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Assessment of epithelial permeability in asthma through nuclear imaging

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Registration date 28/07/2009	**Overall study status** Completed	
Last Edited 23/05/2016	**Condition category** Respiratory	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
RHM MED0880

Study information

Scientific Title
Assessment of epithelial permeability in asthma through nuclear imaging: an observational trial

Study objectives
This study aims to assess whether the increased epithelial permeability seen on a cellular level in asthma can be assessed using nuclear imaging means. It will look at the clearance from the lungs of two radio-labelled compounds, one which can be absorbed through the bronchial epithelium and one which cannot be absorbed. The latter will be used to correct for mucociliary clearance as a route of clearance from the lungs. The study will involve a control group of healthy people, a group of smokers (in whom epithelial permeability has been demonstrated using this method) and a group of asthmatics to test the hypothesis (both controlled and uncontrolled). Uncontrolled asthmatics will only be enrolled if previous analysis of the data from controlled asthmatics confirms both safety and statistical significance.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Southampton and SouthWest Hampshire Local Research Ethics Committee (LREC) - approval pending as of 12/06/2009

Study design
Observational case-control study

Primary study design
Observational

Study type(s)
Screening

Health condition(s) or problem(s) studied
Asthma

Interventions
This is a single centre study occurring at Southampton Hospital. The study will consist of a screening visit, followed by an imaging visit. Three groups (healthy controls, smokers and asthmatics), with 10 patients in each group, will take part. If a preliminary analysis shows statistical significance and safety, the study will be extended to include a further 10 uncontrolled asthmatic patients. The study will consist of a screening visit followed by two imaging visits.

Screening visit:
A screening visit will occur to assess eligibility and stability. At the visit, written consent will be taken, medical history and physical examination will be performed. Lung function testing including provocation tests and exhaled NO measurement will also occur. Blood tests to establish normal renal function will be taken. Electronic recording of lung sounds will be performed. For smokers, a record of number of cigarettes smoked per day will be taken, and 'pack years' calculated (wherein a person smoking 20 cigarettes/day for 1 year = 1 pack year, 40 cigarettes/day for 1 year = 2 pack years, etc). A detailed asthmatic history will be taken from asthma patients including symptoms, medication use and completion of an asthma control questionnaire. It is estimated that this visit will last 2 hours.

Imaging visit A:
The participant will then return between 14 and 28 days later for their imaging visit. This will

firstly consist of a transmission scan to define the lung contours and regions of interest in the lungs, and also allow correction for tissue attenuation of gamma rays. Radiopharmaceuticals will be prepared and nebulised as detailed below. Scintigraphy will occur with the patient in the supine position, with dynamic imaging (1 minute timeframe) for the first hour, together with further images at 60, 90 and 120 minutes. A cumulative urine sample will be collected at 2 hours. A detailed record of number of cigarettes smoked in the preceding 24 hours will be taken from the smoking subjects, whilst a detailed record of asthma medication use in the preceding 24 hours will be taken from the asthmatics. Spirometry and oximetry will be undertaken before and after imaging. It is estimated that this visit will last 3 - 4 hours.

Imaging visit B:
The patient will return 24 hours later for further scintigraphic imaging and a 24 hours cumulative urine specimen. Spirometry and oximetry will be undertaken before and after imaging. It is estimated that this visit will last 1 hour.

Follow-up will cease after the second visit, therefore will only last 4 - 5 weeks.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
Measurement of clearance of Indium 111-labelled DTPA from the lungs of healthy controls, smokers and asthmatics, measured at the time of the imaging visits, between 14 and 28 days from their screening visit.

Key secondary outcome(s))
1. Measurement of mucociliary clearance using technetium labelled albumin as a microcolloid, 99mTc-Nanocoll, in normal subjects, asthmatics and smokers and comparison for statistically significant difference
2. Lung function and volume measurements (FEV1, forced vital capacity [FVC], forced mid-expiratory flow rate [FEF25-75], reversibility with salbutamol, functional residual capacity [FRC] and total lung capacity [TLC]) together with provocation testing (PC20 metacholine) and exhaled nitric oxide (eNO) will be recorded and correlated with degree of permeability if possible
3. History of atopy will be recorded and correlated with permeability
4. Lung sounds will be recorded for analysis and correlation with airflow obstruction

Measured at the time of the imaging visits, between 14 and 28 days from their screening visit.

Completion date
01/10/2009

Eligibility

Key inclusion criteria
General:
1. Subject must understand the procedures of the study and agree to participation in the study by providing written informed consent
2. Subject considered fit enough to undergo lung function testing including provocation tests

3. Either gender
4. Age 18 - 55 years at screening

Group specific:
1. Healthy controls:
1.1. Lifelong non-smoker
1.2. No history suggestive of airways disease
1.3. Normal spirometry, normal exhaled nitric oxide (NO), provocative concentration causing a 20% fall in forced expiratory volume in one second (FEV1) (PC20) (metacholine) greater than 8 mg/ml (non-cumulative)
1.4. No signs of concurrent respiratory infection at time of scanning or within previous 8 weeks
1.5. No significant cardiopulmonary/hepatic or renal co-morbidity
2. Smokers:
2.1. Daily smokers of tobacco cigarettes
2.2. Normal spirometry, normal exhaled NO, PC20 (metacholine) greater than 8 mg/ml (non-cumulative)
2.3. No signs of concurrent respiratory infection at time of scanning or within previous 8 weeks
3. Asthmatics - controlled:
3.1. Asthma defined as per BTS guidelines, on treatment with inhaled corticosteroids +/- long-acting beta-agonists
3.2. Lifelong non-smokers (never smoked)
3.3. Clinically stable with FEV1 greater than 70% post-bronchodilator use, with use of rescue bronchodilators less than 3 x week
3.4. No signs of concurrent respiratory infection at time of scanning or within previous 8 weeks
4. Asthmatics - uncontrolled:
4.1. Asthma defined as per BTS guidelines, on treatment with inhaled corticosteroids +/- long-acting beta-agonists
4.2. Lifelong non-smokers (never smoked)
4.3. Use of rescue bronchodilator greater than 3 times a week
4.4. No signs of concurrent respiratory infection at time of scanning or within previous 8 weeks

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
55 years

Sex
All

Key exclusion criteria

1. Pregnancy (where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive human chorionic gonadotrophin [hCG] laboratory test greater than 5 mIU/ml), an intention to become pregnant or breast-feeding (lactating)
2. Subjects with active lung disease other than asthma
3. Significant medical co-morbidity which in the view of the investigator could impact on the interpretation of results or participation in the trial
4. Active cancer or a history of cancer or radiotherapy
5. Current/previous users of recreational inhaled illicit drugs, e.g. cannabis, crack cocaine, etc.
6. Inability to lie flat for scan for 2 hours
7. Those who have participated in a clinical trial involving an investigational or marketed drug within 12 weeks of screening, or participated in any study involving radiation within 12 months of screening
8. Those in any situation which, in the opinion of the investigator, may interfere with optimal participation in the study
9. Those unable to optimally perform the breathing manoeuvres required for lung function testing, or deposition of the radio-labelled aerosol
10. Signs of concurrent respiratory tract infection on examination at the time of scanning or within previous 8 weeks (can be rescreened after 8 weeks if otherwise eligible)

Date of first enrolment
01/07/2009

Date of final enrolment
01/10/2009

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Department of Nuclear Medicine
Southampton
United Kingdom
SO16 6YD

Sponsor information

Organisation
Southampton University Hospitals NHS Trust (UK)

ROR

https://ror.org/0485axj58

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Southampton General Hospital (UK) - Biomedical Research Unit

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes