail, for example surveillance recommendations, prophylactic surgery or exploring your feelings, please feel free to contact us at any stage on 08 8161 6995.

Genetic testing in familial breast/ovarian cancer

The discovery of the breast cancer susceptibility genes (BRCA1 & BRCA2) in the mid 90's confirmed the suspicion that a predisposition to develop breast/ovarian cancer can be inherited from your parents.

Everyone carries the BRCA genes as part of their genetic makeup. They play an important role in repairing damaged DNA. However, if you have inherited an abnormal copy of a BRCA gene from one of your parents, you may be at increased risk of developing breast/ovarian cancer.

Typically, the families in which an abnormal BRCA gene is most likely to be found are those where there are multiple affected relatives on the same side of the family and where there is an earlier than usual age of onset of cancer.

Genetic testing attempts to identify any abnormalities in the BRCA genes which may alter their ability to function normally. The testing must be performed on a person affected by the familial cancer to ensure the validity of the result. Genetic testing is a very labour intensive process and therefore an expensive exercise at around \$2000 per test.

The Familial Cancer Unit began offering BRCA genetic testing in 1995 to women with breast/ovarian cancer who fulfilled the National Health and Medical Research Council's (NHMRC) guidelines for 'high genetic risk'.

Over time we have seen a significant decline in the number of BRCA gene abnormalities detected in the women that we test. For this reason it has been necessary to re-evaluate which patients we offer BRCA genetic testing. This represents a challenging task given that there is still a lot to be learnt about the role that genes play in the development of breast/ovarian cancer.

After much analysis, we have chosen to adopt a clinical scoring system which was developed in Manchester (UK) to select patients for BRCA genetic testing (J Med Genet 2004;41:474-480). The Manchester scoring system proved to be the most efficient system when applied to our data and we implemented its routine use in October this year.

It should be noted that not being selected for BRCA genetic testing does not necessarily alter the diagnosis of familial breast/ovarian cancer or the patient's status of high genetic risk. It simply means that we are limiting BRCA genetic testing to patients whose familial breast/ovarian cancer is most likely to be attributed to an identifiable BRCA gene abnormality.

These changes to our testing protocol will not alter the provision of other services that we provide to our patients (like genetic counselling, confirmation of family history and on-going surveillance updates) and it is envisaged that our testing protocol will evolve as more is understood about the genetic influences in breast/ovarian cancer.

For more information please contact the Familial Cancer Unit on 08 8161 6995 or cywhs.famcancer@cywhs.sa.gov.au

Data update from the Familial Cancer Unit

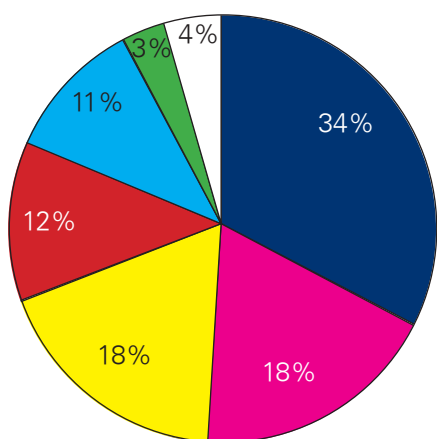
From June 2006 to July 2007 the Familial Cancer Unit had 649 contacts with clients and their family members.

When a client with a family history of cancer but no cancer diagnosis themselves is referred to our service, one of the first things they want to know is 'what is my risk of developing cancer?'

A client's risk of developing cancer is determined by their family history and is assessed using the relevant guidelines which set out criteria to categorise their risk as average, moderate or high.

Once a risk level is ascertained, the likelihood of the client carrying an inherited genetic abnormality which predisposes them to develop cancer is explored. If appropriate and beneficial, genetic testing may be offered and the option to initiate testing is completely up to the client.

The figure below displays the proportions of clients that we saw during the above period according to their genetic risk assessment and genetic testing status. It is interesting to note that an underlying genetic abnormality was confirmed in only 18% of all the clients seen. This reflects how important family history is in predicting cancer risk, as genetic testing provides a clear answer in only a relatively small number of families.



- High risk of cancer determined from family history
- High risk of cancer & abnormal gene identified
- Pre-symptomatic genetic testing performed & no genetic abnormality detected
- Moderate genetic risk from family history
- Support people
- Average genetic risk from family history
- Genetic risk unknown

Healthy eating



Carrot, zucchini and date cake

Preparation: 20 minutes plus
4 hours to stand
Cooking: 1 to 1 ¼ hours

7 serves of vegies in this recipe

Ingredients:

- 2 cups dates, pitted and chopped
- ½ cup bran cereal (e.g. Allbran ®)
- ½ cup untoasted muesli
- 1 ½ cups low-fat milk
- ½ cup brown sugar
- 1 teaspoon cinnamon
- ½ cup low-fat natural yoghurt
- 1 egg, beaten
- 1 cup zucchini, grated
- 1 cup carrot, grated
- 2 cups self-raising flour
- 1 cup wholemeal self-raising flour

Method:

Combine dates, bran cereal, muesli, milk, sugar and cinnamon and allow to stand for 4 hours or overnight. Preheat oven to 180 °C. Line a 23cm square cake tin. Add yoghurt, egg, zucchini and carrot to the date mixture and mix well. Add flour and combine. Pour mixture into tin and bake for 1-1 ¼ hours until firm and browned. Cool on a wire rack.

Serves 12.

Hint

This cake can be frozen. Individually wrap slices for a healthy lunch box treat.

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Resource update

The Cancer Council Helpline 13 11 20

In response to consumer demand, The Cancer Council SA is trialling extended Helpline hours until the end of the year. The Cancer Council Helpline 13 11 20 is now available from 8.30am to 8.00pm Monday to Friday. The trained nurse counsellors can provide information and support and can be reached on 13 11 20 for the cost of a local call.

On the web

NEW on-line breast cancer risk calculator – a new National Breast Cancer Centre (NBCC) initiative that can be completed in a few minutes. Gives the facts about risk factors for breast cancer and provides useful information about lifestyle changes that may reduce risk. Access through the NBCC website www.nbcc.org.au

Breast Cancer Network Australia (BCNA) magazine **The Beacon** – Issue 38 focuses on familial breast cancer. It features many inspiring stories and current genetic facts. www.bcna.org.au/images/stories/pdf/beacon/beacon38_web.pdf

Familial Adenomatous Polyposis (FAP) website for kids (USA) John Hopkins Gastroenterology & Hepatology Resource Centre <http://hopkins-gi.nts.jhu.edu/pages/latin/templates/index.cfm> go to the Digestive Disease Library/Colon & Rectum/Hereditary CRC/kids FAP.

Book watch

My Mum has breast cancer, a family's cancer journey (2006) by Lisa & Harrison Sowards. An illustrated children's picture storybook written by an Australian mother and son. Order on-line at www.leadingedgebooks.com.au or phone 03 9598 5111.

Support groups

The Aussie breast cancer forum – an Australian internet based forum for people who have been touched in some way by breast cancer. You have the opportunity to share your personal experience with other forum members and there are links to valuable resources and information. www.bcaus.org.au

canSA sisters – is a South Australian group of young women with breast cancer experience and a diagnosis at 45 years or younger. They meet monthly to discuss issues, projects and life in general. They have a monthly newsletter and participate in a number of fundraising events like The Cancer Council's Relay for Life. For details contact Julie 0418 894 038 or Nicole 0407 867 786.

Internet club for kids with FAP – a US based internet based club for kids with FAP. www.clubs.yahoo.com/clubs/kidswithgardnerssyndrome Founded in 1999 with over 100 members.

Go green

If you prefer to receive Gene Trek electronically please email your request to genetics@cancersa.org.au.

Important note

- Have you or any of your family members changed address?
- Has there been a new cancer diagnosis in your family?
- Is there any surgery planned for cancer or preventative reasons?

Have you answered yes to any of the above questions? To ensure we can provide you with the best possible service, please let the Familial Cancer Unit know of these changes on 08 8161 6995 or cywhs.famcancer@cywhs.sa.gov.au

Considering surgery?

The Kathleen Cunningham Foundation research project into familial breast and ovarian cancer (kConFab) is seeking women willing to donate a small sample of tissue removed at surgery to support new initiatives in breast cancer research.

Do you have a

- BRCA1 or BRCA2 gene mutation OR
- a family history of breast or ovarian cancer?

Are you planning surgery for

- breast tumour removal OR
- prophylactic (preventative) breast removal?

Please consider donating tissue to the kConFab research project.

Please contact the research nurses, Meryl Aintree or Susan Schulz at the Familial Cancer Unit on 08 8161 6995 for more information or speak with your surgeon.

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