



ASSOCIATE PARLIAMENTARY FOOD & HEALTH FORUM



Links between diet and asthma

5-6.30pm, Tuesday 23 June 2009

House of Lords Committee Room G

Minutes

Introduction – The Countess of Mar

The Countess of Mar welcomed members and the guest speakers to the meeting and explained that she was chairing the meeting in the absence of our Chairman, Lord Rea, who had had to send his apologies because he was unwell. The Countess of Mar acknowledged that the issue of possible links between diet and asthma is a controversial area with emerging evidence often providing conflicting findings on associations between asthma and various foods, including essential fatty acids, antioxidants, vitamin D, sodium and selenium. Epidemiological studies are also difficult because it is not easy to obtain accurate information about previous diets and there are relatively few large intervention studies.

Dr Elaine Vickers, Research Relations Manager, Asthma UK

The World Health Organisation estimates that asthma affects 300m people worldwide. It is the most common chronic disease among children. In the UK 5.4m people are currently receiving treatment for asthma, including 1.1m children. Despite the common perception that asthma is relatively easy to manage, it still causes 3 deaths a day in the UK. Although asthma symptoms tend to be more common in affluent countries like the UK, USA and Australia, they appear to be more severe in poorer countries.

Worldwide asthma cases are increasing. This is more apparent in countries that are becoming more affluent and in which the population is switching to a more urban way of life. Many researchers have suggested that the rise in asthma is linked to changes in lifestyle and environment, including diet. However, family history remains the highest risk factor for asthma.

Genetic variations can mean that some children are prone to allergies and asthma or more susceptible to their parents smoking or at higher risk of viral infections. Other risk factors associated with asthma are modern lifestyles: such as changes in housing and diet and a more hygienic environment. Research has shown that smoking during pregnancy significantly increases the risk of a child developing asthma and children whose parents smoke are more likely to develop asthma. Environmental pollution can make asthma symptoms worse and may play a part in causing some asthma. The onset of adult asthma may follow a viral infection or be linked to irritants in the workplace. It is generally thought that the majority of cases of asthma are caused by a combination of inherited risk of allergies and asthma along with environmental exposures.

Evidence to support or refute a role for diet in asthma fall into two main groups: epidemiological studies and clinical trials.

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Associate Parliamentary Food & Health Forum
Church House, Great Smith Street
London, SW1P 3AZ

Tel: 020 7222 1265 Fax: 020 7222 1250

Epidemiological studies look at the characteristics of a group of people and try to draw conclusions as to how different characteristics are linked. There are three main types: cross-sectional studies, case-control studies and cohort studies.

Cross-sectional studies represent a snapshot in time. For example, a researcher might ask a group of people what foods they eat regularly and whether they experience any asthma symptoms. The researcher might then try to identify foods that are commonly eaten by people who have asthma. The advantages of this sort of study are that they are relatively easy to undertake and cost-effective. However, they establish links not causes and cannot determine cause and effect.

Case-control studies compare hundreds of people who have asthma to hundreds who do not. They might be asked to remember their diet as a child, the diet of each group is compared and the results combined. Again this type of study is relatively easy to undertake and cost-effective, but it relies on people's memories and can be affected by recall bias – their own views as to what foods might be linked to asthma.

Cohort studies collect data on a group of people, say new born babies, keep collecting information on these children for a number of years and then look for links between their diet and risk of asthma. The advantage of this type of study is that they can avoid problems of recall bias and they can provide information on cause and effect, but these studies may take many years to complete and are very costly.

The other main group of studies are clinical trials to test a dietary intervention. The gold standard for this type of study is the double-blind, randomised, controlled trial. These trials can provide reliable information on cause and effect, but they are expensive and time consuming. Again it can be many years before reliable results are achieved. The results will also be affected by the make-up of the study group and it can be difficult to extrapolate the results to the general population.

Certain general factors affect all studies investigating possible links between diet and asthma. It is almost impossible to obtain a completely accurate idea of a person's diet. Studies often use the presence of allergies, wheeze or atopic conditions other than asthma in order to obtain an indication of a child's subsequent asthma risk. However, this is not always an accurate indicator. For example, the majority of wheezy children do not develop asthma. Researchers around the world use many different definitions of asthma, making it difficult to compare studies. There are also thousands of variables which can affect an individual's asthma risk and it is impossible to take each and every one into account when analysing the results of a study.

The evidence so far suggests that asthma and diet can interact in a number of different ways. Some people with asthma are sensitive to certain foods that will trigger asthma symptoms. A woman's diet during pregnancy may impact on the allergy and asthma risk of her unborn child. Whether or not an infant is breastfed may alter their asthma risk. A child or adult's diet may increase or decrease their asthma risk. A diet could lead to the re-emergence of asthma later in life. Asthma is more common in young boys than in young girls, but they tend to outgrow it leading to a reversal of asthma risk in teenage boys and girls. Dietary interventions, such as taking vitamin, fish oil or zinc supplements or probiotics may modify asthma risk, but no clear evidence has emerged to support this. All these interactions have been investigated through thousands of research studies and the only clear evidence to emerge to date is that asthma risk can be reduced by avoiding smoking and alcohol.

The long list of possible dietary triggers of asthma include: cow's milk, eggs, fish, shellfish, yeast products, nuts (both peanuts and tree nuts), food colourings and preservatives, Royal Jelly products, red wine, sulphites and salicylates.

In terms of asthma prevention, the window of opportunity is potentially in utero and the first few months and years of a child's life, while their lungs are still developing. Many studies therefore look at early life, but the evidence is conflicting and confusing. Theoretical evidence is often

interesting and substantial, but it has not yet been transferred into meaningful advice for individuals.

We can tell pregnant women to avoid smoking and alcohol, but studies involving breastfeeding have produced conflicting results. Some of the biggest studies do show that breastfeeding offers some protection against asthma risk. For example, one cohort study of 4,089 newborns, showed a reduced risk of asthma at 4 years for breastfed infants (Kull et al. *JACI* 2004) and current advice is for infants to be breastfed exclusively for the first 6 months. Different studies have had different hypotheses including for example, that it is nothing intrinsic to the mother's milk, but the mechanical action of breastfeeding – which may require greater effort from the baby than bottle-feeding – which helps infants develop strong, healthy lungs.

The traditional view is that postponing the introduction of solid foods until a baby is 4-6 months old may offer some protection against the risk of allergies and asthma, but the evidence to support this view is scarce. A cohort study of over 2,000 children found no evidence to support delayed introduction of solids (Zutavern et al. *Pediatrics* 2008).

The use of probiotics to reduce asthma risk is linked to the hygiene hypothesis, which suggests that infants have “better” bacteria in their digestive system if they are breastfed. Supplements have been tested, but no evidence of a protective effect against allergies for naturally-born children was found, although there was evidence that they offered some protection for those born by caesarean (Kuitunen et al. *JACI* 2009).

Food allergies affect around 1.5% of adults and 6-8% of children. They are a known risk factor for asthma. People with food allergies tend to have more severe asthma symptoms and people with asthma are at greater risk of severe food allergy reactions. Unfortunately there have been very few studies in this area. One of the most interesting was the Isle of Wight prevention study of children at risk of asthma and allergies (Arshad et al. *JACI* 2007). In this study, breastfeeding mothers ate a “low allergen diet” and the infants had low allergen formula. The children also had a restricted diet and ate no dairy, eggs, wheat, nuts, fish or soya for a year. House dust mite levels were also reduced using mattress covers and pesticide. The findings showed these children had fewer allergies and asthma at age 8, but it is questionable whether this significantly constrained diet would be feasible and could be recommended for the general population.

Peanuts also attract much media and popular attention and over the years women have been given conflicting advice. The Food Standards Agency asked the Committee on Toxicology to review all the latest evidence and in December 2008 they published a report on peanut avoidance. It concluded that there is no evidence to support peanut avoidance. Indeed eating peanuts may actually protect against peanut allergy, but it is impossible to say either way; there could be no effect at all.

As well as looking at individual components in the diet, there is increasing interest in looking at dietary patterns associated with asthma. A consensus has emerged that a Mediterranean diet high in fruit and vegetables and low in saturated fat may protect children against asthma symptoms. Cow's milk consumption has been looked at frequently and while there is conflicting evidence, there is some evidence for the view that high consumption of unpasteurised milk may have a protective effect in children. No dietary pattern was identified for adults that could have a protective effect against the development of asthma, although the “western diet” of pies, pizza and puddings may make symptoms worse in people who already have the condition. There is some evidence that a “nuts and wine diet” may offer some protection against asthma attacks (Varraso et al. *ERJ* 2009).

Vitamin D is recognised as being essential for bones and teeth – and this forms the basis for the RDA – but it also appears to be important in maintaining a healthy immune system. The majority of our vitamin D is made in our skin when we are exposed to sunlight, while a small amount comes from the food we eat. The evidence on links between vitamin D and asthma is conflicting, but it is cheap and interesting to test. Two major intervention trials are now underway in which pregnant

women will be given vitamin D supplements and their children will be tested for signs of asthma at age three. These trials should shed light on whether vitamin D can help prevent asthma. Vitamin D levels have also been suggested as a means of increasing the effectiveness of steroid-based asthma treatments and an Asthma UK funded clinical trial is underway to investigate whether vitamin D pills alongside steroid tablets can reduce symptoms in people with severe asthma. The results of this study could be very important because an estimated 10% of people with asthma do not gain any benefit from steroid-based treatment.

Our cells produced millions of chemical reactions, some of which produce free radicals which can be damaging. Anti-oxidants mop up the free radicals and prevent the body from being damaged, so it seems reasonable to suggest that anti-oxidants are good for us. We know fruit and vegetables which are rich in anti-oxidants are good for us, but we lack evidence that this is because they contain anti-oxidants. Moreover anti-oxidants are not benign; they do carry some health risks. Higher levels of free radicals have also been found in the lungs of people with asthma, but we do not know if these cause asthma symptoms or are simply produced as a by-product of such symptoms. A wide variety of cross-sectional and observational studies have suggested that a diet rich in anti-oxidants, or taking anti-oxidant supplements, may reduce asthma risk or prevent symptoms. However, clinical trials to assess the potential benefits of supplements have failed to show that the incidence of asthma or the frequency or severity of asthma symptoms can be reduced through dietary supplementation. More recently a meta-analysis concluded that a low dietary intake of vitamins A and C is linked to increased asthma risk (Allen et al. *Thorax* 2009).

In summary, there is evidence to justify links between diet, asthma risk and asthma symptoms; however the most important risk factor is our genes, combined with lifestyle and exposures. We now know of some associations between diet and asthma, but this information is largely theoretical and further studies are needed to justify interventions to reduce the risk of asthma or to reduce asthma symptoms.

Dr Jo Leonardi-Bee, Lecturer in Medical Statistics, Nottingham University

Jo Leonardi-Bee began by thanking her colleagues Sarah Allen and Professor John Britton for participating in the research, published in *Thorax* online on 30 April.

They recognise the role of diet in many chronic diseases, such as cardiovascular disease, cancer and stroke, but the role of diet, if any, is less well defined in respect of respiratory diseases. A recent Cochrane Review (Kaur, Rowe & Arnold, 2004, updated in 2008) which included 9 trials covering 300 patients looked at vitamin C supplementation and concluded that the evidence was inadequate to recommend supplementation. Another trial looked at vitamin E and concluded that daily supplementation showed no benefit in mild to moderate asthma (Pearson, Lewis, Britton & Fogarty, 2004). There have been no published trials to date looking at vitamin A. Although there have been some promising results from some observational studies, there is inconsistency between epidemiological data and the results of randomised controlled trials (RCTs) (McKeever & Britton, *AJRCCM*, 2004).

In Nottingham they wanted to do a systematic review and meta-analysis that looked at all the studies globally to determine the magnitudes of the overall associations between outcomes of asthma and levels of vitamins A, C and E. Standard methods were used to identify relevant epidemiological studies and statistically analyse the data (meta-analysis). The outcomes that interested them were primarily asthma and, at a secondary level, wheeze, airway reactivity and asthma severity.

Their initial searches identified over 2600 studies, which were looked at by two people independently who identified 40 as meeting the inclusion criterion and being eligible for our systematic review. The majority of these studies (65%) were conducted in adults. The populations studied included Africa (3 studies), Asia (6 studies), the Americas (10 studies), Europe (18 studies) and Oceania (3 studies).

Various definitions can be used to ascertain asthma outcome. The best use an independent evaluation by a physician, as was the case in 16 studies. 12 further studies used a self-reported physician-diagnosed asthma. Other studies used self-reported wheeze (15 studies) or airway hyper-responsiveness (4 studies).

The measurement of vitamins fell into two groups: 26 studied dietary intake and 24 studied biochemical levels in serum, plasma or sputum. The latter are more objective, but produce results based on recent dietary intake, whereas the former can look at diet over a longer period.

They found that people with asthma had on average significantly reduced levels of vitamin A compared with people without asthma. Dietary intake was significantly reduced for people with asthma (182µg/day) in 3 studies; and for people with severe asthma (344µg/day) in 2 studies; but we found no relation between vitamin A levels and wheeze or airway reactivity. Serum levels of vitamin A were significantly reduced in people with asthma (0.25µmol/L) in 2 studies, though for children only; and in cases of severe asthma (0.48µmol/L) in 3 studies involving physician diagnosed cases of adult asthma. There was no data available to assess evidence of a link between vitamin A levels and data for airway reactivity.

Looking at vitamin C they found that dietary intakes of vitamin C were significantly reduced in cases of people with asthma (a 12% increased risk was found looking at 9 studies); wheeze (10% increased risk, looking at 6 studies); airways reactivity (reduced mean levels; 7 times more likely); but no relation was found in cases of severe asthma. Serum levels were significantly reduced in cases of people with asthma (16.8µmol/L in 2 high quality studies); one study found a 22% increased risk of asthma; but again there was no evidence of a relationship between vitamin C levels and severe asthma or wheeze.

Dietary levels of vitamin E were significantly reduced in cases of people with asthma (1.91mg/day, looking at 4 studies) which were physician-diagnosed only; and in severe asthma (1.20mg/day, looking at 2 studies), but there was no evidence of a relationship between vitamin E levels and wheeze or airways reactivity. When they looked at serum levels they found no evidence of a relationship between vitamin E and asthma, asthma severity or wheeze.

They concluded that there is a consistent negative association between dietary vitamin A and asthma (relating approximately to 26% in men and 30% in women of their RDA); consistent increased risks of asthma, wheeze, and airways reactivity seen with lower levels of vitamin C (relating to approximately 20% RDA in studies assessing differences in intakes between people with asthma and those without); and that vitamin E levels are generally unrelated to asthma. There are some mechanisms for action which make these results plausible, including the known anti-inflammatory properties of these vitamins and, possibly, their anti-oxidant actions. They found interesting links, but these studies cannot be used to determine cause and effect. Further work is needed in the form of large, well designed, randomised controlled trials to test these associations between vitamin levels and asthma. However, such trials take a long time to complete and if immediate messages are wanted, they can say that a balanced healthy diet, including lots of fresh fruit and vegetables, reduces the risk of asthma. They cannot go further than that at present.

Questions

The Countess of Mar asked if lower vitamin intakes were associated with lower levels of income. **Jo** said they were, although several studies included in the systematic review were adjusted for socio-economic status.

Rosan Meyer of the British Dietetic Association (BDA) said the studies seemed to be based on UK RNIs and asked if the researchers had compared the findings with American recommendations. **Jo** said they had not, but accepted it was a useful suggestion.

Rosan asked if the researchers had distinguished between studies that looked at treating asthma and preventing asthma whether any of the studies had been early intervention studies involving

children. **Jo** said the best evidence to answer this would be from using cohort studies, but only 2 heterogeneous studies included in their review had involved looking at infants and then following them to see whether they developed asthma. **Elaine Vickers** commented that some studies had shown adverse effects as a result of mothers taking vitamin supplements during pregnancy, including an association with an increased risk of needing more health care. **Rosan** agreed and said that the BDA do not recommend vitamin supplementation during pregnancy; they prefer to recommend a healthy, balanced diet. **Elaine** said that some researchers working on vitamin D are worried that it could have an adverse effect at the levels being used in American studies. There is conflicting evidence, but some studies have shown an increase risk of eczema associated with vitamin D.

Earl Baldwin of Bewdley asked if the researchers had used very high levels of vitamin C in their studies. **Jo** said she was not sure what dose was used in every case, but they were short-term studies. **Elaine** said very high doses of vitamin C have been linked with some severe side effects. **Rosan** agreed saying that normal adult daily doses of vitamin C are measured in milligrams, whereas some trials use between 1 and 15 grams a day.

Dr Jackie Lavin of Slimming World asked if there are any biochemical markers that can be used to identify asthma rather than relying on symptoms. **Jo** said the best measure of asthma is a physician's evaluation or using an airway challenge, but the latter are quite invasive so not many studies have used them. **Elaine** said there are other measures you can use, for example, the level of nitric oxide in expelled air, which correlates with the level of airway inflammation, but it does not always correlate accurately with a person's experience of asthma. She suggested the best way to measure asthma is to look at a GP's evaluation and the overall effect on an individual's quality of life. Asthma in children is notoriously difficult to diagnose. There is a lot of interest in what you can define as childhood asthma. Lots of children are wheezy when young, but this is often resolved. There is no evidence that if you diagnose asthma early that you can prevent it from becoming worse in later life. There is no clear consensus in terms of diagnosis: we do not yet know when we should start intervening to try to control asthma.

The Countess of Mar suggested there were so many variations in asthma from diagnosis to treatment because individuals vary so much and she suggested it may be impossible to determine that one factor will prevent or treat asthma. **Elaine** agreed saying she was aware of one study that looked at teenage boys who typically spent 10 hours a day outside in sunshine without sunscreen which found that some of them were still deficient in vitamin D – against all expectations – demonstrating that our bodies deal with environmental exposure differently and all this interacts with our genetic makeup. Drawing meaningful conclusions from individual dietary components is very difficult, which is why researchers are increasingly looking at dietary patterns.

Rosan suggested that the evidence on diet and asthma adds weight to the case for emphasising the existing public health messages on a healthy diet – including five pieces of fruit or vegetables a day. **The Countess of Mar** agreed that there were no simple, quick fixes, but said she was aware of one case where a 9 month old baby's severe eczema had cleared within several weeks after drinking unpasteurised goat's milk, rather than cow's milk or formula.

Conclusion

The Countess of Mar thanked the guest speakers and announced that the next meeting will be held in October, when we will discuss the results of a systematic review into the nutrient content of organic food. Members will be notified as soon as the date can be confirmed by the guest speaker, Dr Alan Dangour.