CONSENT FORM

TITLE: Dietary Impact on Intestinal Sulfate Metabolism

PROTOCOL NO: 25182

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You are invited to participate in a research study. Your participation is completely voluntary. Before agreeing to participate in this study, it is important that you read this consent form. Please ask one of the study team members to explain any information that is not clear. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

This study is being conducted by Dr. Alexander Khoruts and his colleagues in the Department of Medicine. It is funded by the University of Minnesota. About 30 subjects will take part in this study. People who participate in clinical research are called subjects.

Study Purpose
Sulfur is a mineral naturally found in many foods. We wish to determine whether changing the sulfur content of a person's diet can modify certain aspects of sulfur metabolism in the gastrointestinal tract. It is known that bacteria found in the gastrointestinal tract, known as the gut microbiota, influence sulfur metabolism. Participants in this study will follow two different diet plans for one week each – one that is high in sulfur-containing foods and beverages and one that is low in sulfur-containing foods and beverages. Diet plans will be created by a Registered Dietitian and participants will track what they eat and drink using a food record provided by the research team. We will then examine any changes in fecal bacterial composition associated with dietary modification and will determine if any observed changes have an influence on sulfur metabolism.

Study Length
Your participation in the study will last about 1 months.

Study Procedures
If you agree to participate in this study, we would ask you to do the following:

- Follow the instructions you are given.
- Come to all study visits with the study staff.
- Tell the study staff about any changes in your health or the way you feel.
- Tell the study staff if you want to stop being in the study at any time.
- Not start any new medications or change your medications without approval from the study staff.

The following tests or procedures describe what will be done during some or all of your study visits. Below this section, the procedures that will occur at each visit will be outlined. You may also refer to the chart on page 8, which contains information on each study visit. Of note, 24-hour urine collections, vitals and blood draws during the Study Visits 1-6 may not be collected if the study doctor does not think it is necessary.

Stool Collection
You will be asked to provide a stool sample at numerous study visits. You will have the option to collect the stool sample at home to bring with you to these visits or you can provide a stool sample onsite at the research clinic. Since the time of the collection is important to our research results, you should only collect a sample at home if you can bring it to the study visit within 1 hour. For at home stool collection, the study staff will provide you with containers and instructions to cleanly collect stool samples at home.

We will also ask that you collect stool samples intermittently throughout the study in collection tubes (Day: -4, -2, 3, 5, 9, 11, 16, 18, 23, 25, 30, and 32). Keep the fecal sample frozen until you bring the sample to your next research visit. The sample should be collected no more than 6 days before your next visit. When you bring the sample to your visit, place the ice pack in the cooler with the sample.

24-hour Urine Collection
You will be asked to collect all urine over a 24-hour period at 5 different time points to help us estimate dietary sulfur intake. The sample will be collected at home. The study staff will provide you with containers and instructions. The containers that store your urine will need to be kept in the refrigerator.

Blood Sample Collection
You will be asked to provide a small amount of blood at 6 study visits for research measurements and clinical labs, which will be collected by a trained staff member. Approximately 1.5 tablespoons of blood (4 teaspoons) will be collected at 6 of these visits, and ¾ tablespoon (2 teaspoons) will be collected at 4 of these visits.

Food Frequency Questionnaire and Diet Records
At study visit 1 you will complete a Dietary History Questionnaire (DHQ), in which you will be asked about your eating habits over the past month. This survey is given in a web-based format and should take about 45 minutes. You will also complete detailed dietary records at 6 different time points, each of which will require you to keep track of everything that you eat and drink for three full days.

The procedures that will take place at each visit are outlined below.

SCREENING
- Review of your demographic information and medication history
- Thorough review of the study, including involved procedures and diet
- Dietitian consult to review methods used to record and measure food consumption, with instructions for 3-day diet records
- Measurement of vital signs
- Height and weight measurement
- Collection of blood samples (4 teaspoons) for laboratory testing
- Urine collection kit provided, to be completed prior to visit 1

VISIT 1 (BASELINE)
- Measurement of vital signs
- Weight measurement
- Collection of blood samples (4 teaspoons) for laboratory testing and research measurements
- Collection of stool sample for research measurements
- 24-hour urine sample content collection
- Urine collection kit provided, to be completed prior to visit 2
- Dietitian consult, assessment, and review of 3-day diet record
- Assignment of first intervention diet, to begin immediately after conclusion of visit

- Food frequency questionnaire
- Receive instructions on completing adverse events diary card
- Review of any recent changes in your health and medication

VISIT 2

- Measurement of vital signs
- Weight measurement
- Collection of blood samples (2 teaspoons) for laboratory testing and research measurements
- Collection of stool sample for research measurements
- 24-hour urine sample content collection
- Review of 3-day diet record with dietitian
- Review of any recent changes in your health and medication
- Urine collection kit provided, to be completed prior to visit 3

VISIT 3

- Measurement of vital signs
- Weight measurement
- Collection of blood samples (4 teaspoons) for laboratory testing and research measurements
- Collection of stool sample for research measurement
- 24-hour urine sample content collection
- Review of 3-day diet record with dietitian
- Review of any recent changes in your health and medication

VISIT 4

- Measurement of vital signs
- Weight measurement
- Collection of blood samples (2 teaspoons) for laboratory testing and research measurements
- Collection of stool sample for research measurements
- Dietitian consult, assessment, and review of 3-day diet record
- Assignment of second intervention diet, to begin immediately after conclusion of visit
- Review of any recent changes in your health and medication
- Urine collection kit provided, to be completed prior to visit 5

VISIT 5

- Measurement of vital signs
- Weight measurement
- Collection of blood samples (4 teaspoons) for laboratory testing and research measurements
- Collection of stool sample for research measurements
- 24-hour urine sample content collection
- Dietitian consult, assessment, and review of 3-day diet record
- Review of any recent changes in your health and medication
- Urine collection kit provided, to be completed prior to visit 6
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VISIT 6

- Measurement of vital signs
- Weight measurement
- Collection of blood samples (2 teaspoons) for laboratory testing and research measurements

- Collection of stool sample for research measurements
- 24-hour urine sample content collection
- Review of 3-day diet record with dietitian
- Review of any recent changes in your health and medication

Risks of Study Participation

Risk of Gastrointestinal Symptoms

Changes in dietary intake can trigger gastrointestinal symptoms. However, these are typically minor in nature and occur in a small percentage of healthy volunteers.

Other Study Risks

Study Questionnaires

The screening questionnaires ask questions that are private in nature. Also, some people can be embarrassed by the questions or sharing information on food and beverage eating habits. This may make you feel uncomfortable.

Blood Collection

Blood collection for lab tests can cause:

- Temporary discomfort
- Bruising
- Bleeding
- Swelling at the venipuncture site
- Risk of infection at the venipuncture site
- Light headedness
- Nausea
- Fainting

Infectious Disease Testing

Testing for HIV, hepatitis C, and syphilis can expose volunteers to psychological and social risks if results are positive. By law, positive tests for some of the infectious diseases that you will be screened for must be reported to the Minnesota Department of Health. This includes many of the infectious diseases that can cause diarrhea, HIV, hepatitis A, hepatitis B, hepatitis C, and syphilis.

Feces Collection

You may find it distasteful to provide fecal samples for this study.

Urine Collection

You may find it distasteful to provide urine samples for this study.

Risks for Women of Child-Bearing Potential

Participation in this the study is unlikely to involve risks to a pregnant woman, unborn baby or nursing infant.

Unforeseen Risks

There may be risks from participating in this study that are unknown. All investigational interventions have a potential risk, which if not treated promptly, could become life-threatening.

New Information
The study researcher may receive new information about the diet intervention. If the researcher believes it may affect you to take part in the study, you will be told. If this changes your decision to take part in the study, please talk with the study researcher about your decision.

Notification of Significant New Findings
You will be told of any important new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study.

Benefits of Study Participation
It is possible that your condition or health may improve by taking part in this study. However, there is no guarantee that you will benefit in any way. Information from this study may help other people in the future.

Research-related Injury
In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your insurance company. If you think that you have suffered a research-related injury and that you may be eligible for reimbursement of some medical care costs, let the study physicians know right away.

Will I be compensated for my participation?
If you agree to take part in this research study, we will pay you up to a total of $150 for your time and effort; $25 paid for the completion of each study visit (a total of 6 study visits). Payment will be in the form of gift cards.

Payment you receive as compensation for participation in research is considered taxable income. If payment to an individual equals or exceeds $600 in any one calendar year, the University of Minnesota is required to report this information to the Internal Revenue Service (IRS). Research payments to study participants that equal or exceed $600 during any calendar year will result in a FORM 1099 (Miscellaneous Income) being issued to you and a copy sent to the IRS.

Confidentiality
Records of your participation in this study will be held confidential except when sharing the information is required by law or as described in this informed consent. The study doctor, the sponsor or persons working on behalf of the sponsor, and under certain circumstances, the United States Food and Drug Administration (FDA) and the Institutional Review Board (IRB) will be able to inspect and copy confidential study-related records which identify you by name. This means that absolute confidentiality cannot be guaranteed. If the results of this study are published or presented at meetings, you will not be identified. Data for this study will be transmitted via a secure internet database that has provisions for protection of privacy in place. To these extents, confidentiality is not absolute. Study data will be encrypted according to current University policy for protection of confidentiality.

Blood samples collected during the study will be sent to and processed by hospital laboratory personnel at University of Minnesota Health. Blood will be discarded immediately after testing.

Fecal and urine samples will be stored by the investigator's laboratory. Samples will be anonymized and will not be shared with other investigators. The urine samples will be discarded immediately after testing. The fecal specimens may be stored in the investigator's laboratory for up to 5 years. No human genetic testing will be performed on these samples.

Subjects may withdraw consent for fecal sample storage. If a subject withdraws consent, samples will be destroyed. Any data from fecal samples obtained prior to withdrawal of consent will be used in study results analysis.

Subjects will be asked to agree to re-contact for future research on stored samples.

A description of this clinical trial will be available on http://ClinicalTrials.gov, as required by U.S. law. This website will not include information that could identify yourself. At most, the website will include a summary of the results. You can search this website at any time.

Protected Health Information (PHI)
Your PHI created or received for the purposes of this study is protected under the federal regulation known as HIPAA. Refer to the attached HIPAA authorization for details concerning the use of this information.

Voluntary Nature of the Study
Participation in this study is voluntary. Your decision whether or not to participate in this study will not affect your current or future relations with the University, University of Minnesota Health, or Fairview Hospitals. If you decide to participate, you are free to withdraw at any time without affecting those relationships. If you leave the study early for any reason, the study doctor may ask you to have some end-of-study tests for your safety.

The study doctor or the sponsor can stop your participation at any time without your consent for the following reasons:

- If it appears to be medically harmful to you;
- If you fail to follow directions for participating in the study;
- If it is discovered that you do not meet the study requirements; or
- If the study is canceled

Contacts and Questions
The researcher conducting this study is Dr. Alexander Khoruts. You may ask any questions you have now, or if you have questions later, you may contact him at 612-62 5-5956.

To share feedback privately about your research experience, including any concerns about the study, call the Research Participants Advocate Line: 612-625-1650 or give feedback online at https://research.umn.edu/units/hrpp/research-participants/questions-concerns.. You may also contact the Human Research Protection Program in writing at D528 Mayo, 420 Delaware St. Southeast, Minneapolis, Minnesota 55455.

You will be given a copy of this form to keep for your records.

Statement of Consent
I have read the above information. I have asked questions and have received answers. I voluntarily consent to participate in the study.

Permission for Future Contact

__ Yes, I agree to permit study staff to contact me in the future about testing on stored samples.

__ No, I do NOT agree to permit study staff to contact me in the future about testing on stored samples.

_____
Printed Name of Subject

_____ _____
Signature of Subject Date

_____ _____
Signature of Person Obtaining Consent Date

Schedule of Events

Procedures	Screening	Baseline	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6
		0	Day 7	Day 14	Day 21	Day 28	Day 35
Obtain Consent	X						
Medical History	X						
Vitals*	X	X	X	X	X	X	X
Height	X						
Weight	X	X	X	X	X	X	X
Clinical Labs[1*]		X	X	X	X	X	X
Fasting blood for TMAO and metabolites*		X		X		X	X
Provide stool sample**		X	X	X	X	X	X
24-hour urine collection*		X	X	X		X	X
Diet Assignment		X			X		
Dietary history questionnaire		X					
Provide food diary	X	X	X	X	X	X	X
Review food diary		X	X	X	X	X	X
Adverse Events/ Con meds		X	X	X	X	X	X

[1]Clinical labs include: fasting lipid panel and C-reactive protein (CRP)
*Optional based on PI discretion
**Intermittent stool samples (in frozen collection tubes) will be dropped off at each respective visit following collection. Samples will be collected on days (±2 days) -4, -2, 3, 5, 9, 11, 16, 18, 23, 25, 30, and 32.