Standard Treatments of Irritable Bowel Syndrome (IBS) A cross cultural study

A. Study Purpose

Irritable bowel syndrome (IBS) is a functional bowel disorder where changes in bowel habit are accompanied by abdominal discomfort. In the U.S., 1) IBS occurs in 10% to 20% of a adults and accounts for as much as 50% of the referrals to gastroenterologists; 2) the female to male ratio is 2:1; and 3) the onset of IBS occurs with equal likelihood at all ages. The etiology of IBS is unknown at present and treatment varies in different parts of the world.

The primary aim of this study is to establish the rate of treatment success achieved when IBS is treated according to currently accepted standards of practice for two different medical traditions: western medical practice and Ayurvedic medical practice. Claims of treatment success with IBS vary widely and different medical traditions claim different degrees of superiority for this condition. But prior efforts establish treatment efficacy suffer from a lack of standardized case definition, systematic case follow-up, and common, objective assessment of outcome. This study will employ a common protocol for the identification, case follow-up and outcome assessment of patients with IBS in three different medical settings: an Ayurvedic medicine practice in India, a western medical practice in India, and a western medical practice here in New York City. Successful completion of this study will provide a scientific estimate of IBS treatment success rate in each of these three practice settings and the data needed in order to design future studies for the treatment of this common debilitating condition.

One hundred subjects meeting eligibility criteria for IBS will be recruited from each of the three clinical practice sites: an Ayurvedic medicine practice at Hindu University Hospital in Benares, India; a western gastrointestinal medical practice also at Hindu University Hospital in Benares, India; and a western gastrointestinal medical practice located at the New York Presbyterian Hospital in New York City.

B. Study design and statistical analysis

This is a longitudinal study the clinical course of men and women between the ages of 20 and 40 meeting clinical eligibility criteria for IBS (ROME Criteria). Three different medical practices have agreed to use a common definition of IBS for the purposes of subject inclusion in this study, to treat each subject according to the standard of practice they currently use, to maintain a standardized record of clinical observations at baseline and weeks 12, 24 and 48, and to employ a common definition of treatment outcome for the 24 week and 48 week assessment of treatment efficacy.

One hundred patients meeting eligibility criteria will be enrolled from each site. To ensure that patients enrolled are representative of the potential population of patients meeting criteria at each site, only 2/3's of eligible patients will be enrolled according to a random selection scheme. In any particular month of the study at the respective clinical sites, four of the first five eligible patients will be actually selected for inclusion in the study. Then, 8 out of the first 10, 12 of the first 16, 16 of the first 24, finally 20 out of the first 30. To ensure that the patients enrolled represent eligible patients over a span of time, no more than 20 subjects can be enrolled during a month.

C. Study Procedures

Each patient presenting to one of the three participating clinical sites with symptoms potentially consistent with IBS will be informed of the study and given the opportunity to give informed consent to participate. Consenting patients will undergo routine diagnostic testing to rule out other conditions and confirm the diagnosis. Routine diagnostic testing includes a physical exam, medical history, routine

laboratory tests (CBC, differential count, sedimentation rate, thyroid function tests, electrolyte levels, urinalysis and stool analysis). Patients may undergo routine diagnostic flexible signoidoscopy, colonscopy or endoscopy as determined to be of relevance by the treating physician. The patient will be given a one-week bowel habit diary to take home, complete and return the following week. At this return visit, the physician will evaluate available information and determine whether the patient meets the eligibility criteria of the study. When a patient meets eligibility criteria, the physician will consult a list to determine if this patient is to be monitored according to the study protocol or continue under routine care without the extra visits required for the study.

Subjects meeting eligibility criteria and selected to participate will attend study visits at weeks 12, 24 and 48. The information collected at baseline will be collected again at each follow-up visit and physician and patient assessement of IBS symptom presence and severity will be recorded. In addition, each patient will report on their compliance with treatment and report any adverse events, intercurrent diseases, current non-IBS medications or the introduction of any other treatment they may have begun. In the event a subject chooses to withdraw from the study, the reason will be asked and recorded. If a patient fails to return for a protocol scheduled visit, staff will attempt to track the patient and record their tracking efforts.

Outcome assessment by clinical evaluation (Appendix D) will be based on the patient's IBS symptoms during months four through six. Outcome will be classified at the six month visit as follows.

Failure, if the subject continues to meet ROME criteria for IBS for the past 2 months;

Partial response is if the subject continues to meet at least one of the ROME symptoms for the past 2 months;

Success if the subject fails to meet any of the IBS criteria for at least two months.

D. Study procedures

There are no study procedures required for this protocol.

E. Study drugs

No experimental drugs will be administered as part of this study.

F. edical devices

None will be used

G. Study questionnaires

The initial diary inquires about IBS symptoms and diet over a seven day period. Additional questionnaires inquire about IBS symptoms after 6 months of treatment and after 12 months.

H. Study subjects and recruitment method

Men and women aged 20 to 40 years will be recruited. Study subjects will be those presenting or referred to physicians at each clinical site. All subjects completing routine screening and meeting ROME criteria will be offered the opportunity to participate in the study. Subjects will be excluded if there is another cause identified as responsible for the gastrointestinal symptoms.

I. Confidentiality of study data

All patient identifying demographic information collected at baseline will be stored in a locked cabinet in the office of the investigator at each site. When a patient has consented, meets eligibility

criteria and has been selected to participate in the study, the patient is assigned a unique study identification number. This number is used on all research data forms to identify the patient, and no other patient identifying information is recorded on research data forms.

J. Location of the study.

The study will be performed at the Center for Intestinal Dysfunction and private practices of Drs. Susan Lucak and Joseph Sweeting, at Columbia-Presbyterian Medical Center. In India, the study will be performed Benares Hindu University, Benares. There the western arm of the study will be conducted at the clinic of Dr. Vinod Dixit, a western trained gastroenterologist. The Ayurvedic arm will be conducted in the Ayurvedic clinic of Dr. Manjari Dwivedi.

K. Risk and benefits

Risks are those associated with the local standard treatment of irritable bowel syndrome and the completion of questionnaire information. The patients may derive benefit by having their persistent IBS symptoms treated. The study will adopt a consistent, reliable and quality controlled data collection protocol for measuring subjects' response to treatment which will provide the basis for estimating the rate of success achieved in each of these three clinical practice settings. Furthermore, this study will establish the feasibility of conducting cooperative, protocol-driven clinical studies in India and the US.

K- Alternative therapies

The therapies used in this study are the practices commonly used by these practitioners. In discussions with physicians from both Ayurveda and western traditions, we are assured that the treatments to be employed here are considered common practice and neither innovative nor unusual. Other methods of treatment may be available from physicians not participating in this study.

L. Compensation and costs to the subjects

There will be no compensation paid to subjects. Participation in this study does not change how a patient will pay for treatment, whether by insurance or self-pay. All the tests and treatments are standard and should be reimbursable by insurance. In India, the patients treated with Ayurveda will not incur any cost of treatment.

M. Minors as research subjects

Minors will be be enrolled in this study.

N. Radiation and radioactive substances

None will be used.

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 particiapte in this research study.

Study Title: Standard Treatments of Irritable Bowel Syndrome (IBS) A cross cultural Study

Study Purpose:

You are invited to participate in this research study because you have symptoms of Irritable Bowel Syndrome (IBS) and are seeking treatment for this complaint. IBS is a bowel disorder where changes in bowel habit are accompanied by abdominal discomfort. This disorder, while not leading to serious illness in most cases, is often very disruptive of a person's normal daily functioning, and can lead to significant emotional distress. In the U.S., IBS occurs in 10% to 22% of adults and accounts for as much as 50% of the patients who see a gastroenterologist. It occurs more than twice as often in women. IBS occurs as often in the elderly as in younger people. The causes of IBS are unknown, although in some cases, stress or other emotional factors may play a role. The way people have IBS varies in different countries. In India, for example, the number of men and women who have iBS is about the same. Further, there are slightly different kinds of IBS.

The purpose of this study is to measure the degree of symptom relief that is achieved by different treatment traditions. Although this is a research study because the doctor's will be recording their observations of you and ask you to complete a diary and questionnaires, there is no experimental treatment that is part of this study. In fact, the study is designed to only study the normal routine practice of how physicians treat patients with IBS. Three hundred patients with IBS are being recruited to this study from three physician practices: one in New York City, and in two in India. In New York and in India, the doctors will use the standard western medical practice used by gastroenterologists to diagnose and treat IBS. In India, there will also be an Indian Ayurveda physician who will use this traditional Indian medical practice to diagnose and treat patients with IBS.

Study Procedures:

Participation in this study does not affect the care you will be given for your IBS condition. Agreeing to participate only means that you will be asked to come to see the doctor four(4) more times than you might if you were not to participate in the study. These visits would be scheduled for next week, thirteen weeks from now, 25 weeks from now, and 49 weeks from now. Each of these visits should last about an hour. At each visit the doctor will ask you a series of questions about your symptoms, any other illnesses or symptoms you have had since the last visit, any medications or treatments you have taken since the last visit, any times that you forgot or stopped taking the treatments that the doctor prescribed at the last visit, and for you to rate how your IBS condition has changed since the last visit. If you agree to participate today, you will be given a diary booklet that you are to use to record your bowel movements each day for the next week. You should return this booklet at next week's visit. You may be asked to fill out a new diary booklet for the week before the 25week visit and the week before the 49-week visit.

You should understand that the diagnosis of IBS involves blood tests, urine tests and stool cultures that the doctor needs to rule out other causes of your bowel problems than IBS. In addition, the doctor may require you to undergo endoscopy (in which you swallow a plastic tube down to your stomach so that the doctor can see if you have signs of ulcers, cancer, or other problems with the lining of your esophagus or stomach), or colonoscopy or flexible sigmoidoscopy (in which a flexible tube is inserted into your rectum to a length of about 1 -meter so that the doctor can see if you have signs if cancer in your colon or problems with the lining of your lower bowel). These diagnostic tests are required when other tests, the doctor's examination of you, or family risk factors suggest that IBS may not be the cause of your bowel problems. All of the tests mentioned are part of the process doctors use to diagnose IBS and are not

part of this study. We will record the results of these tests so that we can see how differences in how patients present at the beginning of treatment may be related to the degree of symptom relief attained after treatment.

If any of these tests indicate that you have a cause of your bowel problems that is not IBS, your participation in the study will be finished.

All study visits will take place in this doctor's office (at New York Presbyterian Hospital or Benares Hindu University). There is no involvement on your part that is required by this study other than completing the bowel movement diary(ies) and attending the four additional visits.

Study Risks:

Your participation in this study involves no additional risks, compared to those of other IBS patients who do not participate in the study. The tests and examinations that the doctor orders to make sure that your symptoms are not due to something other than IBS are tests and examinations that would also be ordered if you were not participating in the study. Any medications or treatments that doctor prescribes are the same drugs and treatments that you would have received if you were not part of the study. The doctor will explain the reasons why medications or treatments are prescribed and inform you of any risk they pose to you as is the common practice of the doctor..

As mentioned earlier, you will not have any additional risks compared to people who have IBS and who are not in the study. There are no experimental procedures, drugs or other treatments that are part of this study. All subjects will receive the treatment for IBS that this doctor normally uses.

Study Benefits:

There is no direct benefit to you by participation in this study. The treatment and the doctor providing the treatment are exactly the same were you to not participate in the study. The benefit to society is that this study will help physicians better understand how people in different cultures present with IBS and which patients benefit from different methods of treatment.

Alternatives:

Currently, there is no accepted cure for IBS. Different doctors may vary to a small degree in their use of diagnostic tests and examinations, and medications or treatments that will be used here. You will be given the quality medical care that is available to all patients who present to these physician practices with symptoms of IBS. Any treatments other than those available in this study would be considered experimental treatments for which the benefit has not yet been shown.

Costs:

There will be no financial costs to you.

Compensation:

You will not receive any compensation for your participation in this study. Participation in this study does not change how you will pay for your treatment, whether by insurance or self-pay. All the tests and treatments are standard and should be reimbursable by insurance. In India, the patients treated with Ayurveda will not incur any cost for the herbs prescribed as treatment.

Confidentiality:

We will protect your confidentiality by having all research data collection forms only identified by a unique number and not by name, hospital card number, social security number, or address or phone number. All research data will be kept in a secured room to which only research staff members have access. Any publication or presentation of the results of this research will only give data on groups of patients so that no single patient can be identified individually. Members of the Institutional Review Board may have access to your records so that they can fulfill their role to monitor the safety and ethics of the study.

Participation is voluntary:

Your participation in this study is completely voluntary. You can refuse to participate, or withdraw from the study at any time, and this decision will not affect your medical care at th New York Presbyterian Hospital, now or in the future. If you chose to withdraw, the doctor will ask you to provide a reason for leaving the study. If you do not come to one of the scheduled study visits, the doctor or a research assistant will try to contact you directly, or the people you indicated that they could contact in this event. Signing this form does not waive any of your legal rights. There are no study-related procedures requiring medical action, should you decide to withdraw early from the study.

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. (name at each site) at (phone number at each site). If you have any questions on your rights as a research subject, you can call the Institutional Review Board at (institution name at each site) at (phone number at each site).