ASSOCIATE PARLIAMENTARY FOOD & HEALTH FORUM

The links between diet and behaviour

3.15-5.15pm, Wednesday 28 March 2007

House of Lords Committee Room 3A

Minutes

Introduction

Lord Rea welcomed FHF members and guests to the meeting and explained that the FHF inquiry into the links between diet and behaviour is loosely based on the procedures of a Select Committee, but will be much more informal. The inquiry report will not have the same status as a Select Committee report and the Government is not obliged to respond to it. However, the Parliamentarians on the inquiry team will take note of its recommendations and seek to raise these issues in Parliament, for example by means of Parliamentary Questions.

The presentations given by guest speakers will be supplemented by written statements they have supplied, by published academic papers and by written evidence submitted by FHF members and others.

Lord Rea introduced the first guest speaker, Professor Michael Crawford of the London Metropolitan University. Professor Crawford has been working in the field of essential fatty acids (EFAs) for some 30 years. Indeed he published a report in 1977 on the effects of EFAs on health. Lord Rea noted that work on EFAs had initially focussed on their importance for physical health, but more recently there has been increasing interest in their significance for the development and function of the brain.

Professor Michael Crawford, London Metropolitan University

Michael Crawford (MC) said he would give an introduction to the subject of the importance of EFAs for the brain before focussing on the way in which the nature of our food web has changed in recent times and the extent to which that affects the brain and mental health.

In the last century the dietary focus was on protein consumption and physical growth. MC showed a slide of a rhino (slide 1). The rhino obtains all the protein it needs by eating grass and grows to weight 1 tonne within 4 years. He then showed a slide of a baby and its mother, which showed that their skulls (the "brain case") were roughly the same size, although the baby's hands were much smaller. This, he suggested, illustrated that the brain is the priority for development in the human species. MC explained that the brain is largely made of fats rather than protein and the development of a child's brain is significantly affected by the mother's diet during pregnancy.

The UK has the highest incidence of low birth-weight of any Western European country. Although low birth-weight is only a crude marker of pregnancy outcome, none the less lower birth-weight is the single most powerful predictor of ill health, heart disease, stroke, diabetes, poor learning abilities, mental ill health and crime. At the extreme end, very pre-term, low birth-weight infants, are at high risk to central nervous system disorder such as Cerebral Palsy.

Associate Parliamentary Food & Health Forum
1 Millbank
London, SW1P 3JZ

Tel: 020 7222 1265 **Fax**: 020 7222 1250

The human brain is 60% fat or lipid. Essential fatty acids (EFAs) are required to build lipids. They are called "essential" because they cannot be made in the body and must be obtained from the diet. MC said the brain also requires a specific balance of EFAs (as Joe Hibbeln would demonstrate later).

MC suggested the priority for food policy should be nutrient delivery, especially brain specific nutrients, rather than fast growth and production. MC noted with regret that successive Governments have ignored the issue of low birth weight in babies in the UK and welcomed a Fabian Society pamphlet published today on this issue.

MC described the sources of essential fatty acids. All seeds contain Linolenic Acid (LA) which is the precursor of Arachinoid Acid (AA). Alpha-linolenic Acid (ALA) is the precursor of Eicosapentaenoic Adic (EPA), Docosapentaenoic Acid (DPA) and Docosahexaenoic Acid (DHA) (see slide 5).

Animal brain cells require liquidity in molecules, making Highly Unsaturated Fatty Acids (HUFAs) necessary rather than saturated fats.

MC suggested that the ideal balance of Omega-6 and Omega-3 would be 1:1, as it is believed to have been in prehistoric times. Vision and brains evolved in the marine environment. Early man developed on a diet near the sea. The chemistry of the brain is built to a similar lipid specification in all mammals thus far studied. The differences are the extent to which the brain evolved which in turn appears to depend on the availability of the brain specific fatty acids.

Man became distinguished from the chimpanzee about 7 million years ago, but we are only 1.5% different in terms of our genetic make-up. We are still adapted for a wild food diet and that differs enormously from modern food. MC showed two slides (slides 9 and 10) that described the difference in terms of calories derived from fat between wild food and modern versions of the same food, for example beef and chicken. There are fewer calories and less fat in the wild version of the same food than the modern version. Through the centuries the animals we eat have changed. As we have moved from the wild to extensive animal husbandry to selection for fast growth and intensively fed systems, the proportion of visible fat, and fat between the muscle tissue, has increased. This is also evident when the arteries of wild animals are compared with those of humans. MC showed slides (slides 20 and 21) of a lion's artery and a human aorta; the lion's artery had no visible fat, whilst the human aorta clearly showed fatty deposits.

What has gone wrong?

He ended by making four recommendations:

- domestic science, hygiene, nutrition and health should be included in the curriculum of schools and medical colleges;
- food policy should focus on nutrition and health rather than production and economics;
- there should be a determined effort to halve the incidence of low birth weight in the UK from its present level of 8% of all babies to 4%; and
- a new policy is required on coastal marine productivity through truly clean rivers, estuaries and coast lines to restore, enhance and develop their natural productivity.

Questions

Dr Ian Gibson asked if anyone had predicted what would happen in terms of cardiovascular disease (CVD) if nothing changes. **MC** said 30 years ago he had predicted that brain disorders

and mental ill health would increase if nothing changed; nothing changed and brain disorders had increased hugely. He expects the same to hold true in the future if nothing changes. He emphasised that the cost of brain disorders had now overtaken the cost of all other burdens of ill health in the EU. At 2004 prices the cost was estimated to be E386 billion, including some £50-60 billion for the UK. MC suggested a third of that ill health could be prevented with dietary changes leading to savings of some £20 billion.

Lord Baldwin of Bewdley (EB) asked whether the incidence or the cost of mental ill health had increased or both. **MC** said both had increased.

Baroness Masham of Ilton asked why the UK had the lowest average birth-weight in Western Europe. **MC** attributed it to the great socio-economic disparity apparent in the UK. He said low birth-weight was concentrated in the poorest areas. His research team had over the last 20 years, found in east London that low birth-weight was associated with poor maternal nutrition before and during pregnancy independent of smoking, socio-economic and ethnic differences. MC said that as birth-weight falls the risk of brain disorders increases sharply from 1 or 2 per 1,000 live births to over 200 per 1,000 in extremely low birth-weight, premature infants. This however, is the tip of an iceberg of poor mental development and risk of chronic ill health.

Dr Alexandra Richardson, University of Oxford

Dr Alexandra Richardson (AR) is a Senior Research Fellow at the University of Oxford's Department of Physiology, Anatomy and Genetics, and a Founder Director of the charity Food and Behaviour Research. She is internationally known for her research into the role of nutrition (and particularly fatty acids) in behaviour, learning and mood. She has been investigating the biology of individual differences in behaviour and learning for some twenty years, particularly in relation to developmental and psychiatric disorders. For more than 12 years her work has been focused on the role of diet in these conditions, especially the significance of EFAs for child behaviour and learning.

AR suggested that the current, average UK diet is 'a rotten way to feed our children' (as suggested by a newspaper headline). We recognise that obesity and type-2 diabetes follow from a poor diet, but we do not adequately recognise that the same poor diet will also affect children's brain development and thus their behaviour.

The UK Government has been pressed into improving school food and that is a welcome development.

AR noted that depression is now the top cause of mental ill health in western countries, and that on present trends, the WHO recently predicted a 50% increase in child mental disorders by the year 2020. Various developmental disorders first evident in childhood, including dyslexia, hyperactivity, autism and related conditions all appear to be on the increase, and milder forms of the traits and features that define these disorders are common in the general population

AR expressed regret that huge resources are committed to refining definitions and diagnoses of specific behavioural and learning disorders, such as dyslexia, ADHD and autism, when such diagnoses are currently only descriptions, not explanations. She emphasised the substantial overlap between these conditions and urged the use of a more trait-based/symptom based approach, as well as a primary focus on investigating the underlying causes. These involve complex gene-environment interactions, and nutrition and diet are at the interface of this

It is difficult to get an official "statement" of special educational needs and these are restricted to a small percentage of the school population, but AR is aware that Local Authorities estimate that up to 20% of children have some form of behavioural and/or learning problem that falls into this area.

Omega-3 fatty acids from fish oils are absolutely essential to the visual system. 30%-50% of the retina is made from the omega-3 DHA; and DHA deficiency can reduce the efficiency of the initial

stage of retinal signalling by more than a thousand-fold. Omega-3 deficiency is associated with poor night vision and other problems with visual, spatial and attentional processing.

AR explained that it was from her early research investigating these kinds of visual and attentional difficulties in dyslexia and related conditions that she became interested in the potential role of omega-3 in these disorders. She re-emphasised Professor Crawford's point that the body's requirement of omega-3 for the structure of the brain and healthy vision has not changed through evolution – but that omega-3 intake in modern western-type diets has fallen dramatically since industrialisation, and is effectively at an all-time low in human history..

Two fatty acids are called 'essential' because the body cannot make them from other substances: linolenic acid (LA) (omega-6) and alpha-linolenic acid (ALA) (omega-3). Highly unsaturated fatty acids (HUFAs) are the ones the brain actually needs, but they are not always called "essential" because in theory the body can synthesise them from the respective parent essential fatty acids, LA and ALA.

AR then showed a slide **(**slide 7) depicting the synthesis of highly unsaturated fatty acids (HUFAs) from essential fatty acids and the enzymes involved in HUFA synthesis. AR said that four HUFAs are particularly important for brain development and function: Dihomogamma-linolenic (DGLA) and Arachidonic (AA) from the omega-6 series and Eicosapentaenoic (EPA) and Docosahexaenoic (DHA) from the omega-3 series. AA and DHA are major structural components of neuronal membranes (making up 20% of the dry mass of the brain and more than 30% of the retina). EPA and DGLA are also crucial, but they play functional rather than structural roles.

The conversion of HUFAs from EFAs in the body is poor and it can be blocked by many diet and lifestyle factors**,** including: excessive consumption of saturated fats, hydrogenated fats and trans fatty acids; lack of co-factors such as zinc, magnesium and manganese, and vitamins A, B3, B6 and C; viral infections and the presence of hormones released in response to stress. Alcohol and smoking are also relevant to HUFA status. These do not stop people making HUFAs, but they help strip them from the body.

Constitutional factors also affect the efficiency of synthesis of HUFAs from EFAs. Ageing, atopic eczema, diabetes and being male are all associated with poorer conversion of HUFAs from EFAs. It is interesting to note against this background, that many behavioural disorders, such as ADHD, dyslexia, dyspraxia and autism are undeniably more common in males than females, and also seem to be associated with an increased frequency of atopic and other immune-related conditions.

AR acknowledged that EFAs were only one significant feature of dietary intake. Vitamin A is necessary for vision, for the immune system and for integrity of the gut (as well as for EFA to HUFA conversion), but data from the last official UK survey showed that one in ten children from the general population have a clear dietary deficiency of Vitamin A even when precursor forms are included (i.e. they consume less than the Lower Reference Nutrient Intake) while a majority of children consume less than the population Reference Nutrient Intake. Similarly, zinc is needed for more than 200 different enzymes in the brain and body, including those involved in cell division and replication, immune system function and the building of HUFA from the EFA precursors available from vegetable sources, but again, a clear majority of children (more than 80% in some age groups) consume less than the population daily Reference Nutrient Intake, and again, at least 10% consume less than the Lower RNI – an acknowledged index of dietary deficiency.

AA is very important for the brain and heart, but we are unlikely to be deficient in it because there is an abundance of omega-6 in modern diets. This is particularly true of the omega-6 EFA precursor (LA) – but AA is also provided 'ready-made' by meat, dairy products and eggs. On the other hand, even the omega-3 EFA (ALA) is lacking from most children's diets, being found only in green vegetables and some of the less commonly consumed nut and seed oils. Furthermore, those who are not good at converting EFAs to HUFAs are likely to be deficient in the key omega-3 (EPA and DHA) unless they frequently eat fish and seafood. In particular, vegetarians and vegans may

find it difficult to obtain sufficient EPA and DHA because it is difficult to convert effectively the simplest omega-3 (ALA) – found in foods such as flax oil - into these HUFA.

AR showed a slide (slide 13) which showed how the balance of omega-3:omega-6 had changed as humans moved from a hunter-gatherer diet to the modern diet from 1:1 to some 15:1 to 25:1. Over this period the total proportion of calories derived from all fats has doubled to some 40%, intake of saturated fats has increased and coronary artery disease has soared since the 19th century.

Omega-3 and omega-6 HUFA are essential for all cell membranes and for brain growth and connectivity. These fatty acids and their derivatives improve the flexibility of membranes which is necessary for proper cell signalling. The latter also affect hormone balance, immune function and blood flow.

The consumption of pre-formed DHA in a mother's diet powerfully affects the amount present in breast milk, with important implications for the babies of vegetarian and vegan mothers (see slides 15 and 16). Supplementing infant formula with pre-formed HUFAs (both imega-3 and omega-6), found naturally in breast milk, has been shown to improve visual and cognitive development.

AR said that many studies now suggest that omega-3 deficiences may contribute to a range of developmental disorders of behaviour and learning, including dyslexia, ADHD, dyspraxia and autism – but that properly randomised controlled trials, which are essential to show clear evidence of cause and effect, are still few in number.

There are clinical symptoms associated with omega-3 and omega-6 deficiencies, such as rough, dry skin and hair, excessive thirst, frequent urination and soft or brittle nails. These conditions are found (disproportionately) in children with behavioural problems in comparison with control groups.

AR acknowledged that the impact of omega-3 on mental health is a relatively new field, but suggested that the balance of evidence from the randomised controlled treatment trials (RCTs) undertaken to date is promising (see slide 22 for the results of various trials involving adults investigating the impact of omega-3 supplementation on a range of physical and mental health conditions). She expressed the hope that we could move increasingly to an approach that is trait/symptom based with less focus on specific diagnoses and emphasised that more research is needed.

AR briefly summarised the results of the five RCTs conducted to date of fatty acid supplementation for child behaviour and learning problems, which are reviewed in more detail in an article[1] submitted as written evidence for the FHF inquiry (see slides 23 and 44 for a summary of the trials and their results). Two negative studies showed no benefits from treatment primarily or exclusively with DHA for children with ADHD.

Three of these five randomised controlled trials (RCTs) found benefits for behaviour and learning in children with a primary diagnosis of either dyslexia, ADHD or dyspraxia. These three successful trials used supplements containing both EPA and DHA, a little evening primrose oil and some vitamin E. The biggest trial, though still small (117 under-achieving children from mainstream schools aged 5-12), was the Oxford-Durham trial in which AR was the leading scientist. It did not show an improvement in motor skills because all the children – including those in the control group – improved on this score, possibly because of premature media attention. AR emphasised that this illustrates very clearly why any trials without a proper placebo-controlled design cannot be taken as evidence for cause and effect. However there were significant improvements for those taking the supplement in terms of learning, behaviour and working memory with no placebo effect. Their reading improved at three times the normal rate and their spelling improved at twice the normal rate. Similarly, significant reductions in ADHD-type symptoms (including inattention, hyperactivity, impulsivity and other disruptive behaviours) were found for the children receiving

[1] Richardson, A.J. Omega-3 fatty acids in ADHD and related neurodevelopmental disorders. *International Review of Psychiatry*, 2006 18(2) 155-172.

active treatment compared with placebo. Additional findings of benefits for working memory, which are still being written up, may prove important because working memory is a significant factor in many behavioural disorders (see slides 30-34).

Scientific and medical experts recommend a daily intake of 500mg/day of EPA and DHA simply for cardiovascular health (ISSFAL statement 2004, Joint Health Claims Initiative (JHCI) 2005). In the UK the average intake is some 100-150mg/day and most children consume less.

We still don't know what is needed in terms of optimum intake of these HUFA for mental health or whether there will be greater benefits from higher doses. In the Oxford-Durham trial and other successful trials the supplements used were similar to the minimum recommended intake – some 550-750mg/day EPA and DHA. AR suggested that more RCTs should now be a priority for public policy. She also suggested that both the public and health and education professionals needed better information and advice about the crucial role of omega-3 fatty acids for brain development and function, and thus behaviour, but that this information must be objective and it must be evidence based.

Questions

Earl Baldwin of Bewdley (EB) asked whether it was fair to say that the move away from nutrition in medical colleges in the second half of the twentieth century was partly responsible for our present health problems. **MC** replied that currently every medical student studies pharmacology for a year and it is a subject touched on throughout their studies, whereas students only have three hours of tuition on nutrition. **AR** agreed with the urgent need for better training of all health professionals, and said we need to divorce nutrition as a subject from the food industry, which has its own agenda.

Baroness Masham of Ilton (SM) Asked why children could not be given omega-3 supplements at school. **AR** said that is what they did during their trials, as it is the only practical way to maintain the double-blind placebo-controlled conditions needed for this kind of research. She emphasised, however, that it is always better to get essential nutrients from food whenever possible. Although she agreed that supplements could be useful in some cases, she emphasised that properly controlled trials to assess the relative benefits and costs would be the obvious next step if universal supplementation were to be considered. **MC** noted that during World War II pregnant mothers and children had been given orange juice and cod liver oil every day.

Ian Gibson (IG) asked what the effect of omega-3 deficiencies were in terms of violent behaviour. **Joseph Hibbeln** (JH) said that when pigs were supplemented with omega-3 the levels of serotonin in their frontal cortex doubled and the reasons why deficiencies affect aggression and impulsivity are known.

IG asked whether excesses of either omega-6 or omega-3 were known to cause problems. JH said that epidemiological and nutrition studies show no upper end of benefit for consumption of these nutritients. The Innuits who consume relatively high levels of seafood had lower levels of depression than Innuits who ate less seafood. His 2007 study of pregnant mothers found that even those who ate the most fish and seafood were not placed at risk. **NR** asked whether there were any examples of high omega-3 consumption putting people at risk. **JH** said that (very?) high omega-3 consumption could (slightly?) increase the risk of certain kinds of stroke, but it lowered the risk of either types of stroke and it lowered the overall risk of stroke.

The Countess of Mar (MM) reported that her grand-daughter had been diagnosed with dyspraxia and the family had found that giving her fatty acid supplements had led to a significant improvement in her behaviour. **AR** explained that there is a huge range of different supplements available now – of varying composition and quality - and the public need more information about them in order not to be misled by commercial 'hype'. Different supplements have been used in the existing successful studies, and yet others are under investigation in ongoing trials. AR added that EPA is possibly more important that DHA, but more research is needed to establish this beyond

doubt. The quality of oils is also important and AR strongly recommended that people should obtain their EPA and DHA directly from fish oils rather than relying on conversion of the simpler omega-3 found in some vegetable oils (such as flax), as this process is not efficient in humans – particularly with respect to obtaining DHA. She also emphasised that excess consumption of cod liver oil could put at a person at risk of vitamin A toxicity, so no-one should try to obtain the doses of EPA+DHA used in successful trials (550-750mg/day) in this way - but one teaspoon a day should be safe.

MM said she had also noted that autistic children often improve on a non-gluten diet and she expressed regret that it was difficult for families to access non-gluten foods under the NHS. **AR** agreed with her concerns, but mentioned that this again reflects the serious lack of properly controlled research trials in the area of nutrition and behaviour.

NR asked if there were ways of obtaining the essential fatty acids, omega-6 and omega-3 that we need, other than by eating fish given the concern about sustainable fish stocks. **AR** said various steps could be taken to improve our omega-3 status, and that Dr Hibbeln would be presenting evidence on how dramatically the consumption of omega-6 EFA (linoleic acid) can influence dietary needs for pre-formed EPA and DHA, as there is competition between omega-3 and omega-6 EFA for the enzymes involved in EFA-HUFA conversion. In addition, reducing our consumption of trans fats and saturated fats and ensuring we consume sufficient vitamins and minerals would improve our ability to convert EFAs into HUFAs; and cutting down on the consumption of alcohol and smoking would help because these habits can seriously compromise HUFA status. AR also mentioned that some supplement companies are researching whether we can "skip the fish" and secure the nutrients we need from the algae that the fish feed on. To date, the only controlled trials using algal-derived omega-3 (one for ADHD and one for depression) have not shown any benefits - but this may be because they have provided only DHA with no EPA. She understood that algal sources of EPA were now also becoming available - but again, further studies will be needed to assess these.

Commander Joseph Hibbeln

[NB Joseph Hibblens' presentation was interrupted at various points by questions. In order to present his views in a coherent way, all the questions have been recorded at the end of his presentation.]

Joseph Hibbeln (JH) is a Commander in the Public Health Service in the USA. He is a lead Clinical Investigator at the National Institute of Alcohol Abuse and Alcoholism NIH, with graduated training in lipid biochemistry, epidemiology, statistics and is a Board Certified Psychiatrist. JH initiated research in the field of omega-3 fatty acids in depression and violence in 1995. JH has run rigorous trials looking at the impact on patients with a history of violence of essential fatty acid supplements. He is also involved in the Avon Longitudinal Study of Parents and Children (ALSPAC). ALSPCC, also known as "Children of the 90s", is aimed at identifying ways in which to optimise the health and development of children. Most recently (Lancet 2007) he published the result of a study looking at the impact on child development of maternal consumption of fish and seafood during pregnancy.

JH said it is important to consider what we regard as valid evidence and he showed a slide (slide 1) illustrating the evidence hierarchy:

- Hypothesis
- Epidemiological association (Ecological)
- Direct case based observational associations
- Plausible biological mechanism
- Open (non-blinded) intervention trials
- Randomized masked placebo controlled trials
- Large scale, multi-center placebo controlled trials
- Meta-analysis, weighted analysis of efficacy
- Treatment recommendations

JH said there is a great deal of basic biochemical data on the effect of omega-3 consumption on neurotransmitters and we know it to be effective in the treatment of depression. The only missing link in the chain of evidence now is a large scale multi-centre trial. A meta-analysis of ten trials has been carried out. In summary it found an overall effect size of 0.54, which is considered to be of high significance as antidepressant medications typically have effect sizes smaller that 0.3. He also noted that in the trials under investigation the omega-3 supplements had been used on patients with the worst cases of depression, that is those who had treatment-resistant depression. On the basis of this evidence, treatment recommendations were issued by The American Psychiatric Association. JH believes these, in turn, should be evaluated.

Federal Government agencies in the USA issued recommendations in 2004 advising pregnant women that they should avoid eating fish and seafood because of the potential risk of mercury toxicity (see slide 4). JH believed this advice was in error because they did not take into account the balance of risks with deprivation of beneficial nutrients in fish. So, he decided to evaluate the efficacy of the Federal Government's advice in the largest epidemiological study of pregnancy in the world: the Avon Longitudinal Study of Parents and Children (ALSPAC), initiated by Professor Jean Golding.

ALSPAC is an observational study looking at a representative sample of the British population. Their enrollment included every pregnancy between April 1st 1991 and December 31st 1992 in Avon. The children are now between 11.5 and 15 years of age. Participants mail in questionnaires every 6 months; 1,500 children have been seen in clinics every year since birth and 85% of the children have been seen in clinics every year starting at age 7.

JH and his colleagues allowed for 28 confounding variables, such as housing, education, breast-feeding (see slide 6) and the nutritional variables included 12 food groups so as to ensure the results were tied only to fish and seafood consumption and not other factors. Each of the composite factors taken into account, for example, the "home" score factored in up to 100 contributory factors. The results were published in the Lancet in February 2007. They found that for every dose higher of omega-3 from fish and seafood during pregnancy there was a corresponding higher level of IQ at age 8 of the child (see slide 7).

JH and his colleagues looked at children with a sub-optimal IQ (the lowest quartile) and found that the risk of having a child in this group was 31% where the mother ate no fish and seafood, 23% where the mother ate up to the recommended limit of fish and seafood, and 17% where the mother ate more than the advisory limit. Even at the highest levels of fish and seafood intake, the benefit of consumption outweighed the risk. They also found that children were most protected against the risk of sub-optimal fine motor skills and sub-optimal social development where mothers ate most fish and seafood.

JH and his colleagues also checked that the study was not being biased as a result of the students who dropped out by comparing maternal consumption of fish and seafood against the results of SATs examinations for all the children involved in the study regardless of whether they dropped out. They found that in both groups (those who had dropped out and those who remained in the study) at every level of increased fish and seafood consumption the SATs results improved (see slide 9). They also found a disproportionate attrition of low seafood/disadvantaged families, so the attrition actually resulted in an underestimate of the benefit of maternal consumption of fish and seafood.

The findings of the ALSPAC study were that: maternal limitation of seafood consumption to <340g/week during pregnancy did not protect children from adverse outcomes; this observational study showed beneficial effects on child development when maternal seafood intakes exceeded 340 g/week, with no upper limit of benefit; and these findings were robust after adjustment for multiple potential confounders. They concluded that their evidence indicates that advice for mothers to limit seafood intake, for example, to the the FSA recommended level of 280 gm/week during pregnancy is detrimental.

JH has tried to establish omega-3 intakes based on criteria used to create recommended daily intakes (RDI). He explained that RDIs are calculated so as to protect the majority (>98%) of a population from increased risk of chronic illnesses (for example vitamin C and scurvy) against a risk of adverse effects (see slide 12). Response curves of this kind need to take account of the sensitivities of a diverse population. JH took the world as his sample population and looked at the consumption of omega-3 from fish sources and compared it with World Health Organisation (WHO) databases for various illnesses (see slides 13 and 14). It is notable that Japan and Iceland (with relatively high per capita consumption of omega-3 from fish sources) always do better than the curve. JH also measured omega-3 consumption from fish sources against homicide rates and post-natal depression, not least because omega-3 is rapidly depleted from mothers during pregnancy.

Having produced a dose response curve for each of the twelve variables, including all cause mortality in females (see slide 15), JH and his colleagues calculated the percentage of a vulnerable population that could be protected from various illnesses at different omega-3 doses (see slide 16). They found, for example, that some 48% of cardiovascular disease was potentially modifiable. The data also suggested that 98.5% of major depression was potentially modifiable by omega-3, but JH would like to test this finding further. Only at 750mg/day of omega-3 from all food sources can 98% of the population protected (see slide 15).

JH described the conversion of EFAs to HUFAs and explained that Linolenic Acid (LA)(omega-6) inhibits the conversion of Alpha Linolenic Acid (ALA) (omega-3) to EPA and DHA because they compete for desaturase and elongation enzymes (see slide 17). This is a potential problem if the tissue target is Japan and we want 60% of EPA to be derived from omega-3 because higher amounts of LA (omega-6) mean that the population would require greater amounts of omega-3 HUFAs (see slide 18 showing varying RDIs for different countries). JH and his colleagues found that dietary intakes of long chain omega-3 fats would need to vary more than 10-fold internationally to achieve Japanese tissue levels (98% protection) of long chain omega-3 fatty acids

One alternative to increasing fish and seafood production and consumption 10-fold would be to reduce the intake of LA (omega-6) 10-fold as each would result in similar tissue compositions of EPA and DHA.

A look at changes in the USA food supply over the last century (see slide 20) reveal a huge increase in soya bean consumption from 0.12 kg/year to 12kg/year, that is a thousand-fold increase. Soya bean consumption now accounts for 20% of calories in the average USA diet and half of these calories are derived from LA (omega-6), which creates Arachidonic Acid (AA), which has inflammatory properties. Similarly the consumption of canola (rape-seed) in the USA has increased dramatically. As omega-6 has increased in the diet, the number of homicides in the UK has increased four-fold, despite increasing prosperity (see slide 21).

JH also compared increases in LA (omega-6) consumption with increases in homicide in various other countries, including Australia, Canada, Argentina and the USA and found that they rose in tandem (see slide 22). He noted that these studies do not prove that greater LA intake caused rises in homicide, but noted that increasing EPA and DHA intake has been shown to reduce anger or violence in 3 placebo controlled studies.

JH emphasised that he was speaking from his individual scientific opinion and did not in any way represent the views of the US Federal Government. Thus, he could not make any recommendations to the FHF inquiry team, but he did suggest some issues they might consider for action. He suggested we could:

- support and encourage maternal seafood and omega-3 consumption in pregnancy to protect children from lifelong adverse behavioural and educational harms;
- establish recommendations for minimum daily intakes or EPA and DHA considering mental health outcomes;

- determine if high levels of dietary linoleic acid from seed oils is safe and is not contributing to increasing rates of violence; and

- support fisheries habitats and ecologically safe aquaculture.

JH emphasised that we did not necessarily have to stop eating the vegetable sources of omega-6 because various companies are exploring ways of modifying these crops. For example, DuPont is developing a yeast that produces EPA and Sole is genetically modifying soya beans in an attempt to reduce the amount of LA in them and to see if they can produce EPA and DHA.

Questions

SM asked whether mercury is a problem in all fish. **JH** said that pilot whales had been used to test the level of mercury for the purposes of the USA advice, but pilot whales have relatively high levels of mercury and low levels of omega-3 fats in comparison with other fish. JH believes we cannot assume the level of mercury in other fish is the same as that found in pilot whales. Salmon, for example, has high levels of omega-3 and no significant level of mercury. He is currently working on a specific calculation for each type of fish.

MM asked whether JH had allowed for the effect on their IQ of fish consumption by the children between the age of 0 and 8 years. **JH** said they had investigated this issue and found that English children do not eat much fish and there was little variation between the children in terms of fish consumption during their childhood. Even taking this into account they found that most of the difference between the children was attributable to maternal intake of fish and seafood during pregnancy. He added that this does not mean we should not encourage children to eat fish.

IG noted that the data JH had used depicted correlations rather than cause and effect. **JH** agreed and said epidemiological studies are used to produce testable hypotheses, which he then tests in trials. For example, he had found a 50% reduction in violence among alcoholic patients given omega-3 supplements. JH said he would like to do a large trial to measure the effect of lowering LA (omega-6) in the diet. Finally he noted that the 2004 advice to limit seafood intake was based on observational epidemiological studies.

Baroness Gibson of Market Rasen (AG) asked why there had been so few studies and whether it was because of a lack of money. **AR** said funding was a problem. She and colleagues had responded to a Food Standards Agency proposal, but it would have been very difficult to achieve what the FSA was asking for at the costs suggested. None of the projects offered in response met the FSA's requirements and they are now reconsidering this matter. The DfES has shown some interest in the issue, but unfortunately a significant amount of media attention has generated scepticism about the links between diet and behaviour. AR suggested we need better education about nutrition so that the public, health and education professionals understand the significance of good nutrition.

EB asked whether AR's suggestion in her summary that evidence from RCTs "clearly shows" the benefits of omega-3 on behaviour is valid given the few number of trials that have been conducted and the absence of any large trial. **AR** agreed we need more, larger scale trials. EB pressed AR to say whether there was sufficient evidence to justify recommending universal supplementation of school children and whether there was any danger of causing harm by using supplements. AR said supplementation was unlikely to cause any harm. AR said she does not recommend universal supplementation – we still need to establish the costs and benefits of that– but she does believe that there may be a case for giving supplements to children with special educational needs, given the very high costs of providing other forms of support. She pointed out again that the latter are currently not available to all who need them, and most have not been formally evaluated for their effectiveness in any case. AR reiterated her view that, as with any state-funded interventions, the use of supplements really should be evidence-based so large-scale controlled trials would be the obvious next step.

JH said the FDA's recommendation that it is safe for adults to consume up to 3g of fish oils/day has stood the test of time over twenty years, although no-one has been evaluating the mental health outcomes. He believes it would be safe to consider advising use of fish oils up to this dosage, but he would also like to monitor the outcome of this advice.

MC emphasises that maternal nutrition during pregnancy should be our main focus given its significance for child development and behaviour.

NR asked JH how he could verify his views on the need to reduce LA (omega-6) intake and convince others. **JH** said he would like to actively lower the intake of LA in the diet of violent people and then monitor them to see if lead to reduction in violent behaviour. He would also like to measure the difference between the costs and benefits in terms of reduced crime and health costs. NR asked whether it would be easy to design a diet where omega-6 intake was reduced and JH said he believed this was possible.

JH was asked whether mercury was the only toxin in fish that had resulted in the FDA warning to pregnant mothers, or whether the authorities were also concerned about PCBs and dioxins. **JH** said he believed their recommendation was based purely on their concern about mercury levels because they affect neurodevelopment, whereas PCBs and dioxins are thought to be significant for cancers in later life.

Lord Rea thanked the speakers for their excellent presentations and the meeting ended.

CLC, March 2007