CONSENT FORM TO BE PART OF A RESEARCH STUDY

Title of Research: **Gut Oxalate Secretion and Assessment of Endogenous Oxalate Synthesis**

UAB IRB Protocol #: **IRB-151020005**

Principal Investigator: Sonia Fargue, PhD

Sponsor: National Institute of Health (NIH)

General Information	You are being asked to take part in a research study. This research study is voluntary, meaning you do not have to take part in it. The procedures, risks, and benefits are fully described further in the consent form.
Purpose	The purpose of the study is to determine how much oxalate the body produces and how this varies in certain groups of individuals, with different health conditions.
Duration & Visits	The screening will involve 3-4 days and 2-3 visits to the Clinical Research Unit (CRU). The Dietary Phase will last 5 days. The Oxalate Infusion Phase will occur on the last day of the Dietary Phase at the CRU. The total maximum duration will be 10 days and require a maximum of 8 visits in total.
Overview of Procedures	The screening will require two 24-hr urine collections, one blood draw, a fecal collection and a visit to the Clinical Research Unit (CRU). The dietary phase will require eating a controlled diet for 5 days and collecting two 24-hr urines. The Oxalate Infusion phase will take place at the CRU on the 5th day and will require collecting several blood and urines over 7-hr at the CRU and home collections of urine for the remainder of the day.
Risks	The most common risks include discomfort and bruising from the blood draw, illness from improperly prepared food, and a potential loss of confidentiality
Benefits	You may not benefit directly from this study. Your participation will help us better understand the mechanisms behind the formation of oxalate kidney stones.
Alternatives	This is not a treatment study, and you do not have to participate if you don't want to

Purpose of the Research Study

We are asking you to take part in a research study. The purpose of this research study is to assess how much oxalate the body produces and whether the intestinal bacterium *O. formigenes* can reduce the amount of oxalate excreted in urine. Oxalate is a naturally occurring molecule in many foods, which is absorbed in our intestines and excreted in urine. If oxalate reaches high levels in the urine it can result in kidney stone formation. *O. formigenes* is a normal, harmless, bacteria found in about 30% of the population, and consumes oxalate as its major food source. This study will recruit healthy volunteers as well as individuals with chronic kidney disease and subjects with a history of kidney stones. The study will use the intravenous infusion of a naturally occurring form of oxalate, called carbon 13 oxalate. The concentrations of carbon 13 oxalate injected will increase plasma oxalate by less than 20%. The injection of carbon 13 oxalate and the use of a low oxalate diet to limit its dietary absorption will allow us to measure how much oxalate the body makes as part of its natural processes in the different groups of subjects recruited.

Study Participation & Procedures

Screening Visit

1. The screening will start with collection of two 24-hr urines while consuming foods and drinks of your choice. You will return these urines to the research unit
2. If the results from your urine collections are within the expected range, you will then be invited to come to the UAB Clinical Research Unit (CRU) in the fasted state (at least a 10-hour) fast. The following will occur at this visit:

a. A fasted blood sample will be obtained at this appointment to ensure you are in good health. This will require 2 tablespoons of blood (20 ml) in total.
b. You will meet with a nutritionist at the CRU to determine your caloric requirements and your willingness to consume a diet prepared in the CRU, which will be controlled in their content of nutrients including oxalate and calcium. You will learn about the menu choices available for the diet, as well as the procedure for picking up your food from the CRU kitchen for the dietary phases of the study. The nutritionist will also measure your height, weight, waist-to-hip ratio, and estimate your body fat mass.
c. You will be provided with a commercial stool collection kit, and asked to swab your stool with 2 swabs, insert them in a transport medium, and post them to the research laboratory in a prepaid Fedex Clinical Pak, or return them in-person. This sample will be used to determine if you are colonized with *Oxalobacter formigenes.*

3. If any of the test results exclude you from participating in the study, we will contact you over the phone to let you know that you may not participate. If all the exams and tests show that you meet the requirements to be in this study, and you decide to be in this study, you will be scheduled for the study.

Controlled Dietary Study

The diet will be prepared by the CRU kitchen. It will be controlled for protein, carbohydrates, fat, calcium, oxalate, calcium vitamin C and sodium. You are asked to stop dietary supplements for 14 days before the start and for the duration of this study (e.g., vitamins, calcium and other minerals, herbal supplements, nutritional aids, probiotics). You will be asked to also avoid high oxalate and high vitamin C foods for two days before the start of the controlled diet study. A list of foods to avoid is below. You will be asked to not exercise strenuously during the controlled dietary study. On all days of controlled diet, you will not eat any foods other than those provided by the CRU kitchen. Meals will be divided into specific days, and you may not switch out one day's meals for another, such as eating Day 1's dinner on Day 3. You may however switch up the meals for any one day, such as swapping out Day 3's lunch meal and dinner meal. You will be asked to at least drink 1.5 liters of bottled water per day, which will be provided, but no tap water. You are restricted to 8 oz. of unsweetened or artificially-sweetened black coffee or tea daily.

Foods to Avoid 2 days before beginning the controlled diet

High Oxalate and Vitamin C foods to avoid

Vegetables	Fruits	Other foods
· Spinach	· Rhubarb	· Chocolate
· Potatoes	· Kiwi Fruit	· Cocoa powder
· Potato Chips	· Fruit Juice	· Soy Products
· Potato Fries	· Oranges	· Nuts
· Beetroot	· Grapefruits	· Rice and wheat bran
· Kale and Chard	· Lemons	· Bran flakes
· Broccoli		· Wheat Germ
· Green/Yellow/Red Bell Peppers		

1. After two days of avoiding high oxalate and high vitamin C foods (listed above), you will return to the CRU to pick up the controlled diet, which you will consume for the next 5 days. You will not have to visit the CRU on Days 1 and 2.
2. **Days 3-4:** After two days on the controlled diet, you will be asked to collect 24 hour urines on Day 3 and Day 4 of the study. You will be given containers to collect your urine for each day, and will be asked to drop off these samples with the research coordinator the morning following each collection, meaning that you will drop off Day 3's urine on the morning of Day 4 and Day 4's urine on the morning of Day 5.
3. **Day 5:** You will be asked to perform a 14-hour fast by not eating anything from 12:00 am (midnight) the evening before until 2:30 pm. You will come to the CRU in the morning while still fasting for the Oxalate Infusion phase.

Oxalate Infusion phase

Day 5: This is the day of the oxalate administration. You will perform the following on this day:

1. You will be asked to perform a 14-hour fast by not eating anything from 12:00 am (midnight) the evening before until 2:30 pm. You will come to the CRU in the morning while still fasting for the Oxalate Infusion phase. You will be provided with a meal following this fast, which you will consume at the CRU.
2. **Upon waking**, you will need to urinate to empty your bladder, and drink 500 ml (about 2 cups) of bottled water to ensure an adequate urine flow.
3. **At 7:00 am**, you will arrive at the CRU. An intravenous (IV) catheter (a hollow, flexible tube) will be placed in a vein in your arm to collect blood. An intravenous catheter will also be placed in a vein on the back of the hand of your other arm and will be used to deliver the oxalate constantly with a pump. You will remain at the CRU until the infusion is finished at 2:30 pm, which will be a total of about 7 hours.
4. **From 7:30 am to 2:30 pm**, you will collect your urine hourly in separate containers. To assist with this, you will be asked to drink 200 ml (about 1 small cup) of water per hour.
5. **At 8:30 am**, the carbon-13 oxalate infusion will start. Very small amounts of blood (3 mls) will be drawn from this catheter at 8:00 a.m., 8:30 a.m. and then every half-hour up to 2:30 p.m. A maximum of 17 samples with a total of 50 mls or 3-4 tablespoons of blood will be collected during this visit.
6. **After 2:30 pm**, the blood collections will end and you will be provided a meal at the CRU. You will leave the CRU after completing your meal and complete the last urine collections at home. This CRU visit will take approximately 8 hours.
7. At home, you will collect the entirety of your next bowel movement and collect timed urine until the next morning and return these stool and urine collections no later than the next day at the CRU. You will continue to ingest the controlled diet food until the next morning, and only drink bottled water.

Day	***Time***	***location***	***Diet***	***Procedure***	***Duration***
Day -2-0		Home CRU	Avoid high oxalate foods	 Pick up food	2 days 15 min
CONTROLLED DIET STUDY					
Day 1		Home	Controlled diet		24 hr
Day 2		Home	Controlled diet		24 hr
Day 3	6 am	Home	Controlled diet	24-hr urine collection	24 hr
Day 4	6 am	Home	Controlled diet Fast from 12 pm till 2:30 pm next day	24-hr urine collection	24 hr
OXALATE INFUSION					
	6 am	Home	Wake up, drink 500 ml water		
Day 5	7-7:30 am	CRU	Check-in		8 hr
	7:30 am		Drink 250 ml water	IV Catheters placed	
	Every hr: 7:30-2:30 am		Drink 200 ml water	1-hr urine collection	
	Every 30 min 8:00 am–2:30 pm			Blood draws	
	8:30 am	**START** infusion			
	2:30 pm	**STOP** infusion			
	2:30 pm	CRU	First meal		
	2:30 pm–7:30 am	Home	Controlled diet	Urine collections	17.5 hr
Day 6	7:30 am Or later	Home	End controlled diet	End Urine collections Stool collection	15 min

This completes the Oxalate infusion phase.

Risks and Discomforts

Blood collections

Inserting an IV catheter into your arm or a needle for drawing blood can cause slight discomfort at the puncture site. Some participants may experience dizziness, lightheadedness, or fainting with these types of needle sticks. Bruising or infection at the site could also occur. For fasting blood draws, some people may experience faintness or dizziness from not eating. If you faint, you will be assisted by the nursing staff and be able to rest until you are able to perform normal activities. There is a slight risk that the catheters inserted in blood vessels may become blocked and require removal and re-insertion at a different place.

Carbon-13 oxalate

Carbon-13 oxalate is a stable isolate of oxalate, a naturally occurring substance produced in the body.

The oxalate that will be used in the infusion study is sterilized in a FDA approved facility under the same conditions required for FDA approved intravenous infusions and determined to be free of toxins.

Controlled low-oxalate diet

There is also a risk of illness from improperly handled prepared food. The CRU metabolic kitchen maintains strict policies and procedures to ensure food safety, but you will also need to handle food safely and as instructed to minimize risk.

Benefits

There will be no direct benefits to you for being in this study. The main benefit of the study is that it may assist researchers to understand how oxalate is handled by the body and if the bacterium *Oxalobacter formigenes* has an impact on body oxalate handling.

Alternatives

This is not a treatment study, and your participation is voluntary. Your alternative is not to participate in this research study.

Confidentiality and Authorization to Use and Disclose Information for Research Purposes

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your authorization (permission) to use or give out any health information that might identify you.

What protected health information may be used and/or given to others?

All medical information, including but not limited to information and/or records of any diagnosis or treatment of disease or condition, which may include sexually transmitted diseases (e.g., HIV, etc.) or communicable diseases, drug/alcohol dependency, etc.; all personal identifiers, including but not limited to your name, social security number, medical record number, date of birth, dates of service, etc.; any past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of any kind, including but not limited to drug/alcohol treatment, psychiatric/psychological treatment; financial/billing information, including but not limited to copies of your medical bills; any other information related to or collected for use in the research study, regardless of whether the information was collected for research or non-research (e.g., treatment) purposes; records about any study drug you received or about study devices used; and consent forms from past studies that might be in your medical record.

Your consent form will be placed in your medical record at UAB Health System or Children's of Alabama. This may include either a paper medical record or electronic medical record (EMR). An EMR is an electronic version of a paper medical record of your care within this health system. Your EMR may indicate that you are on a clinical trial and provide the name and contact information for the principal investigator

If you are receiving care or have received care within this health system (outpatient or inpatient), results of research tests or procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing medical record.

If you have never received care within this health system (outpatient or inpatient), a medical record will be created for you to maintain results of research tests or procedures.

All information within your medical record can be viewed by individuals authorized to access the record.

A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time. The ClinicalTrials.gov Identifier is: **NCT03752684**

Who may use and give out information about you?

Information about your health may be used and given to others by the study doctor and staff. They might see the research information during and after the study.

Who might get this information?

All Individuals/entities listed in the informed consent document(s), including but not limited to, the physicians, nurses and staff and others performing services related to the research (whether at UAB or elsewhere). Your information may also be given to the sponsor of this research. "Sponsor" includes any persons or companies that are working for or with the sponsor, or are owned by the sponsor, or are providing support to the sponsor (e.g., contract research organization).

Information about you and your health which might identify you may be given to:

- the Office for Human Research Protections (OHRP)
- the U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- Governmental agencies in other countries
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- UAB Department of Urology
- the University of Alabama at Birmingham - the physicians, nurses and staff working on the research study (whether at UAB or elsewhere); other operating units of UAB, UAB Hospital, UAB Highlands Hospital, University of Alabama Health Services Foundation, Children's of Alabama, Eye Foundation Hospital, and the Jefferson County Department of Health, as necessary for their operations; the UAB IRB and its staff
- the billing offices of UAB and UAB Health Systems affiliates and/or Children's of Alabama and its billing agents
- the sponsor, the National Institute of Diabetes and Digestive and Kidney Diseases
- the University of Texas Southwestern Medical Center

Why will this information be used and/or given to others?

Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study. In addition, people from the sponsor and its consultants will be visiting the research site. They will follow how the study is done, and they will be reviewing your information for this purpose.

This research will be covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Institute of Diabetes and Digestive and Kidney Diseases which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local laws.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

What if I decide not to give permission to use and give out my health information?

By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. If you refuse to give permission, you will not be able to be in this research.

May I review or copy the information obtained from me or created about me?

You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?

Yes, but this permission will not stop automatically. The use of your personal health information will continue until you cancel your permission.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to continue being in this study.

When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Is my health information protected after it has been given to others?

If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others, including others outside of UAB, without your permission.

Voluntary Participation and Withdrawal

Whether or not you take part in this study is your choice. There will be no penalty if you decide not to be in the study. If you decide not to be in the study, you will not lose any benefits you are otherwise owed. You are free to withdraw from this research study at any time. Contact the study doctor if you want to withdraw from the study. Your choice to leave the study will not affect your relationship with this institution.

You may be removed from the study without your consent if the study doctor decides it is not in the best interest of your health, or if you are not following the study rules.

If you are a UAB student or employee, taking part in this research is not a part of your UAB class work or duties. You can refuse to enroll or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research.

Cost of Participation

There will be no cost to you for taking part in this study.

Payment for Participation

You will be paid $30 for completing the screening activities. If you provide stool you will be paid an additional $20. For completing the dietary study, you will be paid $80 for the 24-hr urine collections and a blood draw on the controlled diet. For completing the infusion procedure, you will be compensated a total of $220 at the end of the infusion study. If the infusion is not completed you will be paid $10 for each urine and blood collected up to the maximum. You are responsible for paying any state, federal, Social Security or other taxes on the payments you receive. You will receive a form 1099 in January of the year following your participation in this study. This form is also sent to the IRS to report any money paid to you. No taxes are kept from your check.

Phases	**Subtotal**	
Screening	$	30
Stool Specimen	$	20
Low Oxalate Diet Phase	$	80
Oxalate Infusion Phase	$	220
Total (all phases completed)	**$**	**350**

Payment for Research-Related Injuries

UAB and the NIH have not provided for any payment if you are harmed as a result of taking part in this study. If such harm occurs, treatment will be provided. However, this treatment will not be provided free of charge.

New Findings

You will be told by the study doctor or the study staff if new information becomes available that might affect your choice to stay in the study.

Optional Research

Future Research Use of Private Information and/or Biospecimens

We would like your permission to keep your private information and biospecimens (urine, blood, and fecal specimens) collected in this study for future research. The future research may be similar to this study or may be completely different. Your private information and biospecimens will be stored indefinitely or until used. Your private information and biospecimens will be labeled with a code that only the study doctor can link back to you. Results of any future research will not be given to you or your doctor.

You can take part in this study even if you decide not to let us keep your private information and biospecimens for future research.

If you give us permission now to keep your private information and biospecimens, you can change your mind later and ask us to destroy it. However, once we have analyzed your private information and biospecimens, we may not be able to take it out of our future research. We may share your identifiable private information and identifiable biospecimens, so that others can use it in their research. Their research may be similar to this study or may be completely different. Once we have shared your identifiable private information and identifiable biospecimens with other researchers, we will not be able to get it back. Future research use of your private information and biospecimens will be conducted in compliance with applicable regulatory requirements.

You will not find out the results of future research on your private information and biospecimens. Allowing us to do future research on your private information and biospecimens will not benefit you directly.

The private information and biospecimens used for future research will not be used for commercial profit.

Initial your choice below:

_____ I agree to allow my private information and biospecimens to be kept and used for future research on kidney stones.

_____ I do not agree to allow my private information and biospecimens to be kept and used for future research.

Questions

If you have any concerns or complaints about the research or a research- related injury including available treatments within normal working hours, please contact Dr. Sonia Fargue, PhD at 205-9756932. You can also contact Dr. Kyle Wood, MD, he may be reached by calling 205-934-3411, and request to have him paged.

Any general inquiries about the study protocol can be directed to our study coordinator at kidneystone@uabmc.edu or at 205 9345712. They will be glad to answer any of your general questions.

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll free at 1-855-860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday.

Legal Rights

You are not waiving any of your legal rights by signing this consent form.

Signatures

Your signature below indicates that you have read (or been read) the information provided above and agree to participate in this study. You will receive a copy of this signed consent form.

_____

Signature of Participant Date

_____

Signature of Person Obtaining Consent Date