

ALSPAC NEWS 22



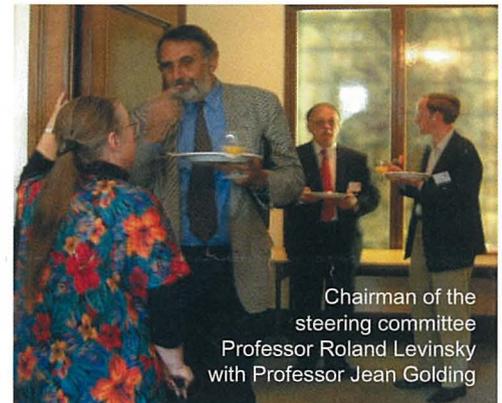
Avon Longitudinal Study of Parents and Children

Researchers from all over the country converged on the Royal Society in London on June 4th to discuss their findings using the ALSPAC data. This is recognised now as the world's most detailed study on how an individual's health is affected by a complex interaction between their genes and the physical and psychological environment. There were collaborators from the USA, Finland and the Netherlands, as well as a group from the ELSPEC Isle of Man.

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- The first 10 years of the study
- The first 100 publications
- The first multi-million £ funding



Chairman of the steering committee
Professor Roland Levinsky
with Professor Jean Golding

The Wellcome Trust and the MRC announced that they were injecting core funding of more than £6 million, and Bristol University £5 million. The Trust is providing an additional £2 million to establish the collection of cell lines. This will allow DNA samples to be used as a long-term resource for future studies.

Dr Mike Dexter, Director of Wellcome Trust said: *'The study has demonstrated the huge power of large population-based studies. It has already saved many lives, and the new core funding and research projects resulting from it will continue to improve the health of parents and children for generations to come. It is a tremendous resource that has stimulated collaborations between researchers all over the world, and a great example of how research should be conducted.'*

Professor Sir George Radda, Chief Executive of the Medical Research Council said *'I'm delighted this partnership will allow the researchers to build on ten*

highly successful years generating vital health information. I would like to express my deep gratitude to the families and researchers for making the project such a great success. Their willingness to share this knowledge for the greater good, is a real and lasting gift to society.

Longitudinal studies provide the perfect opportunity to study biological and environmental influences over a person's lifetime and this long-term view greatly increases our understanding of health and disease.'

Sir John Kingman, Vice Chancellor of the University of Bristol said *'This is a study dear to the hearts of all of us at Bristol University. We are delighted to play our part in ensuring this vital resource will continue to improve our understanding of how nature and nurture interact to cause disease.'*

The Wellcome Trust masterminded the publicity for the occasion and highlighted two of the talks that were being given. These hit the headlines; the study was covered on national news programmes throughout the day. (More inside)



The respiratory allergy group discuss the future

Profile of the ALSPAC Statisticians

As well as the various statisticians working with our distinguished collaborators, there are four who work 'in house'. They are responsible for cleaning, editing and documenting the data, liaising with collaborating groups as well as carrying out their own programmes of research within ALSPAC.

Our four statisticians from left to right:

Jon Heron did his PhD here in Bristol on the foraging behaviour of ducks, otters and small rodents. He has made an impact on the analyses of depression and anxiety within our study. He works with Dr Tom O'Connor of the Institute of Psychiatry, on the relationship between maternal anxiety in the mother and the development of the child, as well as with Dr Sara Meadows of the Graduate School of Education and Dr David Jewell, general practitioner, who are interested in the way teenage mothers differ from the rest of the community. He will also be analysing the data collected in one of the sub-studies that we are carrying out – the influence of noise on the child. We have just finished measuring noise levels in 80 homes and will use this to validate the information given in questionnaires.

Andrea Sherriff is a Glaswegian whose PhD was concerned with diseases in sheep! She has just completed a Wellcome Trust Training Fellowship in Biomathematics during which she spent time at the Rockefeller University in New York, investigating the feasibility of using Artificial Neural Networks to analyse the complexities of analysis of gene-environment interactions. (She concluded that traditional epidemiological methods were less prone to erroneous conclusions). Within the various topics in ALSPAC she specialises in the analysis of information related to asthma and allergies. Andrea has a particular interest in the common genetic polymorphisms which may be linked to an increased susceptibility to these problems and the interaction between genetics and different environmental factors.

Kate Northstone works on a wide variety of topics, particularly diet. She works with Pauline Emmett our nutritionist and also Cathy Williams, our resident ophthalmologist in regard to the various ways in which diet can affect health. Recent papers have included the influence of maternal diet in pregnancy on the child's visual development by age three, the child's birthweight

PEANUT ALLERGY

ALSPAC has made some important discoveries in regard to this disorder. Dr Gideon Lack talked about recent findings in a report given during the recent celebration meeting in London.

He showed that as many as 1 in 100 of our children have peanut allergy by the time they are 7 – a far higher number than previously thought.

He found that of those with peanut allergies approximately 90% are preceded by eczema. 'In eczema, the skin barrier breaks down and there is an abundance of immune cells in the skin that could be exposed to substances that cause allergies,' said Dr. Lack. 'We are currently looking into whether exposure of the skin to products containing peanuts or peanut oils may be responsible for starting peanut allergies,' he added. This is a very important possibility and information given by him at the meeting in June (see page 1) seemed to support this.

There are many over-the-counter preparations (soothing oils and creams and even bath oils) that contain peanut oil. The prevention of peanut allergy may be as simple as ensuring that oils and creams containing peanut oil (it will be listed as arachis oil) are avoided.



Dr Gideon Lack

Peanut allergy is potentially a problematic type of food allergy since peanuts and peanut oil are contained in many foods. Yet a severe reaction can be fatal. One of our mothers has written to us to describe the problems she has.

'I have two children aged 8 and 5 both of whom have peanut and nut allergy. Exposure to even a minute trace of nuts could cause a serious reaction which if not treated immediately could be fatal. This presents us

and the chance of developing the male genital malformation, hypospadias. She has identified dietary influences on the development of headaches and of food allergies in young children. She has also interests in dummy (pacifier) and thumb sucking on child's health and development. Kate is currently working towards her PhD using ALSPAC data.

David Herrick recently completed his PhD in statistics at the University of Bristol. His work with ALSPAC

includes investigating the influence of school and pre-school environment on the child with particular regard to behaviour, non-verbal communication, the child's attention span and later academic achievement. As part of a totally different project he has looked at how sunlight influences the development of melanocytic moles in young children. As we start the 9-year testing, he will be involved in the analysis of oto-acoustic emissions, which will give us an idea about how well the inner ear copes with noise.



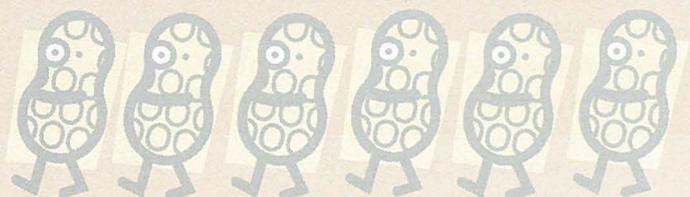
with many problems. We encounter food at least three times a day and food is often central to social activities. My children never eat anything unless it has been checked first. The almost ubiquitous 'may contain nut traces' makes shopping a frustrating experience. We do not buy food from bakeries and we do not risk eating in restaurants or cafes.

The practicalities of living with a severe food allergy are difficult enough, but another more frustrating problem is the chronic lack of awareness which we encounter. This is forgivable amongst the general public as it is such a new condition and most people are keen to understand and concerned to help. But when you are confronted by ignorance amongst those who have responsibility for your children it is nothing less than terrifying. I have encountered head teachers, governors, school cooks, dinner ladies and even school nurses and health visitors who are ill-informed.

A severe food allergy is an invisible condition. People with the condition are usually completely normal in every other respect and yet if they are exposed to the food they are allergic to and do not receive treatment immediately they can die within minutes. I have at times experienced difficulty in convincing others of the

seriousness of the consequences, and the miniscule amounts involved in triggering a reaction. For my children even holding hands with someone who has been eating nuts, especially peanuts, could trigger a reaction.

These children carry the burden of a life-threatening condition and show remarkable responsibility from a very young age. They are aware that they are different. Of course as parents our paramount concern is for our children's safety, but we would also like them to feel as normal as possible and not to be stigmatized or bullied. I know of a child with a severe allergy who was made to sit on a separate table because of his allergy had a peanut butter sandwich thrown at him – this is the worst kind of bullying as he was being threatened with death. I hope I can give my children the emotional strength to cope with their condition and I try daily to keep a balance between safety and normality.'



Contrasts between Children of the 90s born in Britain and in the Czech Republic

To try and shed light on the early origins of asthma we compared wheezing illnesses in infants living in Avon, with those in Brno and Znojmo in the Czech Republic.

We found that, by 6 months of age, 21% of Avon babies had had an attack of wheezing compared with only 10% in the Czech Republic. We tried to see whether this could be explained by smoking habits of the parents. In Avon, 18% of mothers had smoked in pregnancy compared with only 7% in the Czech Republic; the babies were also more likely to be in a smoky atmosphere in Avon (36%) compared with the Czech Republic (10%).

Although we know that the most important factor

influencing early wheezing in Avon was how much the mother smoked during pregnancy, we didn't find this in the Czech Republic. There we found that it was the smoky atmosphere in which the baby was often found that had the most influence.

This does not explain why the Czechs have so much less wheezing, but it does provide clues as to causes of wheezing. Some of the questions to be addressed include the differences between the types of cigarette in the two countries.

Henderson J, Sherriff A, Northstone K, Kukla L, Hrubá D, ELSPAC Study Teams. Pre- and postnatal parental smoking and wheeze in infancy: cross-cultural differences. European Respiratory Journal. In press.



ALSPAC RESEARCHER HONOURED

One of our key collaborators, Dr Ken Ong was awarded the European Society for Paediatric Endocrinology (ESPE) 2001 'Young Investigator Award' at their 6th Joint Meeting of the Lawson Wilkins Pediatric Endocrine Society and the European Society for Paediatric Endocrinology, Montreal, Canada. This was awarded for 'outstanding scientific achievement based on publications and commitment to paediatric endocrinology'. His research with ALSPAC has focused on the growth of the infant and the way this is influenced by both genes and the environment.

Ken is an MRC research fellow working with Professor David Dunger at Cambridge University. Their ALSPAC publications include papers in the prestigious journal Nature Genetics.

Antibiotic Resistant Bacteria

We all carry around with us a large number of bacteria of different kinds. Many of these are good for us and have important functions. However some can cause disease, particularly if we are under stress in any way.

Our colleagues in the Department of Microbiology here at Bristol took mouthwash samples and asked children to post back stool samples. 500 children were chosen to take part in this and gave us a saliva sample at Focus @ 7 – and an impressive 62% sent back a stool sample.

The team found that healthy children who have never been hospitalised carry bacteria around that are resistant to antibiotics. (Most studies on antibiotic resistance are concerned with hospital infections). Many of these antibiotics to

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which the bacteria were resistant are substances that children would never have been given – and so the resistance must have come from elsewhere. There are a number of possibilities including other family members, pets, other children or indeed in the food that we eat. This study will serve as a feasibility study for further sample collections from the ALSPAC children.



Millar MR, Walsh TR, Linton CJ, Leeming JP, Bennett PM and the ALSPAC Study Team. Carriage of antibiotic resistant bacteria by healthy children. Journal of Antimicrobial Chemotherapy 2001; 47: 605-610.

DO TWINS HAVE A SECRET LANGUAGE?

There has been considerable discussion over the years as to whether twins sometimes develop a secret language between themselves

This has been looked at by Dr Karen Thorpe, Sir Michael Rutter and their colleagues. Most of the twins were visited at 20 months and 3 years of age and the way in which they talked to one another and with their mother was recorded. To compare families with twins with other families a comparison group were chosen where there was a study child of the same age together with another brother or sister who was born within 2 years (known as the sibling group).

They found that at 20 months, 60% of twins had a shared understanding (i.e. they understood one another even though their speech was imperfect); this was much more common than in the sibling group although 38% of them also had this sort of understanding. Almost all of the children had grown out of this by age 3.

A real 'secret language' that others could not understand was only found in twins, and only 6% of twins at age 3. Following these children up further they found that none of these twins was still using this secret language once they started school.



Thorpe K, Greenwood R, Eivers A, Rutter M. Prevalence and developmental course of 'secret language'. *International Journal of Language and Communication Disorders* 2001; 36:43-62.

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Anaemia in infancy may be associated with slower motor development at 18 months

A 10% sample of children participating in the Children of the 90s were invited to our Focus clinics at 8, 12 and 18 months. Blood was taken to see if they were anaemic. Their development was tested at 18 months.

A quarter of children were mildly anaemic each time, but their development was just as good as the children who were not anaemic. However the 5% of children who were very anaemic at 8 months of age had, on average, a slight delay in their motor development at 18 months (this included how well they were walking, climbing stairs, etc) but not in other aspects of their development. There were no developmental effects of severe anaemia at the later ages.

A next step in this study will be to look at the later development of these children to see whether there is any indication that there is a long-term effect of severe anaemia on the child before recommending that a

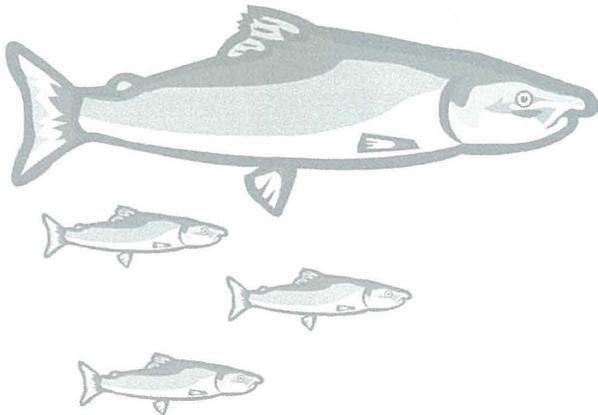


screening programme be started.

Sherriff A, Emond A, Bell JC, Golding J and the ALSPAC Study Team. Should infants be screened for anaemia? A prospective study investigating the relation between haemoglobin at 8, 12, and 18 months and development at 18 months. *Archives of Disease in Childhood* 2001; 84:480-485.

We have found that mums-to-be who eat oily fish such as sardines and mackerel have children who can see better. This positive association was also seen for breast feeding.

The findings were announced by Cathy Williams, the eye expert for the Children of the 90s project. A 10% sample of the Children of the 90s children were regularly invited to 'Children in Focus' where tests were carried out on their eyesight up to age 3 and a half.



Cathy Williams said, 'As far as we know this is the first time that diet in pregnancy has been shown to be associated with a child's visual development. Our results suggest that children whose mothers ate oily

fish in pregnancy or who were breast fed reach the adult grade of depth perception sooner. Other unpublished data from ALSPAC show a strong association between good depth perception and better mental development.'

She added, 'We are not suggesting that pregnant women run out to the supermarket and strip the shelves, as the women we looked at only ate the fish once a fortnight.'

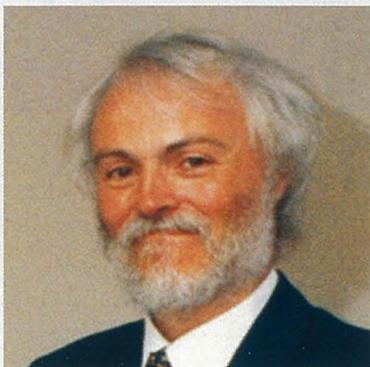
Oily fish include tuna, pilchards, sardines, mackerel, salmon and trout.

Oily fish is the richest source of DHA, a fatty acid which is an important component of neuronal membranes found in the brain. DHA is also present in breast milk but not standard formula milks. These results add to the debate about whether formula milks should be fortified with fish oils.

Williams C, Birch EE, Emmett PM, Northstone K and the ALSPAC Study Team. Stereoacuity at 3.5 years of age in children born full-term is associated with prenatal and postnatal dietary factors: a report from a population-based cohort study. American Journal of Clinical Nutrition 2001;73 :316-322.

What influences women in deciding to breast feed?

Birthday honour for Professor Peter Fleming



Professor Peter Fleming has been awarded the CBE for his important work on cot death and sleeping position. He has been an important member of the ALSPAC Scientific Advisory Committee and had a major impact in advising on questions on early childhood development.

Very few studies have examined whether the way a mother feeds her newborn infant is affected by her plans to go back to work following the birth of her child. We asked mothers in pregnancy about their work plans following the birth of their infant. We looked at these work plans and other factors that have been linked to the way a mother feeds her newborn baby.

We discovered that mothers were less likely to breast feed their infant if they planned to return to work before the infant was six weeks old. We also discovered other features such as age, education, attendance at child-birth classes, smoking, as well as how the mother herself was fed as a baby and number of children she already had, were linked to the way a mother fed her newborn infant.

Noble S, The ALSPAC Study Team. Maternal employment and the initiation of breastfeeding. Acta Paediatrica 2001; 90:423-428.

One of the major questions Children of the 90s can tackle is that concerning the best way of feeding children in the first years of life. We have found that delayed introduction of chewy foods with lumps may lead to difficulty in feeding the child later.

Children who were not introduced to chewy foods by 10 months of age were much more choosy about the foods they would eat by 15 months. Children who are very choosy about food often cause their parents a great deal of worry.

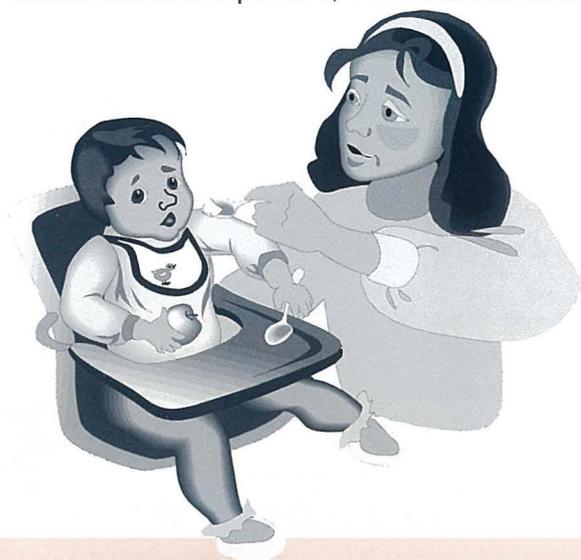
Pauline Emmett explained, 'Previous research had

suggested that babies are ready to learn to chew food at 6 to 9 months of age and that problems might arise if this ideal time was missed. We decided to see if this was so using the detailed information collected in ALSPAC.'

She went on to say, 'The majority had been introduced to lumps between the recommended ages of 6 and 9 months. About 10% had been introduced before 6 months and this did not seem to cause any problems. Nearly a fifth had not been introduced until 10 months or later and this group ate less varied foods at both 6 and 15 months. By 15 months more than half of these children were said to be difficult to feed compared with a third of the other children. They were also twice as likely as the other children to have definite likes and dislikes.'

These results suggest that mothers of six-month-old babies should not delay too long moving from a semi-liquid diet to introducing more lumpy food.

Northstone K, Emmett P, Nethersole F and the ALSPAC Study Team. The effect of age of introduction to lumpy solids on foods eaten and reported feeding difficulties at 6 and 15 months. Journal of Human Nutrition and Dietetics 2001; 14:43-54.



Toddlers diet and iron status

Iron deficiency anaemia is common among toddlers in the UK. We have investigated the relationship between diet and anaemia at 18 months of age. Parents were asked to record in detail what their children ate for three days and a blood sample was taken and analysed for haemoglobin and ferritin – measures of iron status.

We found that the more cows' milk and dairy products the children consumed the lower their ferritin levels – this may be because the calcium in dairy products inhibits iron absorption. Children who still drank an iron-fortified formula milk at 18 months had higher ferritin levels than those who drank cows' milk. ALSPAC nutritionist Dr Imogen Rogers suggested that it is likely that children who drank more than 1½ pints (750ml) of cows' milk a day were too full up with milk to fit in a good range of other foods.

Both haemoglobin and ferritin levels increased as vitamin C intake went up – vitamin C enhances iron absorption from food. Children who ate no fruit or no

vegetables were more likely to have low levels of haemoglobin. Children who ate no meat or poultry were also more likely to have low haemoglobin levels.

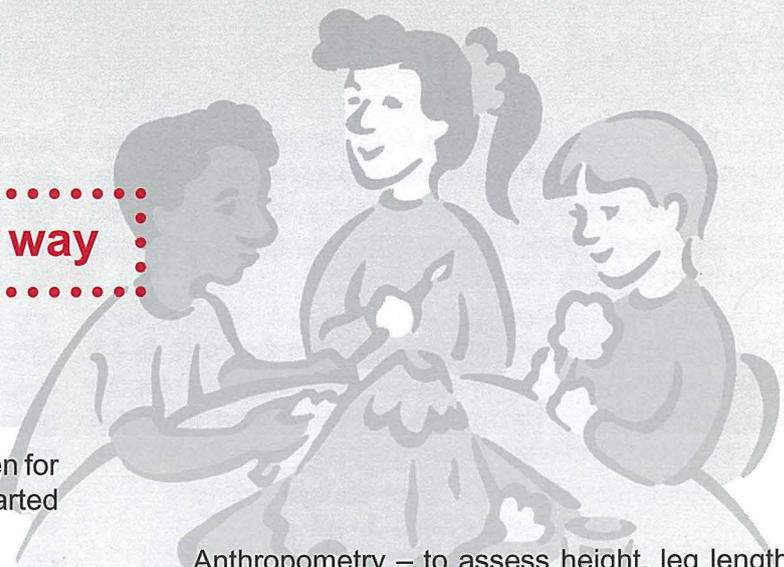
These results reinforce the message to increase fruit and vegetable consumption, and suggest that toddlers should be discouraged from drinking excessive quantities of milk.

Cowin I, Emond A, Emmett P, and the ALSPAC Study Team. Association between composition of the diet and haemoglobin and ferritin levels in 18-month-old children. European Journal of Clinical Nutrition 2001; 55:278-286.



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Focus at 9 is now under way



In keeping with our desire to examine all the children for half a day every year, the 9-year examinations started earlier this year.

The study has taken considerable care to explain to the parents and the children the scientific benefits of laying down immortalised cell lines for future genetic studies. They are told, however, that these can be destroyed at any time, on request. Of the first 1500 children attending the 'clinic', 73% have had a sample successfully frozen down for future culturing.

As well as the collection of blood for immortalised cell lines, there are a number of important measurements being obtained. These include:

DXA scan of the whole body – to provide information on bone mineralisation and body composition.

Anthropometry – to assess height, leg length, weight, waist, head and arm circumferences.

Hearing assessments – audiometry, tympanometry, video-otoscopy, oto-acoustic emissions.

Lung function.

Physical fitness – using a cycle ergometer.

Reading and spelling tests.

The results will allow us to investigate the development of topics as diverse as obesity and dyslexia; they will also provide a baseline against which to measure factors that influence the development of strong bones, respiratory function, cardiorespiratory fitness and the prevalence of hearing loss over time.

... and the last word on our celebration!



Neville Butler with Professor Jean Golding

We were proud to include Neville Butler among our guests at the Royal Society in London. He was the Professor of Child Health in Bristol until 1985, when he retired officially.

He was a key player in directing two of the major national longitudinal studies - of children born in 1958 and 1970. Professor Golding had worked with him on both of these – and that had given her the ideas for what we believe to be an even better study, ALSPAC.



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ALSPAC is a research initiative of the Unit of Paediatric & Perinatal Epidemiology, Institute of Child Health, University of Bristol

The protocol for the ALSPAC study can be found on our website:
www.ich.bris.ac.uk/alspac.html