

**The Raine Study – physical activity levels, respiratory disease,  
and stress responsiveness in early adolescence**

**Parent information sheet**

Dear Parent/Caregiver

As part of the 13 year-old follow-up we plan to assess the children's levels of physical activity and their respiratory status. We asked a number of questions about physical activity when your child was 10 years old. We would now like to assess your child's level of physical activity in a comprehensive manner and relate this information to their level of physical fitness and coordination. We would like to know if daily activities such as walking to school and doing chores around the home contribute significantly to fitness and health. You may remember the respiratory status assessments that took place when your child was about 6 years old. The tests we plan this time are similar but will give us a lot more information as the children are now able to perform more complex tasks. We want to investigate factors that relate to asthma and allergies, particularly to the type of asthma that is likely to last into adult life.

We would like to carry out a three-stage assessment. **Stage one** will involve the assessment of your child at the Telethon Institute for Child Health Research and the Clinical Research Centre, Princess Margaret Hospital. We will be asking you and your child's secondary caregiver (where applicable) to complete separate questionnaires. The questions are similar to those we have asked in previous follow-ups. Parents will be asked to return completed questionnaires at this time. While you are at the institute we will also ask you to complete a food frequency questionnaire detailing your study child's eating habits and ask you questions about your child's general mood. The adolescent assessment will comprise height, weight, respiratory examination, a stress test, lung function test, bronchial responsiveness test, and skin prick test for allergies. Attending parents will also be asked to have height, weight and blood pressure measured. It is envisaged that this assessment will take 2.5 hrs. Details of the stress test and the bronchial responsiveness test are presented below.

**Stress test**

The Hypothalamic-Pituitary-Adrenal (HPA) axis is a vital part of the body and stimulates the body's normal production of steroids. When our body is faced with stress of any type, including emotional or physical stress, the HPA axis stimulates an increase in the amount of steroid (cortisol) our body produces. There is a suggestion that some adults with asthma produce less steroid in response to stress than non-asthmatics. We do not know whether this contributes to the development of the asthma or is a consequence of the asthma. There is no information whether this situation also exists in children. The Raine Study is ideally suited to examine the relationships between the physiological response to stress and asthma in children.

HPA axis responsiveness will be tested using a "single breath test" in which the children will inhale a single vital capacity breath of a gas mixture comprising 65% Oxygen (as apposed to 21% in normal air) and 35% Carbon dioxide (which we breathe out with each breath but which is present in very low concentrations in normal air). Inhaling this gas is not at all harmful, yet it results in the HPA axis stimulating cortisol production. After inhaling the gas mixture, your child will experience a transient (approx 5-10 second) feeling of light-headedness and notice an increased respiratory drive, i.e. their breathing rate increases for a minute or so. We measure the amount of cortisol, in the children's saliva, that is stimulated by the test. We do this by having them hold a cotton swab in their mouth for about one minute each time we want to measure cortisol. There are no blood tests involved. As this is a stress test, it is important that the children are relaxed before the test starts. We will ask them to rest for about 30 minutes in the room where the test is conducted. During this period, and for about 30 minutes after the breath of gas mixture, we will collect a saliva sample approximately once every 5 to 10 minutes, to allow us to measure the cortisol response. We will also store some of the saliva to allow us to analyse it for the presence of antibodies (funding permitting).

## 1 – Full day assessment

We wish to relate how much cortisol is produced by a stress test to how your child deals with life stresses. One way of measuring your child's response to life stresses is to measure how anxious they are, both at the time of the test and in general. We can do this using a standardized instrument (a questionnaire that your child fills out) called Spielberger's State and Trait Anxiety test.

### **Bronchial responsiveness testing**

During the six year follow-up we were able to measure bronchial responsiveness in some of the children. These tests tell us how sensitive your child's airways are. Children with asthma generally have more sensitive airways, which means that they react more than usual to environmental stimuli. However, everybody's airways are sensitive to some degree, so this is a test we want to perform on children who do not have asthma, as well as on those who do. We have two ways of measuring bronchial responsiveness, either using methacholine – a chemical analogue to a naturally occurring body chemical that tells us how sensitive the airways are or using a bronchodilator, such as Ventolin, which is used as an asthma treatment because it opens narrowed airways.

#### Methacholine challenge

The test is done by taking a number of breaths of a nebulized solution and measuring lung function 30 and 90 seconds later. We always start the test using a saline solution, followed by increasing doses of methacholine. People with sensitive airways will have some narrowing of their airways with the methacholine and we can see this as a reduction in their lung function. We stop the test if lung function falls by 20%, a level that most people will not even notice. For comparison lung function usually falls by more than 50% during a moderate asthma attack. Some children may experience some coughing or mild wheezing at the end of the test. All children whose lung function has fallen at all will be given a Ventolin inhalation at the end of the test and this will completely reverse any fall in lung function.

#### Bronchodilator response

Children who are unable to undertake the methacholine challenge will receive bronchodilator inhalation (10 puffs from a large volume aerosol-holding chamber / spacer), as per Department of Respiratory Medicine protocol. Lung function will be repeated 10 minutes post bronchodilator to see if the Ventolin improves their lung function.

We will be asking you for separate permission for each part of the study so that you can feel free to participate in the study without feeling pressured to agree to it all. You may, of course, withdraw your child at any stage without prejudicing your child's right and access to the best medical attention available at Princess Margaret Hospital.

With your permission we will ask your child to complete a questionnaire for us. The questionnaire is mainly about how children perceive themselves, but there are questions about 'risk taking' behaviour, such as smoking and drinking alcohol as well. We have included a copy for you to read. The information contained in this questionnaire is confidential. If your child tells us of a health or social problem he/she does not want you to know about, the matter will be referred to a panel consisting of: two child health nurses; a clinical psychologist; an adolescent paediatrician; and a paediatric social worker. No fewer than three members of this group will determine how to proceed in each case. An appropriate response will be mounted with the knowledge and cooperation of your child.

As part of this study we will be doing a number of tests on you and your child. Some results, such as lung function and allergy tests, we will be able to give you immediately. Other tests will take some time to run in the laboratory; therefore we will send you these results when available. If any of your results are outside the normal range, or we are worried you or your child may have a problem you were not aware of, we will recommend that you see your General Practitioner. However, for some of the tests, such as immunology and genetics, we are not able to send you results, because at this stage in our knowledge we do not know how to interpret what these tests mean for an individual.

## 1 – Full day assessment

**Stage two** will commence in the afternoon, following a brief break for lunch. Your child will need approximately 3 hours to complete a questionnaire (administered on laptop computer – paper copy enclosed for your perusal), a physical fitness assessment, and an assessment of coordination. In addition, height/weight, waist girth and blood pressure will be measured. We will also take a series of digital photos of your child to assess their standing and sitting posture. These photos will be altered to so that all identifying features will be masked. The school principal and your child's form teacher will also be asked to complete questionnaires asking about the school environment, your child's participation within that environment and their academic achievement.

**Stage three** will comprise the period of 7 days following the assessment. At the end of the assessment we will teach your child to use a pedometer (a small instrument that measures the number of steps taken when walking) and a computer based activity diary to monitor their level of activity on a daily basis for 7 days. A small group of children will be asked to use an ambulatory blood pressure monitor for a period of 24 hours. Children and/or parents who have questions about any of this equipment can contact the Raine staff during normal hours on the numbers provided. A phlebotomist/enrolled nurse will visit you at home to take an early morning fasting blood sample and urine from consenting children and their parents. We will need to collect a total of 50 mls of blood from children and 10mls of blood from parents. Just as we have done on previous occasions, local anaesthetic cream (EMLA) will be used for all children and parents who request it.

We will use your child's blood and urine to do a number of studies:

- First, we will measure levels of fats, glucose and insulin;
- Second, we will measure levels of allergic antibodies and markers of inflammation, and the response of the immune system to environmental exposures, especially to infections and allergens;
- Third, we would like to measure the levels of some hormones that are involved in regulating the immune system (eg cortisol, estrogen and testosterone);
- Fourth, we will test for exposure to environmental chemicals and metals, including lead, pesticides, and PCBs (polychlorylbiphenols). We can be exposed to these chemicals without our knowledge as they can occur in the air we breathe, the water we drink and in the food we eat. We want to study these chemicals as they all can have effects on the development of the immune system and may influence the risk of asthma and allergies;
- Fifth, we plan to store plasma which will be used to estimate free fatty acid and vitamin levels as an indicator of dietary intake;
- Sixth, we would like to store your child's DNA so that we can study inherited factors associated with asthma, allergies, blood pressure variability, obesity and sugar metabolism.

We will use your blood to measure levels of fats, glucose and insulin, and we would like to store your DNA so that we can study inherited factors associated with blood pressure variability, obesity and sugar metabolism. We have given you more detailed information about these genetic studies on a separate information sheet.

We would like you to feel free to ask any questions you may have about any aspect of the study. It is important that you understand why we are asking you to allow your child to participate in this part of the study.

We would like to assure you that all information we collect is strictly confidential. The Institute (ICHR) is bound by the Privacy Act 1988 and abides by the National Privacy Principles at all times. If you have any concerns or complaints regarding the way this study is being conducted you can contact the Executive Director of Medical Services on (08) 9340 8222.

1 – Full day assessment

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