ISRCTN15280333 https://doi.org/10.1186/ISRCTN15280333

Exploring the cutaneous immune response to skin massage in early life (CUTIE study)

Submission date 03/11/2025	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 04/11/2025	**Overall study status** Ongoing	
Last Edited 04/11/2025	**Condition category** Other	

Plain English summary of protocol

Background and study aims
Massaging a baby's skin is believed to support bonding between babies and their caregivers. Research suggests that massage may improve blood flow and could positively influence the baby's immune system. However, the effects of massage on the skin's immune response have not been studied in detail. This study aims to investigate how the skin immune system responds to regular massage in healthy infants.

Who can participate?
Healthy babies born at term and aged up to 6 months are eligible to participate.

What does the study involve?
The study is divided into two parts.

Part 1:
The first 9 babies are enrolled to help optimise the method used to collect skin interstitial fluid (ISF)—a fluid found between the top layers of the skin. A non-invasive device is placed on the baby's calf for approximately 5 minutes to collect ISF into a wet gauze. This technique is well tolerated and does not cause significant discomfort or skin damage. Babies are randomly assigned to one of three groups, each testing a different pressure level with the device. This helps determine the most suitable pressure setting. At this visit, parents may also choose to have their baby tested for allergies to house dust mite, peanut, egg, and milk.

Part 2:
100 healthy babies are randomly assigned to one of three groups for an 8-week study period:
-No moisturiser and no massage
-Moisturiser with oil and water-based components plus massage twice a week
-Moisturiser with oil and water-based components plus massage daily
Each baby attends three study visits: at baseline, Week 4, and Week 8. At the first visit, researchers collect a detailed medical and birth history. ISF is collected using the optimised non-invasive device. The ISF samples are analysed to detect molecules released from immune cells and changes in gene expression. Transepidermal water loss (TEWL)—a measure of how well the skin retains moisture—is assessed using a small handheld device. Skin swabs are taken to study

the diversity of bacteria on the skin. These procedures are non-invasive and do not cause significant discomfort. A skin prick test is performed to check for allergies to house dust mite, peanut, egg, and milk. At Week 4 and Week 8, ISF collection, skin swabs, and TEWL measurements are repeated. The skin prick test is repeated at Week 8.

Each visit takes place at the Clinical Research Facility at St Thomas' Hospital and lasts approximately one hour.

What are the possible benefits and risks of participating?
Participants are offered allergy testing for house dust mite, peanut, egg, and milk. After analysis, parents receive information about the diversity of their baby's skin microbiome. While there is no direct benefit to participants, the study may help improve future advice for parents about baby skin massage and its effects on the skin immune system.

The ISF device may cause temporary skin irritation, redness, or pressure marks. All participants are closely monitored, and adjustments are made if needed to ensure safety. There is a very low risk of an allergic reaction to the skin prick test. If a baby develops an allergy during the study, they are referred to the local allergy service for further assessment, as would be done in routine care.

Where is the study run from?
The study is run from St Thomas' Hospital in London.

When is the study starting and how long is it expected to run for?
April 2023 to April 2027

Who is funding the study?
Rosetrees Trust (UK)
Stoneygate Trust (UK)

Who is the main contact?
For questions about the study, the research team can be contacted via email at gstt.cutie.study@nhs.net

Contact information

Type(s)
Public, Scientific

Contact name
Dr Preeti Khurana

Contact details
St Thomas' Hospital, Westminster Bridge Road
London
United Kingdom
SE1 7EH
-
gstt.cutie.study@nhs.net

Type(s)

Principal investigator

Contact name
Prof Carsten Flohr

Contact details
St Thomas' Hospital, Westminster Bridge Road
London
United Kingdom
SE1 7EH
-
gstt.cutie.study@nhs.net

Additional identifiers

Integrated Research Application System (IRAS)
346822

Central Portfolio Management System (CPMS)
69405

Protocol serial number
CF-2021-2\108

Study information

Scientific Title
A randomised controlled trial to investigate how regular skin massage impacts the immune system in early life

Acronym
CUTIE

Study objectives
1. To establish if regular skin massage induces cutaneous immune system changes measured through pro-inflammatory cytokines in interstitial fluid (ISF), and whether this response is amplified in those receiving daily (vs bi-weekly or no) skin massage
2. To measure the impact baby massage has on skin barrier integrity, using transepidermal water loss (TEWL)
3. To measure the impact baby massage has on ISF RNA/protein expression
4. To measure specific IgE to foods and aeroallergens using skin prick testing
5. To detect signals of skin microbiota e.g. bacterial diversity in addition to specific strains such as Staphylococci

Ethics approval required
Ethics approval required

Ethics approval(s)

approved 02/09/2025, London - Hampstead Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 2071048171; hampstead.rec@hra.nhs.uk), ref: 25/LO/0528

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Quality of life, Other

Health condition(s) or problem(s) studied
How regular skin massage impacts the immune system in early life

Interventions
Part 1: ISF (Interstitial fluid) is a fluid found between the top layers of the skin, a non-invasive device will be used to collect this. The ISF device will be piloted in the first 9 healthy babies enrolled in the study. There will be three cohorts with three babies in each cohort, testing three different pressures (for example -2.4 psi, 4.6 psi and 7.5 psi). This will allow us to determine the optimum pressure based on tolerability and cytokine sample sensitivity. This technique is well tolerated and won't cause significant discomfort or skin damage.

Part 2: A total of 100 healthy babies will be randomised using block randomisation into one of the following three groups:
- Group 1: No application of product and no massage
- Group 2 : Application of product containing oil- and aqueous-based components + skin massage twice a week
- Group 3: Application of product containing oil- and aqueous-based components + skin massage daily

This will generate 3 groups of 30 participants each, after a 10% anticipated loss to follow up. Participants randomised to a group that requires massage will be provided with a commercially available baby massaging product and instructed to wash their hands carefully, then apply the product via a whole-body massage for 10 minutes throughout the 8-week study period. Clear instructions on the massaging technique will be given to the participants, which they will then follow at home using video guidance.

Intervention Type
Other

Primary outcome(s)
Levels of IL-10, TGF-β, Th1-related cytokines (e.g. IFN-γ), Th2-related cytokines (e.g. IL-4, IL-5, IL-13), other inflammatory cytokines (e.g. TNF-α, IL-6) are measured using multiplex immunoassay in skin interstitial fluid at baseline, week 4 and week 8

Key secondary outcome(s))
1. Gene expression profiles associated with allergy and inflammation are measured using RNA sequencing with Nanostring nCounter Analysis system on skin interstitial fluid at baseline, week

4 and week 8
2. Protein expression profiles associated with skin biology are measured using mass spectrometry-based proteomics on skin interstitial fluid at baseline, week 4 and week 8
3. Transepidermal water loss (TEWL) is measured using Biox Aquaflux Model AF200 at baseline, week 4 and week 8
4. Sensitisation to egg, milk, peanut and house dust mite is measured using skin prick testing at baseline and week 8
5. Skin microbiota composition including bacterial diversity and presence of specific strains such as Staphylococci is measured using microbial DNA extraction and next generation sequencing from skin swabs at baseline, week 4 and week 8

Completion date
30/04/2027

Eligibility

Key inclusion criteria
1. Healthy babies born at term up to 6 months old
2. Ability of parents/guardians/caregivers to provide written informed consent for study participation
3. Willingness of parents/guardians/caregivers to comply with all study requirements

Participant type(s)
Healthy volunteer, Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
0 months

Upper age limit
6 months

Sex
All

Key exclusion criteria
1. Parents/guardians/caregivers unable to give informed consent
2. Personal history of inflammatory skin disease (in particular AD)
3. Active involvement in another interventional research study

Date of first enrolment
02/01/2026

Date of final enrolment
03/05/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Guys and St Thomas' NHS Foundation Trust
249 Westminster Bridge Road
London
United Kingdom
SE1 7EH

Sponsor information

Organisation
King's College London

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Charity

Funder Name
Rosetrees Trust

Alternative Name(s)
Rosetrees, Teresa Rosenbaum Golden Charitable Trust

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Funder Name
Stoneygate Trust

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from gstt.cutie.study@nhs.net

IPD sharing plan summary
Available on request