A Prospective Randomized Comparison of EGD versus Push Type Enteroscopy for Evaluation of Occult GI Bleeding in Patients with a Negative Colonoscopy

A. Statement of Study and Purpose Rationale

There is still considerable debate regarding the yield of upper endoscopy in cases of asymptornatic patients with positive fecal occult blood tests and negative colonoscopies. Upper gastrointesinal pathology has been reported to be the cause of occult bleeding in 8-55% of patients with a negative colonoscopy. There have been several studies regarding the use of enteroscopy in these cases of occult GI bleeding. Chong et al (1) has reported a 25% diagnostic yield using push-type enteroscopy in patients with occult GI bleeding. The standard diagnostic workup of a patient with heme positive stool ' and/or unexplained iron deficiency anemia is to first perform a colonoscopy. If this does not reveal the source of the bleeding an esophagogastroduodenoscopy (EGD) is performed and, if this is negative, a subsequent enteroscopy is then performed at a later date. It is our intention to determine if there is a cost and time benefit of proceeding directly to an enteroscopy after a negative colonoscopy. An enteroscopy by definition includes an esophagogastroduodenoscopy, however if a lesion is not observed in the esophagus, stomach or duodenum the endoscopist may proceed directly to an enteroscopy without having to reintubate the patient. Proceeding directly to an enteroscopy during the same procedure time has no added risk and could possibly increase the diagnostic yield while decreasing the total number of procedures, cost of the workup and time of conscious sedation. By design the study will also compare the diagnostic and therapeutic capabilities of the EGD endoscope versus the enteroscope which are anecdotally thought to be equal.

B. Description of Study Design and Statistical Analysis

All private and ward patients with the following criteria would be eligible for the study: (1) Heme positive stool with iron deficiency anemia and a negative colonoscopy, (2) Heme negative stool with an unexplained iron deficiency anemia and a negative colonoscopy, (3) Herne positive stool with a negative colonoscopy. All patients who fit the above criteria and consent to be enrolled in the study would be randomized to receive either an EGD or a push-type enteroscopy. If a patient is randomized to receive an enteroscopy and a lesion is found abova the ligament of Treitz which could account for the bleeding, the procedure would be terminated and the patient only charged for an EGD. If a patient is randomized to an enteroscopy and no lesion is found above the ligament of Treitz to account for the bleeding, the endoscopist will proceed to visualize the small bowel and the patient will be only charged for an enteroscopy. If a patient is randomized to receive an EGD and this procedure is negative, meaning no lesion that could account for the occult bleeding is found, the patient would return for a push type enteroscopy, as per the current standard of care. Data would then be collected on the diagnostic yield of all the endoscopies, most notably the nature of lesion and its location, the therapeutic outcome of the endoscopies and the total amount of time and cost of the procedures. There will be no repeated studies on each patient except as warranted by each individual case and as deemed necessary by the patient's physician.

Outcome data including type of lesion, location, therapeutic result, time of procedures and cost will be collected and analyzed using a chi-squared test. With this data we will be able to conclusively determine whether it is more effective to proceed directly to an enteroscopy in evaluating patients with occult bleeding with a negative colonoscopies. In addition we will be able to comment on the comparative diagnostic and therapeutic capabilities of the enteroscope versus the EGD endoscope. To do this we will make three assumptions: (1) 75% of those randomized to EGD and separate enteroscopy (the standard of care) will be diagnosed, (2) a power of 80 and (3) a 1% Type I error. Using these assumptions, by

randomizing 129 patients to each arm and if enteroscopy finds 73% of lesions we can dispute the null hypothesis that enteroscopy is inferior is diagnostic capability to EGD plus enteroscopy.

C. Description of Study Procedures

This study consists only of procedures required for a patient's clinical management. The risk incur-red by patients enrolled in the study is no greater than that normally taken by an patient undergoing an EGD or enteroscopy.

D. Study Drugs

There are no study drugs involved in this study.

E. Medical Devices

There are no medical devices involved in this study.

F. Study questionnaires

There are no study questionnaires involved in this study.

G. Description of Study Subjects and Method of Recruitment

Patients will be recruited from the population of private and ward patients undergoing a diagnostic workup of either heme positive stool and/or an unexplained iron deficiency anemia who have already had a negative colonoscopic exam. This patient population will likely be eldery. Informed consent will be obtained from either the patient or a family member should the patient be unable to make a competent decision. Potential subjects will be identified and approached by either the gastroenterologist performing the procedure, the patient's primary physician, or one of the principal investigators. In accordance with CPMC policy the patient's primary physician will be consulted as to whether the patient is suitable for the study and will ascertain from the patient if he/she is willing to discuss a study with the research team before any approach by the investigators. The study will not be restricted by gender or race.

H. Confidentiality of Study Data

All study data will be coded (without any personal identifiers) and will be stored in a secure location accessible only to the investigators.

I. Location of Study

The location of the study will be limited to the clinical care facilities of Columbia-Presbyterian Medical Center.

J. Risks and Benefits

Gastroduodenal endoscopy and small bowel enteroscopy may be slightly uncomfortable but the risk of serious injury (such as perforation or bleeding) is extremely low (less than I per 10,000 cases). Bipolar electrosurgical devices used to cauterize any potential bleeding lesions are extremely safe and the risk of bleeding or perforation is again extremely rare. Potential benefit to the subject and society include a decrease in the number of endoscopic procedures and the associated cost of these procedures.

K. Alternative therapies

The study does not involve any experimental therapies. All procedures to be performed are considered to be the standard of care.

L. Compensation and Costs to Subjects

The patients will not incur any added cost from being enrolled in the study nor will any compensation be provided.

M. Minors and Research Subjects

This study will not enroll minors as subjects.

N. Radiation or Radioactive Substances

Patients enrolled in the study will not be exposed to any radiation or radioactive substances as a consequence of the study. Fluoroscopy will not be used as the enteroscopies will not be performed with a stiffening overtube.

O. References

1. Chong J, Tagle M Small Bowel Push-Type Fiberoptic Enteroscopy for Patients with Occult Gastrointestinal Bleeding or Suspected Small Bowel Pathology. Am Journal of Gastroenterology 1994;89,12:2143-2146

IRB Lay Summary

Title: A Randomized Comparison of EGD Versus Push Type Enteroscopy for Evaluation of Occult GI Bleeding in Patients with a Negative Colonoscopy

Principal Investigators: Dr Charles Lightdale, Dr Peter Stevens, Dr Reuben Garcia Carasquillo, Department: Division of Gastroenterology

Study Purpose: The usual diagnostic workup of a patient who presents with blood in his or her stool or an unexplained iron deficiency anemia is to first perform a colonoscopy to look for the source of the bleeding. If this fails to localize the lesion the usual next procedure is an esophagogastroduodenoscopy (EGD), which allows the gastroenterologist to visualize the esophagus, stomach and duodenum. If this is negative a push-type enteroscopy is performed to visualize the small bowel. Our study involves randomizing patients to reciceive either the standard EGD, with a possible enteroscopy if this is negative, versus proceeding directly to an enteroscopy after a negative colonoscopy because the esophagus, stomach, and duodenum are just as well visualized with an enteroscope. If no lesion is identified the gastroenterologist can then proceed to examine the small bowel immediately thereby possibly saving the patient the added time and expense of returning for another procedure. There is no loss of diagnostic or therapeutic power in using the enteroscope for upper gastrointestinal lesions.

Study Design: All those patients who fulfill the eligibility criteria and consent to be enrolled in the study will be randomized to initially receive either an enteroscopy or an EGD after having a negative colonoscopy. The data collected will be the type of lesion, its location in the GI tract and the therapeutic outcome. By collecting this data a conclusion can be made as to whether proceeding directly to an enteroscopy has diagnostic, therpaeutic and economic advantages.

Study Subjects: The study subjects will be limited to (1) adults with herne positive stool and a negative colonoscopy, (2) adults with heme positive stool, iron deficiency anemia and a negative colonoscopy and (3) adults with heme negative stool, an unexplained iron deficiency anemia and a negative colonoscopy. The approximate number of patients to be enrolled will probably be in the I130 range for each study arm.

Recruitment Method: The study's recruitment method involves first consulting the patient's primary physician to deterine whether the patient is willing to discuss being enrolled in a research study. If the patient fulfills the eligibity criteria and agrees to be enrolled in the study after having the risks and benefits explained, he or she will be recruited. Patients will not be excluded by race or gender.

Study Procedures: The only procedures to be conducted for the study is either an esophagogastroduodenoscopy or a fiberoptic push-type enteroscopy. The are no added procedures or visits for patients enrolled in the study except those deemed necessary by the patient's physician in caring for the patient's condition.

Issues: There are no ethical or physical risk concerns in being enrolled in the study except those normally taken by a patient undergoing endoscopy.

IRB approval date: Approval expiration date:

Columbia Presbyterian Medical Center--Consent to Participate in a Research Study

The purpose of this consent form is to provide you with the information you need to consider in deciding whether to participate in this research study.

Study title: **A Prospective Randomized Comparison of EGD Versus push-Type Enteroscopy for the Evaluation of Occult GI Bleeding in Patients with a Negative Colonoscopy**
IRB study number:

Study Purpose: You are invited to participate in a research study of whether patients who have occult GI bleeding would benefit from proceeding directly to a fiberoptic enteroscopy to visualize the small bowel in addition to the esophagus, stomach and duodenum rather than an just an initial esophagogastroduodenoscopy (EGD). In the usual diagnostic workup of "blood in the stool", after the patient has undergone a colonoscopy which does not reveal the source of the bleeding an esophagogastroduodenoscopy is performed to try and localize the lesion. If this too is negative an enteroscopy is performed to visualize the small bowel, a possible site of blood loss. We believe that since the esophagus, stomach and duodenum are just as well visualized with an enteroscope, proceeding directly to an enteroscopy instead of an EGD could possibly save the patient the anxiety, time and expense of an additional procedure.

Study procedures: If you decide to participate in the study you will be randomized to receive either an EGD (the standard of care) or an enteroscopy.If you are randomized to receive an enteroscopy your gastroenterologist will examine your upper gastrointestinal tract with an enteroscope allowing him or her to proceed to visualize the small bowel immediately should your esophagus, stomach and duodenum not reveal the source of the bleeding. If the usual esophagagastroduodenoscopy is performed you may have to return for an enteroscopy if this does not reveal the bleeding lesion. By participating in the study you will not have any extra blood drawn, will not be taking any experimental drugs or undergoing any experimental procedures. Your participation will not involve any additional visits to your physician other than those he or she deems necessary to treat your condition.

Study Risks: By undergoing an enteroscopy rather than an esophagogastroduodenoscopy you will not be assuming any increased risk other than that usually incurred by an enteroscopy. There is no loss of diagnostic or therapeutic capability in using the enteroscope rather than the EGD scope. The usual risks of an enteroscopy are similar to an EGD and include bleeding, gastrointestinal tract perforation and infection.

Study Benefits: You may or may not personally benefit from this study. Benefits to you may include avoiding the inconvenience, time and expense of returning for an additional procedure. This potential benefit depends on the site of the responsible lesion. If it is present in the small bowel where it would not have been visualized on a routine esophagogastroduodenodcopy you will have benefited from being enrolled in the study. If enteroscopy is shown to have a higher diagnostic yield than EGD in the evaluation of GI bleeding in patients with a negative colonoscopy the benefits to society may include avoiding additional procedure time and expense without sacrificing diagnostic or therpaeutic benefit.

Alternatives: The alternative to being enrolled in the study is undergoing an esophagogastroduodenoscopy which will only visualize the esophagus, stomach and duodenum.

Costs and Compensation: You will incur no additional costs by being enrolled in the study and may, in fact, benefit financially from being a participant if it is found that the site of bleeding would not have been visualized by EGD and you have avoided an additional procedure.

Confidentiality: Any information obtained during this study and identified with you will remain confidential.

Participation is voluntary: Your participation in this study is completely voluntary. You can refuse to participate or withdraw from the study at any time a such a decision will nott affect your medical care at Columbia-Presbyterian Medical Center now or in the future. Signing this form does not waive any of your legal rights.

Questions: If you have any questions, please ask and we will do our best to answer them.
If you have additional questions in the future, you can reach Dr. Peter Stevens at (212) 305-1909. If you have any questions on your rights as a research subject, you can call the Institutional Review Board at (212) 305-5883 for information.

I have discussed this study with _____ to my satisfaction. I understand that my participation is voluntary and that I can withdraw from the study at any time without prejudice. I have read the above and agree to enter this research study. Signing this form does not waive any of my legal rights.

I have been informed that if I believe that I have sustained injury as a result of participating in a research study, I may contact the Principal Investigator. Dr. Charles Lightdale, at (212) 305-4382, or the Institutional Review Board, at (212) 305-5883) so that I can review the matter and identify the medical resources which may be available to me.

I understand that:

a. The Presbyterian Hospital will furnish that emergency medical care determined to be necessary by the medical staff of this hospital;

b. I will responsible for the cost of such care, either personally or through my medical insurance or other form of medical coverage;

c. No monetary *compensation for* wages lost as a result of injury will be paid to me by the Columbia-Presbyterian Medical Center, and;

d. I will receive a copy of this consent form.

Signatures:

_____

Participant Date

_____

Investigator eliciting consent Date

The solicitation of subjects into this study has been approved by the ColumbiaPresbyterian Medical Center Institutional Review Board.