



ASSOCIATE PARLIAMENTARY FOOD & HEALTH FORUM



The links between diet and breast cancer

5-6.30pm, Tuesday 12 June 2007

House of Commons Committee Room 10

Minutes

Introduction

Lord Rea welcomed members and the guest speakers to the meeting, noting that it is the first meeting the Forum has held to discuss the links between diet and breast cancer. Lord Rea pointed out that breast cancer is now the most common cancer among women and more prevalent than the most common cancer in men, prostate cancer.

Lord Rea introduced Professor Tim Key, the Deputy Director of Cancer Research UK's Epidemiology Unit at Oxford University. Timothy Key's main interests are the roles of diet and hormones in the aetiology of cancer, particularly cancers of the breast, prostate and colon. He currently works mostly on the European Prospective Investigation into Cancer and Nutrition (EPIC), as the principal investigator of the Oxford cohort of 60,000 subjects and the chairman of the EPIC prostate cancer group. He also co-ordinates the Endogenous Hormones and Breast Cancer Collaborative Group, which conducts pooled analyses of the world-wide data on endogenous hormones and breast cancer risk.

Professor Timothy Key

Timothy Key thanked the Forum for its invitation to speak and explained that he would provide an overview of the links between diet and cancer, focusing on factors other than dietary fibre and meat consumption, which would be covered by Professor Janet Cade.

Timothy said that we have known for 40-50 years that breast cancer rates vary by a significant amount (five-fold) in different parts of the world. This variation led scientists to believe that there is something about the way we live that affects the rate of breast cancer. Timothy showed a slide (slide 2) which shows that the highest rates of breast cancer are largely in westernised countries, including Canada, America, Europe, Australia and New Zealand.

It is also known that the incidence of breast cancer worldwide is not related to the genetic make up of the population in these different countries because, for example, Japanese women have the same, higher, risk of contracting breast cancer as American women after they have been living in America for one or two generations.

One of the factors that has come under consideration in response to this evidence is diet. In 1966 a researcher working for the Imperial Cancer Research Fund found that those countries with a high rate of fat consumption had a high rate of breast cancer and that countries with a low rate of fat consumption had a lower rate of breast cancer. Of course, epidemiological studies of this kind illustrate correlations between two factors, but they do not explain cause and effect.

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Although scientists have not yet found good ways to prevent it, many of the factors that increase a woman's risk of contracting breast cancer are known. They include: hormones, early menarche, being tall, obesity and alcohol consumption. Some dietary factors, such as fruit and vegetable consumption, are not associated with the risk of contracting breast cancer. Other factors, including consumption of meat, milk, fat, fibre, folate and phytoestrogens are still under investigation.

The five-fold variation worldwide can be partly explained by the differences in parity (number and timing of births) and breastfeeding rates worldwide. These factors increase in significance when one takes into account the number of babies that are born on average to mothers in different countries and the variation in breastfeeding length which is affected by cultural norms and other factors. When these factors are taken into account it appears that having several children at a young age and breastfeeding can reduce the risk of breast cancer by up to 50%.

Early menarche and being tall are both associated with an increased risk of contracting breast cancer. Both relate to childhood growth and can be influenced by diet and infections.

The knowledge that diet is important has led to two hypotheses: first that nutrition may affect hormones (for example, soya intake and phytoestrogens) affecting the cancer risk; and, second, that diet may have a protective effect independent of hormones (for example, anti-oxidants in vegetables).

The Endogenous Hormones and Breast Cancer Collaboration (Key et al, JNCI 2002) found that in postmenopausal women the risk of breast cancer increases with increasing levels of circulating oestrogen (see slide 6). Women with the highest level of natural oestrogen in their blood have 2.5 times the risk of contracting breast cancer compared with women with the lowest levels. This is now an accepted relationship.

All the studies of obesity have found the same pattern (see slide 7). The most obese women do not have a higher risk of breast cancer before menopause, but after menopause increasing obesity clearly increases the risk of contracting breast cancer. Why this is the case is well understood.

In post-menopausal women, those who are over-weight have almost twice as much oestrogen in their blood as lean women, because the fat cells produce oestrogen. When allowance is made for the oestrogen difference between obese and lean women, it accounts for the whole amount of increased risk. Women who are obese have a risk 40% higher than lean women.

This data can be compared with the rates of breast cancer among women who are taking oestrogen as part of hormone replacement therapy (HRT). Women taking oestrogen HRT have a slightly higher risk than overweight women. Women taking combined (oestrogen with progestagen) HRT have a substantially higher risk than overweight or obese women not taking HRT.

The other dietary factor that clearly increases the risk of contracting breast cancer is alcohol consumption. There is a more or less straight line relationship (see slide 11) between increasing alcohol consumption and increased risk of breast cancer, though the size of the effect is quite small. The evidence, drawn from data for 59,000 cases and 95,000 controls from 53 studies worldwide (Beral and Collaborative Group on Hormonal Factors in Breast Cancer 2002), shows there is a 6% increase in risk for every UK unit of alcohol consumed per day. The mechanism for this effect is not yet fully understood, but it may be because alcohol affects hormones.

A recent American study found that women with the highest dietary fat intake had a higher risk of breast cancer than women with a low fat intake, but the difference was small.

Timothy Key and his colleagues had hoped that many of the questions about the links between fat intake and breast cancer risk would be answered by the Women's Health Initiative, an experiment in America involving 50,000 women. 40% of the women were put on a low fat diet and 60% followed a normal diet. The researchers found, however, that it was difficult to achieve the target low-fat intake and in fact fat intake in the "low-fat" group was only reduced from 38% to 27% of their energy intake. After 8 years there were 1727 incidents of breast cancers and the researchers found that risk in the low-fat group was reduced by 9% and this difference was not found to be statistically significant. However, the difference was not far from being statistically significant and the researchers believe that if the low-fat group had consumed less fat as part of their overall energy intake, significant results could well have been achieved. As it is, there will be follow-up to see if a stronger pattern emerges. Part of the explanation for the reduced risk could be attributed to weight-loss, and thus reduced levels of oestrogen, achieved by those following the low-fat diet.

Timothy Key was disappointed to report that the EPIC study had found that there is no significant difference in risk of breast cancer between women who eat a large amount of fruit and vegetables and women who do not.

The significance of soya foods for breast cancer risk has been receiving increasing attention in recent years, not least because Japanese women who eat a lot of soya have lower levels of breast cancer. It is hoped that phytoestrogens may have a protective effect by blocking stronger, natural oestrogen levels, but the results of trials so far have been inconsistent. A study Key undertook with colleagues in Japan in 1999 found no conclusive result.

In Oxford EPIC conducted a study involving nearly 600 women with breast cancer and 40,000 women without breast cancer, which found no significant difference in risk between vegetarians and non-vegetarians. They also looked at isoflavones (found in soya), but again they found no significant association with breast cancer risk (Travis et al. In press 2007)

There have been lots of studies to see whether insulin-like growth factor 1 (IGF-1) increases the risk of breast cancer. High plasma concentrations of this growth factor are positively associated with breast cancer risk and it is known that a high intake of animal protein, especially dairy protein, increases plasma IGF-I, but more research in this area is needed to explore the relationship and the mechanism of effect.

Timothy summarised his views by saying that obesity and alcohol consumption are two clear risks and areas where action should be taken in order to reduce the risk of contracting breast cancer. Beyond that he would recommend women eat a balanced healthy diet with adequate fresh fruit and vegetables and only a small amount of saturated fat. In his view we need more high quality research to answer the outstanding questions about the links between consumption of fibre, meat and dairy products and breast cancer.

Professor Janet Cade, University of Leeds

Lord Rea introduced Janet Cade, the Professor of Nutritional Epidemiology and Public Health at the University of Leeds. She is head of the Nutritional Epidemiology Group, developed in 1990, in the Centre for Epidemiology and Biostatistics. Her current research projects include the UK Women's Cohort Study of 35,000 women to study diet and cancer risk.

Janet Cade is one of the authors of the study published in the British Journal of Cancer in April 2007, which found that women generally consuming most total meat, red and processed meat were at the highest increased risk of breast cancer compared with non-meat consumers, though red and processed meat were only statistically significant in post-menopausal women.

Janet Cade thanked the Forum for inviting her to speak and expressed her entire agreement with the views expressed by Timothy Key.

Janet illustrated the context of her study by showing two slides which describe some general dietary risks for cancer.

Alcohol consumption increases cancer risk, particularly among smokers. However, in England 47% of men and 30% of women exceed Government recommendations for alcohol consumption. A high fibre, low fat diet with plenty of fruits and vegetables reduces cancer risk, but on average British people are eating only 2.5 portions of fruit and vegetables per day. On a more positive note, the consumption of salt in the UK has fallen by 2% over the last 20 years. However, only 28% of British men and 13% of British women are meeting the recommended daily average intake of fibre. On average people in Britain get 35% of their daily energy intake from fat, and red and processed meats account for as much as 11% of total energy intake.

Changes in diet could prevent up to half of all breast cancer cases. Eating at least five portions of vegetables and fruits each day could, in itself, reduce cancer rates by 20%. Eating healthily, plus staying physically active and maintaining a healthy weight, can cut cancer risk by 30-40%. As many as 100,000 cases of cancer could be prevented each year in the UK through healthy diet and lifestyle choices

The average intake of meat is 124g/day, whereas the recommendation is we should eat moderate amounts, and choose lower fat options.

Janet emphasised that assessing relationships between diet and disease is challenging. Results can be inconsistent due to a variety of potential biases, including: measurement errors (for example people who are overweight have been shown to underestimate their energy intake); different assessment methods (some studies measure average intake, others actual intake). Moreover we do not know in which period of our life diet has the most effect and our diets change throughout our lives. Many studies have used relatively homogenous populations in terms of diet. EPIC and the UK Women's Cohort Study includes people with a wide range of dietary intakes making it easier to tease apart the affect of variations in diet.

Janet suggested that if similar levels of resource had been applied to environmental factors as had been devoted to genetic components of disease, more might have been achieved.

Janet showed a slide (slide 6) which illustrates the fact that increasing alcohol intake is associated with an increase in the risk of contracting breast cancer, as is obesity and weight gain in postmenopausal women.

The key issue which Cade and her team looked at was whether nutrients or foods influence risk of breast cancer. The main focus of their attention has been on dietary fibre and meat.

The national average intake of dietary fibre is 12g/day, whereas the recommended intake is 18g/day. Good sources of fibre include: a medium sized bowl of bran cereal, a bowl of muesli, 2 slices of wholemeal bread, a small can of backed beans or a jacket potato. Other sources include an apple (with the skin on), a (peeled) orange, a portion of peas or carrots, a handful of peanuts and a dried apricot.

Janet gave an overview of previous fibre and breast cancer risk cohort study results (see slide 8). Studies to the right of the bar indicate an increased risk of breast cancer with higher intakes of dietary fibre, whilst studies to the left show a lower risk. Of these studies, the Nurses Health Study found no relationship, but a subsequent publication suggested a possible reduced risk in women eating more than 30g fibre/day compared with those women eating less than 10g/day. The Canadian National Breast Screening study initially appeared to find an effect, but it was later established that it found no associations between intake of dietary fibre and breast cancer risk.

A high fibre diet has been associated with a reduced risk of colorectal, but not usually with breast cancer.

There are various hypotheses concerning the mechanism by which fibre affects cancer risk. Fibre may: inhibit oestrogen reabsorption; inhibit oestrogen synthetase, leading to lower oestrogen synthesis; reduce androgens which affect oestrogen levels and the proliferation of breast tissue; act via insulin/IGFs (high IGF1, leading to breast cancer); or it may be that high fibre foods are rich sources of other significant dietary constituents, such as indoles and isoflavones.

Janet referred to previous studies which have looked at the influence of meat consumption on breast cancer risk. Boyd et al. in 2003 undertook a review of studies looking at meat intake and risk of breast cancer. Results from case-control studies looked at what women ate after they contracted breast cancer, and so results from this type of study may have been influenced by the women's knowledge of their illness. Cohort studies are a stronger design asking people about diet before they develop illness.

Meat cohort studies have shown strong evidence of a 17% increase in risk of contracting breast cancer in the highest meat consumers compared with the lowest meat consumers. The Nurses Health Study, which looked at more than 90,000 pre-menopausal women, found that meat consumption may affect the type of breast cancer that occurs. For example, those who ate more than 1.5 serves of red meat per day experience almost double the risk of hormone receptor positive breast cancer, compared to those who ate less than three servings of red meat per week.

The mechanisms by which meat consumption affects breast cancer risk are not yet understood. It may be because of the saturated fat content of meat, because saturated fat affects cholesterol production, which is a precursor of oestrogen. It may be because of certain compounds (heterocyclic amines) formed during cooking of meat, which may be carcinogenic in their own right. Alternatively it may be because of nitroso-compounds found in processed meat.

The UK Women's Cohort Study, which Janet has worked on for more than ten years, aims to study nutrition and cancer incidence and mortality in middle-aged UK women. There are more than 35,000 women in this cohort. Its work has taken place over two phases between 1995-98 and 1999-2004. In the first phase, the women were sent a questionnaire about their diet so their baseline diet could be assessed. In the second phase they were sent another questionnaire and asked to keep a food diary. Over the entire study period more than 1,400 deaths have occurred and there have been over 700 cases of breast cancer and more than 160 cases of colorectal cancer. The number of cases of breast cancer is expected to double over the next six years.

The women involved in the study have a mean age of 52; the vast majority are white (99%); middle class (lots of teachers and nurses); married; educated to degree level; living in all areas of the UK (33% in the south and east); and with a below average Body Mass Index of 24.5kg/m² - perhaps because they are health conscious, although 11% of them currently smoke.

The researchers hoped to find a broad range of dietary patterns. They found that 28% of the women were self-defined vegetarian (9593 subjects) although more than half of these women ate some meat and fish. Only 1% of the women were vegans (433 subjects). 58% of the women involved in the study take vitamin or mineral dietary supplements. Janet felt this factor merited further investigation, not least because the researchers found that over 4000 (different) dietary supplements were being consumed by the women. 27% of the women recorded that their diet had changed in the last 12 months.

Janet and her colleagues undertook a survival analysis of the women, all of whom had been healthy when they first filled in the questionnaire. The researchers found that in pre-menopausal women those with the highest intake of dietary fibre had almost half the risk of breast cancer as those women with the lowest intake. In post-menopausal women there seems to be no relationship between intake of dietary fibre and risk of breast cancer (the detailed results are described in slides 18-20).

Their meat study aimed to assess meat consumption from the UK Women's Cohort Study on breast cancer and to explore whether there was a relationship between the consumption of different types of meat and breast cancer. The detailed results are shown in slides 23-26.

Their results (which were adjusted for various factors including age, energy intake, BMI, physical activity, smoking status, HRT use, and total fruit and vegetable intake) were that premenopausal women with the highest intake of total meat consumption had a 20% increased risk of breast cancer compared with the women with the lowest total meat consumption. As the amount of total meat eaten is increased the risk of breast cancer steadily increases. The risk in post-menopausal women is even higher for the highest consumers compared to the non-consumers (63%).

When they looked at processed meat consumption, they found that there was no significant increase in risk in pre-menopausal women, but in post-menopausal women those with the highest intake had an increased risk of breast cancer.

They also found that there were no significant associations between poultry intake and risk of breast cancer.

Janet Cade's overall conclusions are that meat intake is associated with an increased risk of both pre-menopausal and post-menopausal breast cancer and that fibre intake is protective only in pre-menopausal women.

Janet concluded by thanking her colleagues and all the women who had contributed to this research by completing their questionnaires.

Questions

Sarah Stacey of the Mail on Sunday asked whether the Women's Health Initiative study had distinguished between different types of fat and looked to see whether omega-3 fatty acids had a protective effect and whether the omega-6:omega-3 ratio was significant. **Timothy** said that the women had been asked to reduce their total levels of fat so this issue was not addressed. Other studies which have looked at fish and breast cancer have found no protective effect. Although there were a lot of inconsistencies between the studies, it would be fair to say there is no conclusive evidence as yet.

Timothy suggested that it may be that obesity and alcohol are the best known dietary risk factors for breast cancer at the present time because they are relatively easy to measure. Every few years an expert panel is convened to look at these issues and this panel will be reporting again in November 2007. It may be that new information emerges then. **Janet** Cade has been involved in some of the systematic reviews which have been undertaken to support this panel's work. She highlighted the variable quality of some of these studies and both speakers agreed that more high quality research is needed.

Priya Venkatesan of the Sugar Bureau asked if research has been undertaken to see if there is a link between sugar consumption and breast cancer risk. The speakers suggested an academic at Leeds University had undertaken a study for the Sugar Bureau a few years ago, which found no significant relationship. **Timothy** said there had only been a few studies and their results were not consistent.

Dr Jenny Lisle of the RCP Faculty of Public Health asked about the timescale of risk and whether if women changed their diet they could reduce their risk of contracting breast cancer, in the same way that the longer a person has given up smoking the more their risk of contracting lung cancer is reduced. **Janet** said she and her colleagues have not looked at this, but she thought it was an interesting question. She thought that among her cohort of women dietary changes to reduce their risk of breast cancer may be underway, but she and her colleagues are not yet aware of them. **Timothy** said there is no simple answer because although some dietary risk factors are

clear, there are other risk factors which have a quicker influence. For example, a woman who has experienced the menopause immediately has a higher risk of breast cancer than before the menopause, although this risk does not continue to rise. Timothy pointed to studies of migrants which show that it takes one or two generations for their risk of breast cancer to match that of the population of their host nation, but this may be because it takes one or two generations for their diet to mirror that of the host nation.

Alan Long of Vega Research asked the speakers for their comments on the value of screening in comparison with epidemiological studies; whether they had considered investigating the relationship between fractures and breast cancer; and whether a difference in risk of breast cancer between meat and non-meat consumers is because the vegetarians tend to eat more fish and dairy products than meat eaters. **Timothy** said that the EPIC study had considered the incidence of fractures, which are associated with low levels of oestrogen, and people need to find a balance between dietary factors and various health risks. He said that the vegetarians in the EPIC cohort do not appear to eat more dairy products than meat eaters. EPIC has tried to recruit vegans, but currently they do not have enough to produce informative results. In terms of the balance of risk between genetic and dietary factors, Timothy said that those with a genetic disposition towards contracting breast cancer may have a higher risk whatever their exposure to dietary factors, but the dietary factors will remain significant.

Maureen Strong of the Meat Livestock Commission referred to saturated fat intake as a mechanism for increased cholesterol levels and increased risk of breast cancer; and questioned whether it was fair to make comparisons between meat and non-meat consumers in the same way that intake of, say, alcohol was compared, when 97% of the people in the UK eat meat and only 3% are vegans. **Timothy** said there is not much evidence concerning the relationship between blood levels of cholesterol and oestrogen and although it cannot be said that it is not important, it is not obviously important. Timothy thinks there is clear evidence that obesity and alcohol affect breast cancer risk, but he does not believe the evidence linking meat consumption and breast cancer has been as well established yet. In his view more high quality evidence of the kind that Janet has collected is needed. **Janet** emphasised that the relationship of risk between meat consumption and breast cancer may change over time.

Lord Rea asked whether, if the effect of diet on breast cancer risk is because it affects women's hormone metabolism, there are other factors that may be significant. **Janet** said that direct acting carcinogens may be created as a result of some methods of cooking meat. **Timothy** said that we know hormones are important, so it is interesting to look at the effect of diet on hormones, but the effect of diet is not necessarily limited to their effect on hormones and we should keep an open mind.

Lord Rea said that the variation in breast cancer rates between different countries seems to be much greater than the difference in rates between women in the UK eating different diets. **Timothy** agreed and said this was because, although other factors are significant, you would expect to see a greater variation in diet between countries than within a country.

Lord Rea thanked the speakers for their very interesting and illuminating insights into the current state of knowledge of an elusive subject.

CLC, June 2007