

CHILDREN OF THE 90s - EVIDENCE FOR HOMEOPATHY?

Professor Jean Golding

Transcript Of Tape Of Blackie Memorial Lecture 2006

Dr. Sara Eames: For those of you whom I haven't yet met, my name is Dr. Sara Eames. I am one of the doctors here at the Homeopathic Hospital and also one of the Trustees of the Blackie Foundation Trust.

It is my pleasure to tell you just a little about the Foundation. I am sure most of you know about Dr. Margery Blackie, who, during the middle part of the last century was a wonderful Homeopathic Physician both at the London Homeopathic Hospital and in private practice in London. She founded the Blackie Foundation Trust with the dual aims of supporting research in homeopathy and for the training of doctors in homeopathy.

The biennial Blackie Memorial Lecture has recently become a part of the Royal London Homeopathic Hospital's Research Conference and is why we are here today. Without further ado I would like to welcome and invite Dr. David Spence, the previous Blackie Memorial Lecturer, who is consultant at the Bristol Homeopathic Hospital to introduce our Lecturer today.

Dr. David Spence: It is a great pleasure to fulfil my duty as the previous Blackie Lecturer and to introduce this evening's Blackie Lecturer, Professor Jean Golding, Professor Emeritus in Paediatric and Perinatal Epidemiology at the University of Bristol.

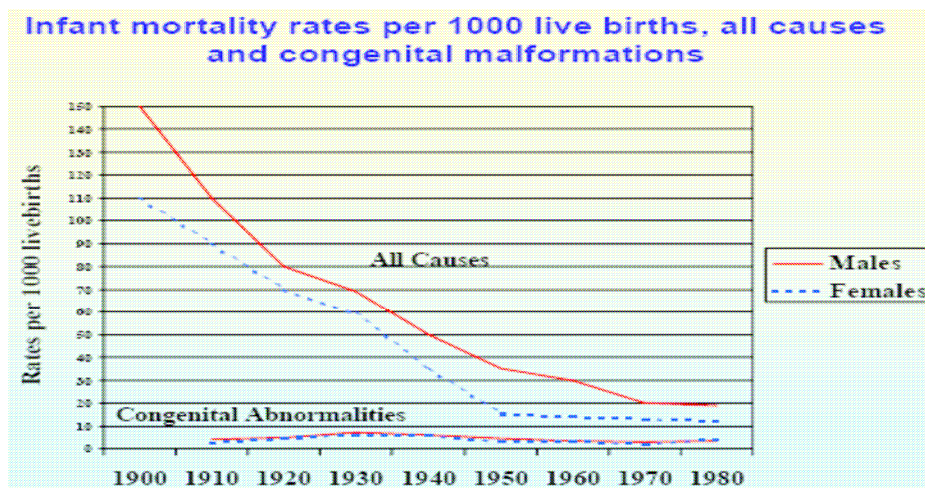
She trained as a mathematician at Oxford and, when she had two young children and needed to find some work based from home, she helped out with some epidemiology research. In her own words she became entranced with it! At the same time she met and worked with Professor Neville Butler and, as he was based in Bristol, she relocated there and became involved with many long-term epidemiological studies. She found it frustrating that there were often large gaps of time when following cohorts of people between capturing information and this gave rise to how she would like to design and run her own studies.

When chatting with Jean yesterday in her office about the Children of the 90s I asked her how the study began and she actually said “it happened by accident!” I wasn’t sure whether to believe her! So without further ado, may I introduce the Eleventh Blackie Lecturer, Professor Jean Golding.

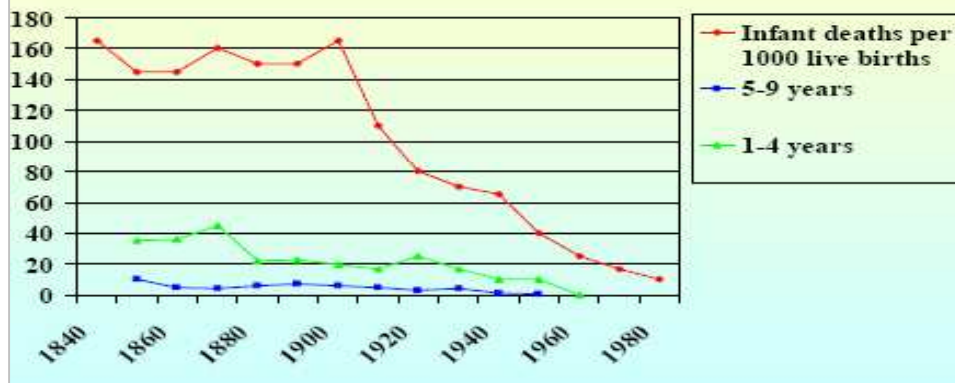
Professor Golding: David, thank you very much indeed. I am indebted to your lecture for enlightening me as to the character of Margery Blackie, whom I just wish I could have met. Her picture on the web doesn’t do her justice although she does look elegant and charming. As my first contact with this organisation was Anita Davies, I instantly recognised a sort of characteristic that perhaps runs through all of you, well the women anyway! I will try and live up to her reputation.

Let me describe what was happening at the time in which I was asked to start planning such a study as the Children of the 90s. Back in the 1980s, a time when the most obvious thing to measure in terms of health was mortality (and mortality was falling dramatically), there was an assumption that if you measured deaths, the converse was health – therefore the nation’s health must be improving dramatically. If you looked at young children you could see that the trend with falling death rates was quite fantastic. However, if you looked at the causes of death you could see that the things that were vanishing were the things that we were immunising against and that there were a number of causes of death that were staying static or even increasing.

So, instead of looking at deaths, if you actually looked at hospital admissions, this is what you would find.



Mortality rates in various ages per 1000 children in different age groups (1846-1981) (Macfarlane and Mugford 1984))



Death rate of children aged 1-14 (rate per 10000) by specific causes.

Cause of death	1911-15	1931-35	1956-60	1976-80
Diphtheria	63	43	0	0
Measles	131	36	0	0
Pertussis	54	19	0	0
Gastroenteritis	68	11	1	0
TB	124	46	1	0
Scarlet fever	26	8	0	0
Rheumatic fever	9	8	0	0
Cancer	6	9	12	8
Pneumonia/bronchitis	2205	89	10	4
Accidents	49	38	20	14

(adapted from Court & Alberman, 1988)

RHSC Edinburgh Admissions to Medical Wards



Is there really an increase in morbidity or is it just that they are admitting children more readily and discharging them quickly? What is going on? Looking at specific causes, we found that there were a number of conditions that were rising quite dramatically such as Type 1 Diabetes, Coeliac Disease and asthma. It could be that people are labelling children as having asthma more readily, but if you look at wheezing, especially wheezing in the past twelve months, you can see an increase and, if you measure lung function, you can see a decrease. Something was happening that was very dramatic and, biochemical tests looking at the total IgE antibodies, showed a dramatic increase over time.

**Prevalence of juvenile-onset diabetes:
Scotland – age 14 school medicals**

	Prevalence per 1000
1969	1.0
1978	1.5
1985	2.4

(from Logan and Cole, 1988)

**Prevalence of asthma symptoms;
South Wales 12 year olds**

	1973	1988
asthma ever	6%	12%
wheeze ever	17%	22%
wheeze in past 12 months	10%	15%
>36% fall in PEFr on expiration	0.9%	2.3%

(from Burr et al, 1989)

Coeliac disease in Sweden

Birth cohort	Prevalence per 1000	(no)
1978 – 82	1.7	(657)
1983 – 87	3.1	(1287)

(from Cavell et al, 1992)

**IgE antibodies
13-14 year old girls, Japan**

Year	Prevalence	(No. Positive)
1978	21%	(30)
1981	25%	(29)
1985	36%	(38)
1991	39%	(37)

(Nagkagomi et al, 1994)

Thus although mortality was dropping, it looked as though chronic diseases were increasing quite dramatically. All those diseases which were increasing had a genetic component but the gene pool cannot possibly have changed so rapidly or readily, so we decided that what we needed to look at were the environmental factors that were influencing these diseases. We developed our overall objective, which was to understand the ways in which the physical and social environment interacts over time with genetic inheritance to affect health, behaviour and development in children and to follow them into adulthood. And the resulting study, the Children of the 90s, is also known as ALSPAC, the Avon Longitudinal Study of Parents and Children.



The advantages of being in the Bristol and Avon area is that it is a defined geographic area that people tend to stay in and not move out of. It has Bristol City as a part of it with half the population of half a million and another half a million outside the city tending to be in suburbs, small towns, villages and farming communities. As a whole it is very similar to England and Wales. At the time we were starting out the health professionals, teachers and employers were all enthusiastic.

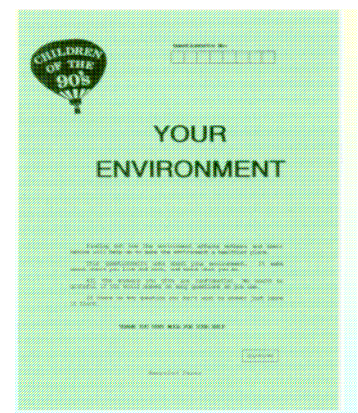
In order to study the effects of the environment we didn't just confine ourselves to the physical pollutants that might have adverse effects, we particularly emphasised the structure of the family and what was going on within the home and outside the home, in the school, as well as the sort of healthcare that the parents were using. And of course within that Anita Davis influenced me very much to add questions on homeopathy and other complementary medicines.

The idea was that those environments would interact often with different genotypes and that we would find influences on all sorts of outcomes. You can see that we are not just looking at health outcomes but also psychological ones, and many aspects influencing the way in which a child will turn into an adult. We are looking at ways in which they develop in childhood like their growth and mental ability, how they get on at school, their reading, writing and any problems such as dyslexia, the accidents they have and so on. The whole design of the study was very much looking way into the future to try and decide what factors we ought to be measuring.

We decided that the earliest we should start collecting information was as soon as the mother became pregnant. This was a challenge because we needed to enrol pregnant mothers even before they got to the health service if we could. We flooded the area with information about the study and tried to raise the enthusiasm of the whole pregnant population of the area for the study. We were very fortunate because our local media thought this was a great idea. The sort of information we decided to collect included questionnaires that were completed by the parents and later by the children, health records, biological samples, the environment, education records and by actually examining the children.

Once the mother had contacted us to say she was pregnant and she met our criteria for inclusion - which was falling within our geographic area of residence and having an expected date of delivery between April 1991 and the end of 1992, we sent her a brochure saying that she was not going to get anything out of the study, that we would be asking a lot of her, but that her participation would be for the common good. Appealing to her sense of altruism, we said that we didn't think that it was likely to help *this* child but the results of the study should be able to help *subsequent* generations. We promised her that all the information they gave us would be kept in absolute confidence and that we would never link the information given on questionnaires to her name or any other identifying information.

Mothers were told to think upon it and if they didn't want to take part to ring and let us know. After waiting a week if we hadn't heard from them we sent them their first questionnaire called 'Your Environment'. It was one of the shortest ones being 32 pages long and was aimed at abstracting all sorts of environmental features that might influence early development of the foetus or embryo. It went into details of the sorts of household chemicals the mother used, the jobs she had had and a variety of other features of the environment that we thought might have an effect.



To encourage compliance, if we hadn't received the questionnaire back after two weeks we sent a reminder, followed by a further reminder after another week and finally by a knock at the door from a charming member of our staff. We had a 94% response rate. One of the reasons why we hassled so much was that we wanted to get four different questionnaires completed during pregnancy.



The next questionnaire was called 'About Yourself' and was concerned with the mothers themselves. It went into a lot of detail about all sorts of aspects of their childhood, medical history, social history, how many siblings they had; it also asked information about their parents such as the sort of occupation they had and their medical histories. At 18 weeks gestation a questionnaire was aimed at measuring various things that had

happened during the pregnancy and also asked a bank of questions that measured depression and anxiety as well as relationships with the partner. Finally, their fourth questionnaire, at 32 weeks gestation, included a very detailed dietary history.

We had done a lot of validation studies before we started to ensure that mothers could actually answer questionnaires accurately. The fact that we had promised confidentiality meant that, as far as we can tell, we got very accurate responses to questions - obvious examples are drug abuse and various aspects of lifestyle which in a face-to-face interview might not be revealed at all.

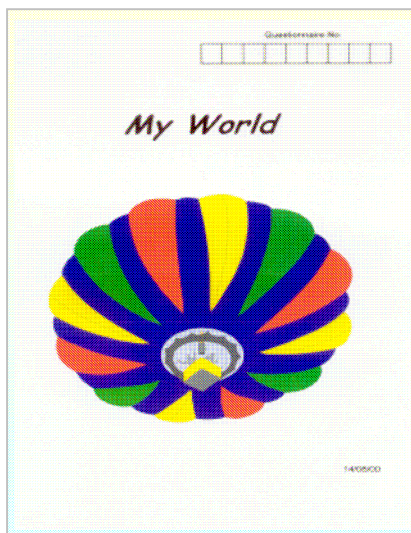
One of the things we had planned to do was include the mother's partner but it was up to her to decide whether she wanted her partner involved. Therefore we sent the questionnaire for the partner to the mother to give to whomever she decided her partner was. We had to say that it needn't be the father of the child as we were aware that the partner needn't necessarily be male. What we don't know is actually how many mothers passed the questionnaire onto their partners but, out of the 14,000 mothers who enrolled, we had responses initially from 10,000 partners. Considering how reluctant in general the opposite sex is in regard to filling in questionnaires, this response rate was pretty good. It did drop off a lot after that, but we think this may have been due to the mother protecting her overworked partner.



We kept an eye on the birth records and, as soon as we identified a birth to one of our study mothers, we sent a congratulations card. They were happening at a rate of 30 a day. Four weeks later we sent a gender specific boy or girl questionnaire about the new baby that was rapidly followed at eight weeks with a questionnaire about the mother and her family with a questionnaire for her partner as well. This is the way that we have continued, with

questionnaires focussing on the child and the child's development, questionnaires on the mother and how she is, and also questionnaires on the partner.

After a while, when the children were five, there was growing agitation from the children that they wanted to join in themselves. They thought it unfair, mummy was getting these things and they weren't! As a bonding exercise to start with, we sent them their own questionnaire, which was more of a colouring book initially but gradually overtime it became more and more like the questionnaires the parents were receiving and obtained very good information.



This is the way it has continued. The children are now aged 13 and 14 and are, of course, becoming young adults and we have to consider all that goes with that. They are extraordinary, because some have developed very fast and others are still small and look like children. Trying to design questions that will cover the whole range of development is fascinating but more and more of a challenge.

Regarding the health records, we have accessed all sorts of records but mostly the nightmare from our point of view has been the information about pregnancy, labour and delivery. Fortunately or unfortunately, depending on how I feel, we did a validation study very early because we had thought that the computerised system of records that was started at the maternity hospitals would be all that we needed and we discovered the accuracy for the sort of data that we wanted was abysmal. So we are going back to records and abstracting all the information we need.

We were anxious to obtain biological samples and asked mothers for their consent to analyse them. In the beginning we obtained the samples very much on the hoof, for example, during pregnancy whenever the midwife was taking a blood sample, we asked her to take an extra aliquot in a vacutainer and send it to us. This worked very well but, as well as collecting those vacutainers, we also had an exercise whereby we went round the clinical laboratories and picked up any blood samples that were left, so we would have more blood than originally taken. We did the same with maternal urine. At the time of delivery, the midwives in the two major maternity hospitals, which covered 94% of the births, took cord blood for us. They also collected the placenta for us and, if you can think of the size of a placenta, we have

the whole placenta of 12,000 children fixed in formalin stored in a secret place. Before fixing the placentas, we took a piece of umbilical cord for freezing.

Once the children were born we asked for samples of their hair and toenails, because the storage of those was so much simpler. And then, when the children started losing their teeth, we decided to collect those as well. At various times we have seen the children and taken blood and also saliva and urine samples. We have a huge bank of biological samples, much of which hasn't been used yet, but one of the major uses has been to extract DNA. From the mother's blood, the children's cord blood, or the blood taken later, we have extracted DNA. We have over 10,000 samples of maternal DNA and over 10,000 of children's DNA. Interestingly, everybody was worried about looking at genetics and whether it would put the families off but they haven't batted an eyelid. They have the option to opt out of any genetic studies and less than 1% do so which is very reassuring indeed.

The environmental monitoring included indoor air pollution, radiation, and hygiene. We took all sorts of measurements of the housing and socio-economic circumstances. We measured stress, both chronic stress and acute stresses. We have looked at schooling and the type of school, the physical environment in the school as well as the quality of the teaching, and the characteristics of other children that go to that school. We have gone into a lot of detail about the diets of the children as well as of the mother and the partner and that information has proved to be extremely important and exciting. In addition we have measured medications administered throughout the child's life and the way in which the parents behave in regard to the children.

The schools give us information on the child and the child's behaviour. We have asked the teacher to administer various tests. We have accessed the national SATS results and we have measured the school's ethos – whatever that might mean – but we have measures of what it might feel like in that school for the teachers and for the children. We get the teachers' views of the school's physical environment, how noisy it is, how near it is to a heavy road or other polluting area. And finally the most exciting thing has been our hands-on assessments of the children.

These were done in a variety of different ways. There was a sub-study looking at the development of the children at the age of 3 that was specifically funded by the Americans to

test whether women who were breastfeeding and drinking alcohol after delivery were damaging the development of their children. It was perhaps unexpected to find that the children of women who breastfed and drank alcohol did better than the children of mothers who breastfed without drinking alcohol. I'm talking within limits – once you go over 3 drinks a day it's not so good.

There have been a variety of studies looking at the quality of family life in step-families, single-parent families and families with lesbian parents, all of which have had very important policy results. We had a detailed study of twins, looking at the development of language. Twins are on average later at beginning to speak, was it something biological due to the pregnancy or is it due to the way in which the mother tries to interact with two children at once? Perhaps the twin doesn't quite ever get the quality of interaction that a mother of a singleton would have given?

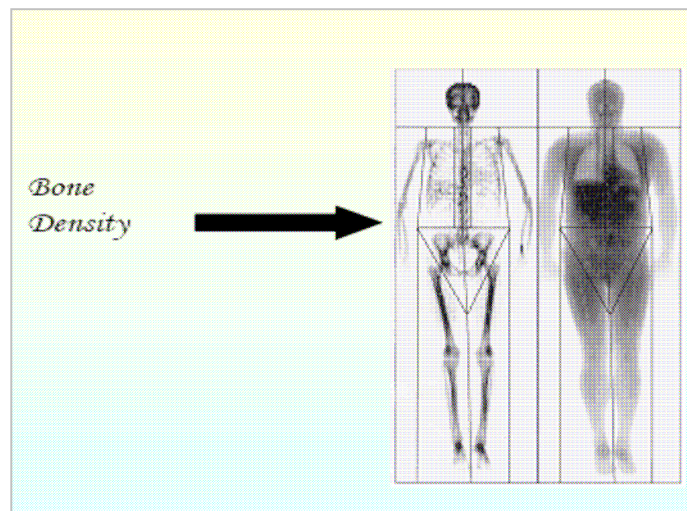
One of the most important sub-studies during the first 5 years was 'Children in Focus', which was chosen from a 10% sample of children from the whole cohort. For two reasons they were invited to come and see us at 4 months of age, 8 months, 12 months and every six months until they were 5 years of age. The first reason was to measure things that we couldn't measure in any other way, and the second was to have examinations of the children that we could compare with the results from the questionnaires. We were very reassured to find that the mothers' report in questionnaires on the development of the children gave very similar results to those obtained when we tested them, using trained psychologists and standard tests.

Then, once the children were 7, we decided that as we could do a 10% sample quite well we could also do the whole lot of children. At age 7 we did very detailed measurements of them, looking at their blood pressure and pulse rates; they had detailed vision tests and hearing tests; we did skin-prick tests for a number of allergies; we tested their motor ability, reading and spelling and phoneme awareness which is related to development of dyslexia. We asked our poor long-suffering parents to do a 3-day diary of everything the child ate or drank prior to coming to the clinic and a nutritionist then interviewed them.

We continued to see all the children on a yearly basis. At 8 years we looked at the neuro-cognitive side, - IQ, memory, and all sorts of speech and language tests. Non-verbal accuracy is the measurement of how good the child is at recognising expressions on others'

faces, so they can detect the difference between happy and angry, which is a very important concept to measure. We also measured attention as well as lung function and we started interviewing the child in regard to things like self-esteem and locus of control.

Once the children were 9 years of age, we started using a whole-body very low-dose X-ray to look at the bone mineralisation of the skeleton and also the fat and lean distribution within the body. We have always tried to give the child something to take away and they absolutely adored having pictures of their skeletal 'insides'!



We have carried on in this way, every year having different measures but also having a repeat of some of the same measures, so that we can look at the long-term trajectory. We hope the future of the study will continue in the same way.

As to some of the results, we measured the anxiety level of the mother during pregnancy, at 18 weeks and at 32 weeks, as well as taking a measurement postnatally. There is animal experimental evidence to say that if you stress a pregnant animal then the resulting baby has abnormal behaviour. So we have looked at the behaviour of our children and there is now a bank of publications to show that the mothers who have been stressed, especially in the third trimester, are twice as likely to have a child that is hyperactive at 4 years of age. The old wives' tale that as soon as somebody was pregnant to let them put their feet up, relax, and don't stress them in any way, can perhaps ring true! When you think of the way in which our obstetric care works, it is very much a lot of stressors in terms of results of this and that test and what do you want to do about this or that?

Maternal anxiety and adjusted odds of hyperactivity in 4 year old boys

Anxiety at:	AOR [95% CI]:
18 wk antenatal	1.1 [0.7, 1.7]
32 wk antenatal	2.0 [1.4, 2.9]**
8 wk postnatal	1.6 [1.1, 2.4]*

** P<0.01, * P<0.05

There is a study that we did on peanut allergy. We found that if the child had been exposed to oil or cream that contained peanut oil in the first months of life then that child is over 7 times more likely to develop peanut allergy. When we took into account of all sorts of other factors like social circumstances, the likelihood dropped slightly, but it is still nearly 7 times as much. I think that many manufacturers of creams and the mild bath oils, did use peanut oil but they have now removed it from their products.

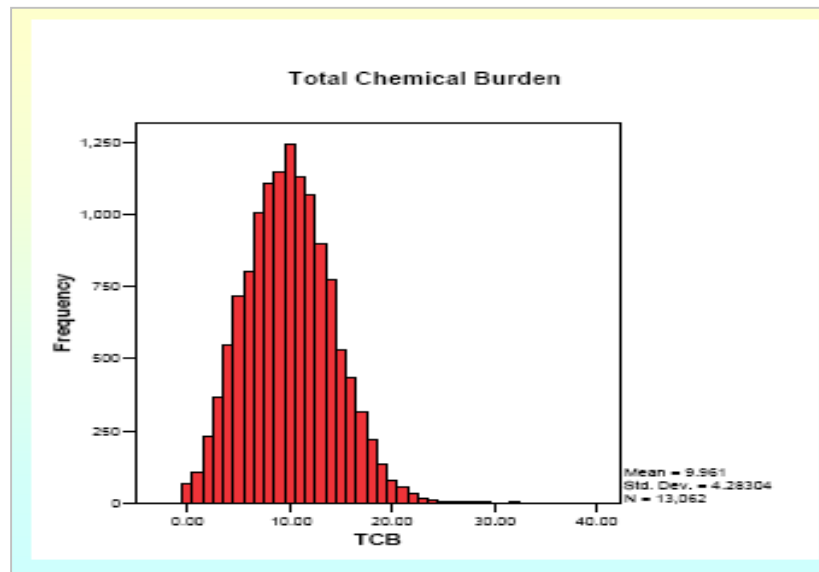
Odds [95% CI] of peanut allergy according to prior use of creams containing arachis oil

▪ Unadjusted	7.49 [1.71, 32.8]
▪ Adjusted	6.81 [1.41, 32.9]

Looking at the early environment that we measured in the very first questionnaire and how often the mother used all sorts of different chemicals in the home we created a score called the Total Chemical Burden. There is a relationship such that the most exposed children are well over twice as likely to develop persistent wheeze compared with the least exposed. They started wheezing in the first months of life and they carried on until 7 years of age. If we look at the effect in pregnancy, which nobody else has ever looked at, we find a reduction in birth weight of 99 grams, which is half what you would get if your mother smoked.

One of our very exciting findings, which isn't published yet, is looking at the importance of mothers eating fish in pregnancy. The recommendations of the Food and Drug

Administration in America are that pregnant mothers mustn't eat more than 2 portions of fish a week, the reason being that there is a fear that mercury in fish will harm the brain and the development of the foetus. Actually the biggest association in fish is with Omega 3 fatty acids, which is essential for brain development, particularly during foetal life and what we show is that those mothers who eat very little fish, or no fish, have children who do much worse in terms of behaviour and IQ than children whose mothers are actually exceeding the recommendation.



Total chemical burden (TCB) in the home in pregnancy and birthweight (g)

	Unadjusted birthweight	Adjusted* birthweight
TCB (continuous)	-4.8[-7.1,-2.5]	-6.3[-11.9,-0.73]
TCB >90 centile v. rest	-56.5[-89.5, -23.6]	-99.8[-171,-28.3]

*adjusted for maternal smoking, parity, maternal education, housing tenure, gender

Total chemical burden (TCB) in the home in pregnancy and risk of persistent wheeze

	Unadjusted OR[95% CI]	Adjusted* OR[95% CI]
TCB (continuous)	1.08[1.05, 1.11]	1.06 [1.03,1.09]
TCB >90 centile v. <10th	2.84[1.17,4.51]	2.30[1.20,4.39]

*adjusted for environmental tobacco smoke, maternal smoking in pregnancy, parity, crowding, pets, damp, housing tenure, gender and breast feeding
Thorax 2005;60:45-49

This is just a little taste of what is coming out of the study. Most of the things we are looking at are not high tech but are things that can be changed just by advice without major expense to the health service.

Last year in the summer we held a party where we invited the study's 12 and 13 year olds, as they were then to come along. Over 2000 came. The weather was good and we had a great time!



I would like to thank all our families for taking part. They have provided fantastic data which I hope is going to be used for the next 50 or even 100 years to come.

Lesley Wye and Elizabeth Thompson are both giving talks tomorrow on the use of homeopathic medication within our study.

Robin Holland-Martin: On behalf of us all I would like to thank Professor Jean Golding very much indeed for such a stimulating, revealing and thought-provoking talk. It is impressive that such a huge number of individuals entered into the survey and what a high response rate you achieved. A remarkable achievement and, judging by the amount of information, the story will run and run.

Question and Answer Session

Q: What has it cost?

Professor Golding: Too much! In the last 5 years, it has cost about £4million a year and the major part of that is spent in collecting data and examining the children. Fortunately the University of Bristol, the Medical Research Council and the Wellcome Trust have put in a substantial amount. They have just renewed a 5-year programme. The rest has come from writing grants. Quite a substantial amount has come from America and various research trusts over here.

Q: Have you found any patterns with vaccination to morbidity?

Professor Golding: We have looked at a limited amount of outcomes in regard to vaccination such as wheezing and asthma and have found no association at all. We have looked at the MMR vaccine, particularly in regard to neurological outcome, and there are a few associations but they are not the same as anybody else has found. We found nothing with autistic behaviour. That's all we have done so far.

Q: What percentage of children are fully vaccinated?

Professor Golding: A very high percentage. You have to take account of all sorts of social circumstances that distinguish the two. At the time our children were born, the MMR/autism story hadn't hit the headlines, so uptake was very good.

Q: Is all this extra attention helping the children, or to rephrase it, are you spoiling your sample by close scrutiny?

Professor Golding: This is a difficult one because what we want to do is make the children extremely excited by what's happening and for them to enjoy the study and come and enjoy their examinations. Not only do they take home pictures of their insides, pictures of their eardrums but also their retinas! I haven't been able to detect that we are creating a healthier bunch of children which would be worrying from the epidemiological point of view, of course.

We have always told them that what we are looking at is what actually happens, not what they feel should happen. For example, when we were starting out, the sleeping position of the baby was still supposed to be on its front, because that was the healthiest. We've shown

very clearly that sleeping on the back is the healthiest for the baby. Not only does it prevent cot deaths, but it has all sorts of other health benefits

Q: Is there any way to measure the effect of socio-economic factors?

Professor Golding: Yes, we have collected a large amount of different socio-economic information on the family. The social scientists are extremely interested and many economists are looking at our data. All sorts of analyses are being undertaken such as family income and what's now called the 'social capital' of the families and how that relates to the development of the child.

Q: Have you looked at causation factors for juvenile onset diabetes?

Professor Golding: One of the things we had to recognise when we started the study was that, although we were targeting 14,000 children, the numbers of certain conditions was still going to be too small to look in detail at the aetiology of certain conditions, such as juvenile diabetes or childhood cancer. We will look at the small numbers anyway to see whether there is something startling, but we haven't done so yet.