

Cover Page

STUDY TITLE:

Abnormal Food Timing and Circadian Dyssynchrony in Alcohol Induced Colon Carcinogenesis

Short title:

AFT

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Principal Investigator : Faraz Bishehsari, MD

Sponsor: NIH - National Institute on Alcohol Abuse and Alcoholism (NIAAA)

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Investigator: Faraz Bishehsari, MD

Contact Information: 1725 W. Harrison St. Suite 207, Chicago, IL 60612; Phone #312-563-4092

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Subject Information Sheet and Consent Form

Introduction

You are being invited to take part in this research study. Before you decide, 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 information in this form carefully, as it may contain words you do not understand. You may wish to discuss it with your doctor, family, and/or friends. If there is anything that you do not understand or you would like more information, please ask questions and the study doctor or study staff will try their best to answer them. Once the study has been explained and you have had all your questions answered to your satisfaction, you will be asked to sign this form if you wish to participate. Before anything is done for this study, you must sign this form. A copy of this signed form will be given to you.

You do not have to take part in this study. You are free to withdraw from this study at any time you choose without giving a reason. This will not affect any future care you will receive. No promises can be made about the outcome of this as far as your current condition, either positive or negative. People who take part in research are called “subjects” instead of “patients”.

Why are you being invited to participate in this study?

You are being asked to take part in this study because you have had advanced tubular adenoma which are considered pre-cancer growths found during a colon (large bowel) examination within the last year and you have no history of alcohol abuse.

What is the purpose of this study?

The purpose of this study is to study the impact of Western lifestyle, including moderate alcohol consumption and delayed eating patterns on studying individuals’ susceptibility to colorectal cancer. This study aims to increase our ability to identify individuals at risk for colorectal cancer in the future.

How many study subjects are expected to take part in the study?

We hope to have 44 subjects to take part in the study which is being conducted only at Rush.

What will you be asked to do?

Screening Visit (Study Visit 1):

After you have reviewed this information sheet and signed it, we will check to see if you are eligible for this study by answering questionnaires and having a physical exam. We will ask you to complete a questionnaire related to demographic information (such as age, race, sex,

occupation, education) and medical history. You will then complete the weekly Food Timing/Sleep Questionnaire and online 24-hour food recall to gather information about timing of food intake and diet. You will also be interviewed by the clinical coordinator with the Lifetime Drinking History assessment tool to evaluate your alcohol drinking history. A study doctor or assistant will do a physical exam and take your vitals (such as height, weight, waist circumference, and blood pressure). If you are eligible, you will be given an actigraphy, an electronic device which monitors your rest/activity cycles during the study period. You will be randomly assigned to one of the interventions. You will then be told to eat normally with no alcohol for 1 week before you start the first intervention week. You will also be asked to complete the daily Food Timing/Sleeping Questionnaire until visit 2. As an option, you can take a picture of each meal/snack and email to the study coordinator and only complete the sleep questions in the Food Timing/Sleep Questionnaire.

Intervention Visits (Study Visit 2, 3, 4, and 5)

You will come in for your visits 2, 3, 4, and 5 after completing each intervention week. You will experience all four conditions of (1) “right-time eating” / no alcohol, (2) “right-time eating” / with alcohol, (3) “delayed-eating” / no alcohol, (4) “delayed-eating” / with alcohol at the end of the study. “Right-time eating” means breakfast before 8am, lunch before 1 pm, and dinner before 6pm. “Delayed-eating” means eating each meal 3 hours later than the “Right-time eating.” Moderate alcohol drinking means 0.5 g/kg alcohol daily, which will be not more than 3-4 glasses of wine depending on your weight. Alcohol will always be consumed in the evening with food or after food (e.g., dinner). The timing of alcohol consumption will be consistent for each individual. You will be provided with red wine for your 2 alcohol intervention weeks. The order of conditions will be random. After each week of intervention, you will come in for an intervention visit, then you will have one week of wash-out period (+/- 2 days) before starting another intervention week. Wash-out period means that you will eat as you normally would during this time.

During the intervention weeks, you will be asked to complete two online-24 hour food recalls for one week day and one weekend day. You will also be asked to complete the daily Food Timing/Sleep Questionnaire between each visit. As an option, you can take a picture of each meal/snack and email to the study coordinator and only complete the sleep questions in the Food Timing/Sleep Questionnaire.

At each intervention visit, you will complete the weekly Food Timing/Sleep Questionnaire, a dietitian will ask you to do a 24-hour food recall, and you will undergo an unprepped sigmoidoscopy. If we were unable to collect enough stool during sigmoidoscopy, we will ask you to collect your stool at home and bring the next day.

Flexible Sigmoidoscopy

You will undergo unprepped sigmoidoscopy to collect tissue and stool sample at each intervention visits (visit 2, 3, 4, and 5). Flexible sigmoidoscopy will not require any colon cleansing and it will be very limited to the most distal (closest to the end of the anus) 20 centimeters (approximately 8 inches) of your colon and thus will be far less uncomfortable than the routine flexible sigmoidoscopy. This type of procedure is not associated with much discomfort. Most patients either experience no discomfort or minimal bloating. During the flexible sigmoidoscopy, you will not receive any sedation (agent that makes you sleepy) or anesthesia (numbing agent). This type of procedure occurs routinely without any sedation or anesthesia and is completed in less than five minutes. You will not require any assistance in getting home. Sigmoidoscopy will happen in the morning on a mid-week day, and be kept

consistent during the study.

Circadian (sleep cycle) assessment

At the end of each intervention week, you will have 3 choices on how to do the circadian assessment. Once you choose one type of assessment, you will be asked to keep the same chosen assessment for the entire study. You will be performing the assessments 4 times. Your choices are the following:

1. You will undergo a 24 hour assessment in the Biological Rhythms Research Lab. During this assessment, a saliva sample will be taken every hour, a mouth swab will be done every 2 hours, and rectal swab will be done twice (every 12 hours). You will be kept awake in dim light on a recliner chair. You can watch a television with dimmed light, or talk to each other. You will be provided with food and drink during the assessment. Driving after staying awake for 24 hours can be dangerous. We recommend to have your family or friend drive you, or to take other transportation (such as public transportation) to arrive and to leave after the assessment.
2. In addition to the 24 hour assessment explained above, you will collect your urine first thing in the morning of your visit in a jug provided by the study staff, prior to the intervention visit at home and will bring the jug with you to your visit. Voids from additional nighttime bathroom trips should be collected in the same jug and kept in the refrigerator. Instruction on how to collect the urine will be provided.
3. You will only collect your urine first thing in the morning of your visit in a jug provided by the study staff, prior to the intervention visit at home and will bring the jug with you to your visit. Voids from additional nighttime bathroom trips should be collected in the same jug and kept in the refrigerator. Instruction on how to collect the urine will be provided.

Table 1. Study Timeline example

Week #	1	2	3	4	5	6	7	8	Final Visit
Visit #	Visit 1		Visit 2		Visit 3		Visit 4		Visit 5
Intervention	Normal Eating	Condition 1*	Wash-out**	Condition 2*	Wash-out**	Condition 3*	Wash-out**	Condition 4*	
Sigmoidoscopy			#1		#2		#3		#4
Circadian Assessment+			#1		#2		#3		#4

*Intervention will be one of the following conditions in random (by chance) order: (1) “right-time eating” / no alcohol, (2) “right-time eating” / with alcohol, (3) “delayed-eating” / no alcohol, (4) “delayed-eating” / with alcohol

** You will eat as you normally would during the wash-out period

+ Subject can choose from 3 options: 1. Only 24 hour circadian assessment, 2. 24 hour circadian assessment and urine collection, and 3. Only urine collection

How long will you be in the study?

You will be in the study for 8 weeks.

You may be removed from this study without your consent. Possible reasons may be that the study doctor decides that continued participation in the study will be harmful to you, you will need a treatment not allowed on the study, you are unable to follow the schedule as directed, or the study is canceled.

If you decide to participate, you are free to withdraw your consent and discontinue participation at any time without prejudice. If you sign the GI Tissue Repository consent in addition to this consent, then any data that has been collected and any remaining samples that are untested will

not be discarded. If you choose to withdraw at any time during the study, please contact the principal investigator (study doctor), Dr. Faraz Bishehsari at 312-942-5861.

What are the possible risks of the study?

- 1) There are minimal risks of the study, which are mainly related to discomfort with unprepped sigmoidoscopy. For this procedure, a doctor will look at part of your colon in order to collect tissue samples from the colon. There is a risk of bleeding when tissue samples are taken with any endoscopic procedure. If bleeding happens, it will usually stop by itself and does not usually require hospitalization, transfusion (administration of blood) or other interventions. There is also a risk of a tiny tear (perforation) and infection in your colon with sigmoidoscopy and tissue sample collection. This is extremely rare but a possible complication. If an infection or tiny tear occurs, you may experience pain and fever. If you experience an infection and/or tiny tear and fever, you should contact the study doctor, Dr. Faraz Bishehsari, immediately, by calling 312-942-5861. In order to minimize these small risks of complication, all procedures will be done by Dr. Faraz Bishehsari.
- 2) Being awake for 24 hours cause fatigue. We recommend not operating heavy machinery or driving until you get enough sleep. We recommend that you have your family or friend drive you, or take other transportation (such as public transportation). Giving rectal and mouth samples every 12 and 2 hours respectively can be uncomfortable. Our technicians are trained and will make this process as simple as possible.
- 3) You may choose to collect urine sample. You may experience emotional stress related to handling with your own urine. Mishandling urine can lead to infections, however, a safe hand washing technique will be taught and reduce this risk.
- 4) Alcohol can aggravate certain medical conditions and some medications can have drug interactions with alcohol. You should inform any medical conditions you have and medications that you take or plan to take (both prescription and over the counter) to the study doctor to prevent any harmful interactions by consuming alcohol. During the weeks of alcohol consumption, do not do things that require skill, coordination, and alertness after drinking, such as driving a car or operating hazardous equipment.
- 5) In addition, exposure to moderate alcohol intake and 3-hour delay in food timing are possible risks. According to the "Dietary Guidelines for Americans 2015-2020," U.S. Department of Health and Human Services and U.S. Department of Agriculture, recommended alcohol intake is up to 1 drink per day for women and up to 2 drinks per day for men. Depending on your weight, you may be asked to consume up to 2 to 4 times more of what is generally recommended for total of two weeks during the entire study duration. The risks of this level of drinking are fully described in the brochure "Beyond Hangovers." Key risks associated with consumption of moderate drinking may include interaction with certain medications, sleep disruption, and clouding of judgment. In this study, we do not recommend participating in our study and drinking alcohol if you don't usually drink; we advise against higher doses of alcohol, and limit the duration of moderate alcohol consumption to one week (the study duration for each intervention). We will further minimize any potential risks that could be associated with one week of moderate dose of alcohol drinking by going over your medications prior to study; if any major interaction is identified you will not be recruited. Moreover, prior to each visit before the study intervention, we will review with you any new medications or conditions

that you may have developed and provide you specific instruction on consumption of alcohol. If new conditions or medications have potential dangerous interaction with alcohol, you will be excluded from the study.

Are there any anticipated pregnancy risks?

Women

If you are pregnant, breastfeeding, or planning to be pregnant, you cannot take part in this study. You are responsible for using an effective birth control method such as birth control pills, barrier method (such as condoms or diaphragms), intrauterine device (IUD), hormone implants or surgical sterility while you are taking part in this study. If you become pregnant, you must notify the study doctor immediately.

Are there benefits to taking part in the study?

There may be no direct benefit to you for participating in this study. However, if you were found to have the most dramatic responses to alcohol and delayed food timing you could be advised to follow a circadian (time) -friendly based food timing to prevent colorectal cancer. Additionally, the knowledge from this study will help shape the future recommendation for colorectal cancer prevention.

What other options are there?

The only alternative to the study is not to participate. Choosing not to participate in the study will not affect your health care.

What about confidentiality of your information?

Records of participation in this research study will be maintained and kept confidential as required by law.

Unique assigned identification numbers will be used along with your initials for identifying your written information. Any records identifying you will also be kept confidential to the extent permitted by applicable laws and/or regulations. The researchers are HIPAA (privacy) trained and will abide by HIPAA rules. Your study information will be kept under lock at the Section of Digestive Diseases Offices at Rush University in Suites 222, 224 or 206, under double lock. Your study questionnaires will only contain your unique study subject number. The study database is secured in an electronic database (also known as a firewall) at Rush, and the Rush system is compliant with HIPAA. This database will be password protected by research personnel and will have no identifying information.

If you withdraw from this study, the data already collected from may not be removed from the study records. The study doctor and/or study team may ask you whether they can continue to collect follow-up data on you. If follow-up information will be requested, you will be asked to sign a separate consent form before this information can be collected.

In order to conduct the study, the study doctor, Dr. Faraz Bishehsari, will use and share personal health information about you. This includes information already in your medical record, as well as information created or collected during the study. Examples of the information that may be shared include your medical history, physical exam and laboratory test results. The study doctor

will use this information about you to complete this research. Your identity will not be revealed on any report, publication, or at scientific meetings.

Confidentiality and disclosure of your personal information is further described in the attachment to this form. The attachment is titled HIPAA Authorization to Share Personal Health Information in Research (2 pages).

The Rush Institutional Review Board (IRB) will have access to your files as they pertain to this research study. The IRB is a special committee that reviews new and ongoing human research studies to check that the rules and regulations are followed regarding the protection of the rights and welfare of human subjects.

What are the costs of your participation in this study?

All costs that are part of this research study will be free of charge.

If you are driving to Rush, we will provide you with parking stickers for the Rush parking garage. We cannot reimburse you for valet parking or for cab fare to and from Rush. We will provide a paid parking sticker at your visit good only for parking at Rush University Medical Center. If you take public transportation to Rush (such as CTA) we will reimburse you for the round trip fare up to a maximum of \$10.

What financial disclosure(s) apply to this study?

Rush University Medical Center is being paid by NIH- National institute on Alcohol Abuse and Alcoholism (NIAAA) to conduct this research. A portion of this money may go to the study doctor to compensate for other institutional research related costs.

Will you be compensated or paid?

You will be compensated a total of \$450 if you complete the entire study. You will not be compensated for the screening visit (visit); however, you will be compensated \$100 for completing Visit 2, \$100 for Visit 3, \$100 for Visit 4, and \$150 for Visit 5 (study completion).

If you choose to do a 24-hour circadian assessment, you will be compensated total of \$950 if you complete the entire study. You will be paid an additional \$125 each time you complete the 24-hour circadian assessment, in addition to the compensation mentioned above for the study visits. For example, \$225 for completing Visit 2, \$225 for Visit 3, \$225 for Visit 4 and \$275 for Visit 5. Extra cost of transportation above \$10 is considered to be part of compensation for completing the 24-hour circadian assessment. You will also be provided with food and beverages during the 24-hour assessment.

You will be required to provide your Social Security Number to be paid.

Your participation in this research study may contribute to the development of commercial products from which the Sponsor company or others may derive economic benefit. You will have no rights to any products, patents or discoveries arising from this research, and you will receive no economic benefit.

What happens if you experience a research related injury?

If you experience any injury or illness as a direct result of your participation in this research study, immediate treatment will be provided. However, the cost of that treatment will be

billed to you or your insurance company. Please check with your insurance company regarding coverage.

If you have any medical problems during the study, please contact the study doctor. He or she will explain your treatment options to you and/or help you find a place to get treatment.

Rush University Medical Center has no program for financial compensation or other forms of compensation for injuries which you may incur as a result of participation in this study.

What happens if you need emergency care?

If you need emergency care while you are participating in this study, it is important that you tell emergency personnel of your participation in this study and notify the study doctor as soon as possible.

Whom do you call if you have questions or problems?

Questions are encouraged. If there are any questions about this research study or if you experience a research related injury, please contact: Dr. Faraz Bishehsari at 312-942-5861. Questions about the rights of research subjects may be addressed to the Rush Research & Clinical Trials Administration Office at 1-800-876-0772.

By signing below, you are consenting to participate in this research study. You have read the information given or someone has read it to you. You have had the opportunity to ask questions, which have been answered satisfactorily to you by the study staff. You do not waive any of your legal rights by signing this consent form.

SIGNATURE BY THE SUBJECT

Name of Subject

Signature of Subject

Date of Signature

SIGNATURE BY THE INVESTIGATOR/INDIVIDUAL OBTAINING CONSENT:

I attest that all the elements of informed consent described in this consent document have been discussed fully in non-technical terms with the subject. I further attest that all questions asked by the subject were answered to the best of my knowledge.

Signature of Individual Obtaining Consent

Date of Signature

☐ *Check here if the Individual Obtaining Consent observed the signing of this consent document and can attest, to the best of their knowledge, the person signing the consent form is the subject and the person signing the form has done so voluntarily. By checking this box, the Individual Obtaining Consent does not need to sign on the Witness signature line (below).*

SIGNATURE BY WITNESS/TRANSLATOR

(for use if this consent is being used as a written summary of the research along with a short form consent OR when the person obtaining consent is not the witness):

I observed the signing of this consent document and attest that, to the best of my knowledge, the person signing the consent form is the subject and the person signing the form has done so voluntarily.

Signature of Witness/Translator

Date of Signature

☐ Check here if a separate witness signature is not necessary.

SIGNATURE OF THE PRINCIPAL INVESTIGATOR

I attest that I am aware of the enrollment of this subject in the study discussed in this consent document.

Signature of the Principal Investigator

Date of Signature

☐ Check here if Principal Investigator obtained consent and a separate signature is not required.