Dr Hayley Scott
Immune Health Research Program
Level 2 West Wing, HMRI Building
Lot 1 Kookaburra Circuit,
New Lambton Heights NSW 2305
T: 02 4042 0113
Fax: 02 4042 0046

Participant Information and Consent Form

Exploring the Impact of Sex Hormones on Asthma Outcomes in Women with Asthma (SHE-Asthma Study)

Invitation

You are invited to participate in a research study examining how the menstrual cycle, the contraceptive pill and menopause affect asthma symptoms and inflammation in the airways of women with asthma. This study is being conducted by Dr Hayley Scott, Prof Lisa Wood, Prof Peter Wark, A/Prof Katie Wynne, A/Prof Jay Horvat, Dr Bronwyn Berthon, Dr Evan Williams, Dr Alexandra Brown, Prof Chris Grainge, and Ms Olivia Carroll from The University of Newcastle and Hunter Medical Research Institute.

Before you decide whether or not you wish to participate in this study, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish. A member of the research team will also explain the study to you. If you do not understand any of the information or have any worries, please ask us.

What is the purpose of this study?

There is some evidence that some women might experience changes in their asthma symptoms, both throughout their menstrual cycle and after menopause. The effect the contraceptive pill has on asthma symptoms is not known. This study aims to look at asthma symptoms in three groups of women with asthma: pre-menopausal women using no hormonal contraception, pre-menopausal women using the combined contraceptive pill, and post-menopausal women.

This research aims to improve our understanding of how the menstrual cycle, the contraceptive pill and menopause affect asthma, in women with asthma.

Why have I been invited to participate in this study?

This study may be suitable for you if you are a female aged ≥18 years with a doctor's diagnosis of asthma. The study includes women who are still having periods, and women who have gone through the menopause and have not had a period for 12 months. This study may not be suitable for you if you:

- Are a current smoker;
- Are pregnant or breastfeeding;
- Have a disorder that has caused you to stop menstruating (e.g. thyroid disease);
- Have an irregular menstrual cycle (varies by >15 days between shortest and longest cycle over 12 months, or your cycle length is outside the range of 26-34 days); or
- Use hormone replacement therapy (HRT) or a hormonal contraceptive other than the combined contraceptive pill

What if I don't want to take part in this study, or if I want to withdraw later?
Participation in this study is voluntary. It is completely up to you whether or not you participate. If you decide not to participate, it will not affect the treatment you receive now or in the future. Whatever your decision, it will not affect your relationship with the staff caring for you.

If you decide to withdraw from the study, you have the option of withdrawing all data relating to you and have any samples that have been taken destroyed. An exception to this is in the case of an adverse event, or a serious adverse event, where the data needs to be retained for regulatory reporting.

The researchers may withdraw someone if it is considered in their best interest, or it is appropriate to do so for another reason. If this happens, the researchers will explain why and advise you about any follow-up procedures or alternative arrangements as appropriate.

What does this study involve?

Telephone Screening
We will need to check that the study is suitable for you. To do this, we will ask you some questions about your medications and medical history.

Screening Visit
If you agree to take part in this study, you will be asked to attend a screening visit. This visit will be conducted at the Clinical Trial Facility on Level 4 of HMRI. At this visit you will be asked to sign the Participant Consent Form if not already signed. During this visit we will:

- Measure your height, weight and blood pressure;
- Complete some questionnaires;
- Collect a blood sample; and
- Complete some breathing tests (see below for more information).

We may look at your medical record to find information about your asthma and other health conditions. We would like to access and record the visits and lung function results in your medical record. This will involve our staff accessing your medical record and recording the results of your visit in your patient notes. We may invite you back for an additional screening visit if we need to do another breathing test.

If this study is suitable, we will organise a convenient time for you to begin the study.

How many visits and how long will each visit take?
The screening visit will take approximately 1.5 hours. The total number of visits you will attend depends on the group you are assigned to.

Post-menopausal women and pre-menopausal women using the contraceptive pill: In addition to the screening visit, you will attend ONE visit at HMRI which will take approximately 2 hours to complete. For pre-menopausal women using the contraceptive pill this will be during the last (third) week of your active pill (i.e. the week before you start the sugar pills). If you usually skip the sugar pills, we can do this visit at any time.

Pre-menopausal women not using any hormonal contraception: As well as the screening visit, you will attend THREE visits over a 1 month period, which are outlined below. These visits will be based around your menstrual cycle, with day 1 being your first day of menstruation (your "period"):

- Visit E: Around *day 10-14* of your menstrual cycle
- Visit P: Around *day 19-23* of your menstrual cycle
- Visit L: Around *day 26-2* of your menstrual cycle

The timing of these visits will be based on the results of an at-home urine ovulation test, which we will provide you with. This test has been described on the following page.

What will I need to do to prepare for my visit?

- *Withholding asthma and allergy medications*: Before your face-to-face visits at HMRI, you will need to withhold your asthma medications for certain amounts of time. The amount of time will depend on what medication you are taking. Study staff will advise how many hours each medication would need to be withheld for each visit. Medications to withhold include asthma inhalers for 8 hours to 3 days, and allergy medication (antihistamines) for 3 days. However, if you feel that your symptoms become significantly worse during this time, you should use your normal medications. We will still see you in the clinic as planned.

- Bring a *list of current medications and supplements* to the Screening Visit, including doses.

Study staff will remind you of how you need to prepare for each visit.

What procedures will be carried out?
If you agree to participate in the study, you will be invited to attend the Clinical Trial Centre on Level 4 of the Hunter Medical Research Institute (HMRI). The study visits will include all the procedures listed below, except body composition and bone density using DXA, which will be completed at Visit L only. Post-menopausal women and women using the contraceptive pill will complete one visit, which will include everything listed under 'Visit L'. Each visit will take about 2 hours to complete.

Visit E	Visit P	Visit L
Weight	Weight	Weight
Blood pressure	Blood pressure	Blood pressure
Breathing tests	Breathing tests	Breathing tests
Mannitol sputum induction	Mannitol sputum induction	Mannitol sputum induction
Blood test	Blood test	Blood test
Questionnaires	Questionnaires	Questionnaires
		Body composition and bone density (DXA)

- **Breathing tests** –
  Spirometry: Your lung function will be measured by blowing into a spirometer, a machine that measures the amount of air you can breathe out of your lungs. You will be asked to blow into the spirometer until your lungs are empty (approximately 6 seconds). This is a routine breathing test with no known adverse effects, except for perhaps some breathlessness and/or dizziness which usually lasts for a few seconds only.

  Forced Oscillation Technique (FOT): You will be asked to breathe in and out normally into a machine. The machine will vibrate slightly while you are breathing. This test measures the mechanics of your lungs. This test is generally well tolerated, is comfortable and quick to perform.

  Fractional Exhaled Nitric Oxide (FeNO): This test involves slowly breathing out into a machine, and measures inflammation in your lungs. This test is generally well tolerated, is comfortable and quick to perform.

- **Mannitol Challenge OR Sputum Induction:** You may be asked to complete a mannitol challenge at the screening visit. You may also be asked to complete a Mannitol Sputum Induction at your other study visits. These are breathing tests where we will ask you to

breathe in a small amount of powdered sugar, called Mannitol. For both tests, Mannitol powder is breathed in via a dispenser in increasing doses, up to a maximum of 9 doses. A breathing test will be done at the end of each dose. Throughout the test, you will also be asked to cough up a sample of sputum (phlegm). This is a routine test, which allows us to look at the amount and type of inflammation in your lungs. This is measured by counting types of cells in the sputum sample. These tests will be stopped at your request or if you develop any problems with your breathing. If you have any problems with your breathing, you will be given a reliever medication (Ventolin). We will closely monitor your symptoms and breathing throughout the test.

Some asthma and allergy medications may need to be withheld for certain amounts of time before the Mannitol tests. We will discuss suitability of this with you and give you more information about the withholding times, if applicable.

Instead of doing either test, we may instead ask you to cough up a sample of sputum (phlegm).

- **Blood Test** – Approximately 50mL (2.5 tablespoons) of blood will be taken from a vein in your forearm to measure sex hormones, levels of inflammation, immune function and a full blood count.

- **Body Composition and Bone Density** – Your weight and waist circumference will be measured at each visit. Your height will be measured at your screening visit. We will also measure your body composition and bone density on one occasion, using a dual energy x-ray absorptiometry (DXA) machine. This is a very low dose form of x-ray, which is used to study body composition and bone strength. It is not painful and takes about 10-15 minutes to complete. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 to 3 millisieverts (mSv) each year. A DXA scan delivers <0.010 mSv. At this dose, no harmful effects of radiation have been demonstrated and the risk is negligible. The dose of radiation from this test is similar to the dose of naturally occurring background radiation that everyone is exposed to in two days. All radiation exposures will be carried out in accordance with the ARPANSA Code of Practice “Exposure of Humans to Ionizing Radiation for Research Purposes” (RPS8)”.

- **Blood Pressure and Oxygen Saturation** – Your blood pressure will be measured using an automatic blood pressure monitor. Your oxygen levels will be measured using a machine called an oximeter, which clips onto your finger.

- **Questionnaires** – You will be asked to complete questionnaires related to your medical history, medications, asthma, menstrual history, quality of life, diet and physical activity. These questionnaires will take approximately 20 minutes to complete.

Pre-menopausal women not using hormonal contraception only:

- **Menstrual cycle and asthma symptom tracking** – You will be asked to complete an online questionnaire each day for around 28 days. Each morning, you will be asked two short questions about how your asthma was overnight and will complete a peak flow measurement. Each evening, you will complete another four short questions about how your asthma was during the day, and record any menstrual symptoms from that day. This will be done online and will take only a few minutes each day. Your lung function will be measured using a peakflow meter, which we will give you. This is a small device that you blow into and it will measure how fast air comes out of your lungs when you exhale forcefully.

- **Urine ovulation test** – We will give you some urine test strips to start using from day 10 of your menstrual cycle (with day 1 being your first day of menstruation (your “period”)). Using

your first urine of the day, either hold the strip in stream or dip it in a cup of fresh urine and wait for the result to appear on the screen. You will need to do this once a day for up to about 10 days, until you ovulate. You will need to come in to HMRI for your first visit within 2-3 days of receiving a positive result ("high fertility" flashing smiley face reading). Once you receive a positive result you will need to continue testing for a few more days, until you receive a "peak fertility" result (solid smiley face).

Are there benefits or risks to me in taking part in this study?
Your participation in this study will benefit our understanding of asthma but you are unlikely to benefit personally. All information about your condition will be available to you. All car parking for the study will be free of charge. If you are in the group attending 3 study visits, you will be given a peak flow meter to record your lung function, which you can keep.

The side effects of having blood collected may include bleeding or bruising at the injection site and possible dizziness and/or fainting. Please advise the research team if you normally feel dizzy or faint when you have blood collected. The sputum test can cause coughing, some minor chest discomfort and wheezing. This is brief and responds quickly to Ventolin.

What happens if I suffer injury or complications as a result of the study?
If you suffer any injuries or complications as a result of this study you should contact the study coordinator as soon as possible, who will assist you in arranging appropriate medical treatment.

How will my confidentiality be protected?
Of the people treating you, only the researchers named below and other clinical staff involved in your care will know whether or not you are participating in this study. Any identifiable information that is collected about you for this study will remain confidential and will be disclosed only with your permission, or except as required by law. Only the researchers named below will have access to your details and results, which will be held securely in the Centre for Healthy Lungs, The University of Newcastle.

What happens with the results?
Your participation in the study will help us learn more about asthma management. All information about your condition will be available to be sent to your general practitioner at your request. A summary of the results of the study will also be sent to you in an email, or a letter will be posted to you, at the completion of the study; however, you should be aware that the study may take several years to complete.

We plan to discuss/publish the results of the study. In any publication, information will be provided in such a way that you cannot be identified. We may also use the stored data in future trials, for which ethical approval will be sought beforehand. Samples collected in this study will be stored securely and may be used in further research, only if you agree and the research has been approved by the Hunter New England Human Research Ethics Committee.

If you are enrolled in another study within the Immune Health Research Program and both studies need the same data/information from you, you can give us permission to share the data collected during our study with these other researchers to reduce the need for you to have further testing.

What should I do if I want to discuss this study further before I decide?
When you have read this information, one of the named researchers will discuss it and any questions you may have with you. If you would like to know more at any stage, please do not hesitate to contact any of the investigators on the numbers listed on the following page.

Tamara Blickisdorf Research Assistant Immune Health Research Program Level 2, HMRI Building Lot 1 Kookaburra Circuit, New Lambton Heights NSW 2305 T: 02 4055 0983 tamara.blickisdorf@uon.edu.au	Catherine Delahunty Research Assistant Immune Health Research Program Level 2, HMRI Building Lot 1 Kookaburra Circuit, New Lambton Heights NSW 2305 T: 02 4042 0135 catherine.delahunty@newcastle.edu.au	Dr Hayley Scott Chief Investigator Lecturer in Nutritional Biochemistry Immune Health Research Program Level 2, HMRI Building Lot 1 Kookaburra Circuit, New Lambton Heights NSW 2305 T: 02 4042 0113 hayley.scott@newcastle.edu.au

Who should I contact if I have concerns about the conduct of this study?

Ethics:

This research has been approved by the Hunter New England Human Research Ethics Committee of Hunter New England Local Health District, Reference 2021/ETH01221.

Governance:

The conduct of this research has been authorised by the Hunter New England Local Health District to be conducted at the John Hunter Hospital site.

Complaints about this research:

Should you have concerns about your rights as a participant in this research, or you have a complaint about the manner in which the research is conducted, it may be given to the researcher, or, if an independent person is preferred, please contact the HNE Research Office, Hunter New England Local Health District, Level 3, POD, HMRI, Lot 1 Kookaburra Circuit, New Lambton Heights NSW 2305. Telephone: 02 4921 4140. Email: HNELHD-ResearchOffice@health.nsw.gov.au and quote the reference number: 2021/ETH01221.

Thank you for taking the time to consider this study.
If you wish to take part in it, please sign the attached consent form.
This information sheet is for you to keep.

Dr Hayley Scott
Immune Health Research Program
Level 2 West Wing, HMRI Building
Lot 1 Kookaburra Circuit,
New Lambton Heights NSW 2305
T: 02 4042 0113
Fax: 02 4042 0046

Participant Consent Form

Exploring the Impact of Sex Hormones on Asthma Outcomes in Women with Asthma (SHE-Asthma Study)

I agree to participate in the above research project and give my consent freely.

I understand that the project will be conducted as described in the information statement, a copy of which I have retained.

I understand I can withdraw from the project at any time and do not have to give any reason for withdrawing.

I consent to-

- ☐ Completing the tests involved in the study
- ☐ Completing questionnaires to obtain research data
- ☐ A copy of my results being sent to my General Practitioner
- ☐ A copy of the study results being emailed or posted to me. My email address is:

  _____
- ☐ Allowing research personnel access to my medical record and to record attendance and results in my file
- ☐ Allowing other studies that I am enrolled in within the Priority Research Centre for Healthy Lungs to access data that is duplicate to the data collected in this study.
- ☐ Having my blood/sputum/stool/nasal swab samples stored for use in future research. I understand my samples will be retained for a minimum of 15 years. If I decline to have samples stored, I am still able to participate in the study

I understand that my personal information will remain confidential to the researchers.
I have had the opportunity to have questions answered to my satisfaction.

Name _____

Signature _____ **Date** _____

I have informed the above person about this research and am sure that they understand both the content of the Information statement and the additional information I have provided.

_____

Investigator/Delegate Name (printed) Signature Date