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Ongoing study examines links between genes and environment

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LONDON Peanut allergies are preceded by eczema in nine out of ten cases, according to the latest findings from the world's largest study examining how the interaction between genes and environment affects children's health.

The Avon Longitudinal Study of Parents and Children ([ALSPAC](#)) celebrated its ten-year anniversary this month (June 2001) with a conference at the [Royal Society](#) in London. ALSPAC was set up in 1991 to try to unravel the way in which physical and social environments interact over time with genetic inheritance to affect a child's health, behaviour and development. The study hopes to uncover the underlying causes of a number of common conditions such as asthma, food and other allergies, autism, hyperactivity, dyslexia, anxieties and phobias, obesity, depression, deafness, eczema, epilepsy, and cerebral palsy.

The study, also known as Children of the Nineties, initially recruited 14,000 women during pregnancy. Around 12,000 families are still being followed 10 years later. The study has been very fruitful so far. Over 100 publications have resulted from ALSPAC over the last ten years. In particular, it has gathered an enormous amount of high quality detailed data from early pregnancy. This information has been based on physical examinations, questionnaires completed by parents, health records, assays of biological samples and specific measurements of the environment in the home. In addition, both maternal and child DNA have been collected.

The children were examined when they reached the age of seven years to assess physical characteristics such as blood pressure, atopic status, vision and hearing. At the age of eight, they were assessed for cognitive and behavioural attributes.

One of the most significant discoveries to come out of the ALSPAC programme so far was that babies are healthier when put to sleep on their back ([Pediatrics](#) 1997, **100**:e11). Conventional thinking was that sleeping on the front was healthier, even though it might be responsible for cot death. "Our part of the ALSPAC study showed that sleeping on the front leads to increased numbers of infections, particularly those involving the chest. These findings convinced the US and UK governments to change their advice to mothers, and saved thousands of lives throughout the world," Jean Golding, Professor of Paediatric and Perinatal Epidemiology at [Bristol University](#) and scientific and executive director of ALSPAC, told BioMedcentral. "This is a study that we know had a big impact and undoubtedly saved lives."

Another interesting finding from ALSPAC was that eating oily fish during pregnancy improves the visual development of the child ([American Journal of Clinical Nutrition](#) 2001, **73**:316-322). Study leader Cathy Williams, an ophthalmologist at the University of Bristol, said: "This is the first time that diet in pregnancy has been shown to be associated with a child's visual development. Our results suggested that children whose mothers ate oily fish in pregnancy or who were breastfed reached the adult grade of depth perception sooner." Oily fish is the richest source of docosahexaenoic acid (DHA), a fatty acid that is an important structural component of neuronal membranes found in the brain. DHA is also present in breast milk but not in formula milk. The findings added to the debate about whether formula milk should be fortified with fish oils.

Another key finding was that female fertility is reduced by passive smoking ([Fertility and Sterility](#) 2000, **74**:725-733). If for example, a non-smoking woman is exposed to passive smoke in the workplace

or at home, the odds of her taking more than 12 months to conceive increase by 14%. If her partner smokes more than 20 cigarettes a day the odds of delayed conception are increased by 34%.

The most recent results show that peanut allergies occur in as many as one in 100 children, a far higher number than previously thought. Eczema preceded peanut allergies in approximately 90% of children. Study leader Gideon Lack, from [St Mary's Hospital in London](#), said: "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." He added: "We are currently looking into whether exposure of the skin to products containing peanuts or peanut oils may be responsible for starting peanut allergies."

Large-scale studies such as ALSPAC are useful in trying to identify the various genetic and environmental factors leading to different diseases. "Life is complex," said Golding. "Genes and environmental factors do interact. It is not as straightforward as saying if you have this gene then you have asthma; rather, if you have this gene and another gene and there are certain environmental factors present then you will develop asthma."

Because ALSPAC recruited during pregnancy, it is in a strong position to address questions about genetic and other influences on foetal and infant growth and the way these relate to risk factors for common adult diseases such as coronary heart disease and type 2 diabetes. A study of a sub-cohort, Children in Focus, has shown that maternal restraint of foetal growth, resulting in small size and thinness at birth, may be associated with insulin resistance and type 2 diabetes in adulthood ([Lancet 1999, 353:1499](#)).

Professor Sir George Rada, chief executive of the [Medical Research Council](#), noted: "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."

"The big advantage of the ALSPAC study is that it is prospective and longitudinal," Golding agreed. "For example, if we have a child with asthma we already have the information on what the mother was eating in pregnancy. If you have to look retrospectively, the mother probably won't remember and so you get inaccuracies."

The sheer size of the cohort is another plus point for the study. Mike Dexter, director of the [Wellcome Trust](#), said: "The ALSPAC study has demonstrated the huge power of large population-based studies. ALSPAC is a tremendous resource that has stimulated collaborations between researchers all over the world, and a great example of how research should be conducted."

The future for the ALSPAC study looks assured, at least for the next five years. The Wellcome Trust and the Medical Research Council have injected core funding of more than £6 million and Bristol University has added a further £5 million. The Wellcome Trust is also providing an additional £2 million to establish a collection of cells from children and their parents, which will allow DNA samples to be used as a long-term resource for future studies.

"I hope we can continue for as long as the families want to take part," said Golding. "We are planning studies on a number of different aspects of puberty such as bone mineralization, the onset of acne and criminal behaviour. We hope to follow the children through adolescence and into adulthood. One particularly fascinating area we hope to look at is their reproductive lives. The future is very exciting."

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