

# IHAST2 Update

July 2000, Volume 1, No. 3



<b>Inside</b>	<b>page</b>
1. Kudos!	1
2. More Kudos!	2
3. IHAST2 Annual Meeting	3
4. Follow-up Exams	3
5. Completion of Screening & Eligibility forms	4
6. Enrolled but not Randomized Patients	5
7. Temperature-Related Issues	6
8. Intercurrent Events	8
9. Body Mass Index (BMI)	12
10. Making Corrections to the Patient Log	13
11. Wrong Telephone Number	13
12. Contact Follow-up	13
13. Physician Protocol Monitor	14
14. <i>Update</i> Newsletters and IHAST2 Operations Manual	

## *Kudos!*

We would like to give some well-deserved recognition to those centers and individuals that have performed "above and beyond". As of July 27<sup>th</sup>, the seven centers with the largest number of randomized patients are: University of Iowa (12), Harborview in Seattle (9), University of Virginia (8), St. Vincent's (8), University of Western Ontario (7), Donauspital (7) and University of Michigan (7). These centers are enrolling patients at an overall rate that is about 150% of expected. After a lot of discussion with people at these centers, it's clear that their "secret" goes beyond simply having more eligible patients, but rather stems from a well organized system to insure that all eligible patients are screened by the study group. *Congratulations!*

We thought that it might be helpful to share some comments from these centers on how they have organized themselves to identify potential IHAST patients. Teresa Novick, study coordinator from the **University of Western Ontario, London, Canada**, searches daily for prospective patients. She checks the OR schedule herself, has requested that the OR booking clerks call her if an aneurysm is booked

### **Please File Your IHAST2 Updates**

Just a reminder. Please file one copy of each edition of the IHAST2 *Update* in your Site Regulatory Binder (See Chapter VII.A.5 of the Operations Manual).

for the OR, and that the neuro-angiography technician page her when a positive angiogram for SAH is diagnosed. She has also asked the ICU database manager to notify her if a patient with a SAH has been admitted to the ICU. Although at the time of admission, these patients do not usually meet the inclusion criteria, their condition may improve and their eligibility status may change. Therefore she checks on these patients daily to assess their status. To help make sure that prospective patients are not missed on weekends, Teresa has asked the neurosurgical residents and neurosurgeons to page her. But she still does not rely only on them to alert her. She also contacts the OR nurse on weekend call to request that s/he page her if an OR case is scheduled. In addition she has arranged that the nurse practitioners on the neurosurgical floor get in touch with her; however, as you might guess, she is usually already aware of the patient by the time they call.

At the **University of Iowa** Mrs. Alice McAllister, study coordinator, and Dr. Mazen Maktabi, the PI, view the neurosurgeons and neurosurgery residents as an important part of the recruitment process. Maintaining a level of commitment to the IHAST2 study not only by the anesthesiologists, but also by the neurosurgery team is a way to avoid missing potential study patients. The neurosurgery team serves as the primary alert system. They are provided with a call schedule and concise instructions on how to reach an IHAST2 anesthesiologist on-call. The schedule not only includes a list of the persons on call for that day, but lists all IHAST2 team members and their pager/cell phone numbers. Also listed are the names of the PI as well as one other anesthesiologist who may be called if back-up is needed. It is also important to follow those patients with SAH who do not meet inclusion criteria at the time of admission in the event that their condition might change.

The **University of Virginia Health System**, another center with high enrollment, reports that their notification system occurs at multiple levels

to ensure that all prospective patients are screened. Ms. Julie Shafer and Ms. Angel Morris, study coordinators, have posted a sign at the nurses' station to "page clinical research for ANY SAH patient being admitted to the hospital". Julie wants to make sure that IHAST certified people actually determine the eligibility. Julie and Angel have also made sure that all residents are aware that the IHAST2 study is ongoing and have provided them with cards stating the study name and pager numbers of the study coordinators to call if a SAH patient comes onto their service.

The coordinators have also requested that the anesthesiologist alert them if they hear of a prospective patient. NNICU is called daily to find out if any SAH patients have been admitted. Julie feels that regular calls also serve to remind them that the study is ongoing. She says they sometimes get up to three calls on one patient and that's when they know "every one is thinking IHAST". Finally, Julie provided us with the real secret to not missing prospective patients: ☺ "We have a tent set up and camp out in front of the ER and monitor all patients entering. Angel and I have a little bonfire going at all times."☺

## 2. More Kudos!

We would also like to extend our appreciation to Ms. Jennifer Hunt, study coordinator at **The Alfred Hospital** (Pahran, Australia). When a patient was unable to return for the 3-Month Follow-up, she and their neuropsychologist, Ms. Pauleen Bennett, personally drove 200 miles to see the patient!!! Then, just two weeks later another patient refused to return for follow-up making it necessary for them to drive another 170 miles. While coordinators should not be doing 3-month Follow-up exams (rather, these should be done by "blinded" Neurologic Examiners), this kind of effort to avoid "losing" a patient clearly takes precedence. **Thanks a million!**

Thanks to another dedicated study coordinator from **St. Vincent's Hospital** in Australia, Ms. Karen Martin, discharge data was obtained even after her patient left the hospital without the IHAST team being notified. After a ward clerk failed to notify her that her study patient was being discharged, Karen decided to visit the patient the very next day. She drove a total of 350 miles to obtain the discharge information. **Now that's going the full distance!!!!**

### 3. IHAST2 Annual Meeting

The IHAST2 Annual Meeting is scheduled for Saturday, October 14, 2000 in San Francisco, California. All Study Coordinators are invited to meet with the IHAST2 CCC and DMC personnel at 8:00 AM in the Yosemite A room of the San Francisco Hilton. All IHAST2 Investigators will join us in the afternoon from 12:00 noon until 5:00 PM. The agenda will include important information about the progress of the trial, safety issues, and discussion of problem areas.

### 4. Follow-up Exams

As of today (July 25<sup>th</sup>), 85 patients have been randomized. The first patients were randomized in March – which means that they are now beginning to start coming back for the 3-Month Follow-up.

So far, the CCC, the DMC, and participating centers have been focusing on more “immediate” problems: local personnel, recruiting patients, working out protocol bugs, etc. However, it's important that everyone begin to prepare for the 3-Month Follow-up visits. Please remember - in a very real sense - this entire trial is based on the data collected at the 3-month visit. If this visit/exam is missed, or if it isn't done correctly, everything that was done before is worthless (really!).

Here are a couple of thoughts and comments based on questions that we have received.

**1. Think ahead.** Local Coordinators, PIs, and Co-PIs need to prepare for this visit by staying in touch with patients and the clinics. Ideally, patients should be coming in specifically for their IHAST exam. Many (most) of these exams will be done in conjunction with a scheduled return visit to the Neurosurgery clinic. You will need to work closely with that clinic to make sure that patients return at the correct time (see below) and that you are notified of the scheduled visit. What we want to avoid is the “*Oh yeah, Mr. Jones was in the clinic yesterday and we forgot to call you....*”. or “*Mr. Jones is down here in clinic, can you come and see him?*” - an hour after your neurologic examiner has left on vacation.

**2. The final follow-up exam is scheduled to take place at 3 months following surgery, NOT following discharge.** In a few cases, patients may still be in the hospital at 3 months (although I hope not too often) or they may have been home for only a short while. Nevertheless, they need to be seen.

**3. The exam does not need to take place precisely at 3 months, but should be done within a 2-week window (e.g., between 11 and 13 weeks after surgery).** We realize that there may be situations where this is not possible - but please do everything possible to meet this goal. Also remember - *better late than never!* If various roadblocks prevent a patient from being seen during this window, it doesn't mean that the exam can be skipped. Please get them back!

**4. There still seems to be some confusion about who does this 3-month exam.** The answer is pretty simple - the designated Neurologic Examiner. While we have “relaxed” the protocol to permit the study coordinator to administer the interim neurologic exams (e.g. post-op NIHSS), coordinators **CANNOT** do any part of the 3-month exam. Even if you have two coordinators and only one worked with a patient, you still need to get an

outside examiner for the 3-Month Follow-up. There are simply too many opportunities for coordinators to talk with each other about patients. Therefore the "other coordinator" may actually know a fair amount about a patient (including group assignment) - in spite of all our best blinding efforts, even if they've never personally seen them before. The examiner needs to be someone who, a) has nothing to do with this trial other than to perform neurologic assessments, and b) can't possibly be unblinded.

**5. GET THE EXAM DONE!** Do everything in your power (short of kidnapping) to complete this follow-up. Seriously, based on other trials, we would expect that in a trial of this size, no more than 2-3 patients should be "lost to follow-up". If we lose more, the validity of the project is jeopardized. So get them back, go to them, or arrange for them to see another certified examiner somewhere else - *whatever is necessary*. Any follow-up is better than a lost patient is!

Overall, everyone out there is doing a great job. The 3-month exam is the "next big hurdle" - but it is unquestionably the most important one of all. If you have questions or concerns, please call us.

## 5. Completion of SCREENING & ELIGIBILITY forms

IHAST2 is a prospective trial. Therefore, screening and eligibility evaluations are made when a patient with an intracranial aneurysm presents for surgery- not before and not after.

### **A. Prospective Form Completion**

All patients who have an intracranial aneurysm for whom surgery is planned within 24 hours are to have a SCREENING form completed. Practically, what does this mean?

- First, if surgery is not planned to take place within 24 hours, then do not complete a SCREENING form. One purpose of the SCREENING form is to measure the overall

surgical activity of each center with respect to cerebral aneurysm surgery. So, if a patient is not going to have surgery (*e.g.*, the patient is neurologically devastated from their hemorrhage or if plans call for endovascular coiling rather than surgery) they should not be screened. *What if surgery is planned several days in advance - is it okay to complete the SCREENING form a few days ahead?* **Answer:** You could, but we suggest you do not. Why? - Simply because the patient's status may change such that surgery is cancelled. If that happens, you will then have to go through the process of correcting and modifying both your local log and the SCREENING form.

- Second, patients with UNruptured cerebral aneurysms should also be screened. Why? - Again, in addition to obtaining demographic information, one purpose of the SCREENING form is to measure the overall surgical activity of each center with regard to cerebral aneurysm surgery. We want to know the total surgical experience of your center - both for ruptured and UNruptured aneurysms. However, because only patients with ruptured intracranial aneurysms are eligible for IHAST2, only those patients who have an acute subarachnoid hemorrhage (SAH) (*i.e.*, the aneurysm has ruptured; item #4 of the SCREENING form is checked "Yes") should then be evaluated for IHAST2 eligibility (ELIGIBILITY form).

Thus, all patients who have an intracranial aneurysm for which surgery is planned within 24 hours and have acute SAH are to have an ELIGIBILITY form completed. Practically, what does this mean?

- First, as before, if surgery is not planned to take place within 24 hours, then do not complete the ELIGIBILITY form more than 24 hours before surgery. Why? - Things change. The patient's status may change such that surgery is cancelled or perhaps a new condition presents that makes the patient ineligible (*e.g.*, endotracheal intubation, life-threatening arrhythmias, etc.). In fact, because things can change quickly in these

patients, the patient's WFNS score (item #7 on page 1 of the ELIGIBILITY form) is determined no more than twelve (12) hours prior to planned surgery. The further ahead of time the ELIGIBILITY form is completed, the greater the chances are that something will change, such that you will have to go through the process of correcting the ELIGIBILITY form (and possibly the SCREENING form and/or your log too!).

• Second, because key elements of IHAST2 eligibility are the patient's pre-SAH Rankin score (Section A, item #5) and WFNS score (Section A, item #7), the person who assesses eligibility must be Rankin- and WFNS-certified. All IHAST2 Study Coordinators are Rankin- and WFNS-certified. All IHAST2 Anesthesiologists are WFNS-certified. Thus, if your Anesthesiologists are frequently performing the eligibility assessments, we highly recommend they get their Rankin certification. IHAST2 Neurosurgeons are not required to be either Rankin- or WFNS-certified. Therefore, if your Neurosurgeons (faculty, fellows, and residents) are, in fact, performing eligibility determinations, they need to be Rankin- and WFNS-certified.

### **B. Retrospective Form Completion**

Patients who are enrolled in IHAST2 MUST undergo the process of screening and eligibility determination prior to surgery. That means all elements on the SCREENING and ELIGIBILITY forms must be fully addressed by IHAST2-certified personnel prior to surgery if the patient is to be enrolled in IHAST2 - no exceptions, **ever**, regardless of the day or time.

*What about patients who are NOT eligible? We understand that patients with ruptured cerebral aneurysms often present for surgery at very inconvenient times. Quite reasonably, the study coordinator or anesthesiologist may ask the following questions: If *the patient is going to surgery at some inconvenient time (say 2:00 AM or on the weekend) and we are told by a person seeing the patient that the patient is clearly NOT**

*IHAST2 eligible (e.g., WFNS of IV or V, intubated, too obese, pregnant, etc.), can't we just complete the SCREENING and ELIGIBILITY forms at a more convenient time (after surgery) instead of coming in and filling out the forms at that exact moment Isn't it pointless to ask us to come in "off-hours" to complete forms on patients that are clearly NOT eligible? **Answer:** Only in this circumstance, is it acceptable to complete the SCREENING and ELIGIBILITY forms retrospectively - in other words, after the patient has had surgery. However, we respectfully ask you to be "on your honor" about this. Be sure you have confidence in the people who are giving you the information. Also, if the patient is considered ineligible on the basis of their pre-SAH Rankin score or current WFNS score, the person making that determination needs to be Rankin- and/or WFNS-certified. *In this circumstance, how do I fill out the SCREENING and ELIGIBILITY forms?**

**Answer:** 1) With respect to **patient-related information** on the SCREENING and ELIGIBILITY forms, please provide answers that reflect the patient's status at the time the eligibility determination was actually made (e.g., 2:00 AM, whatever); 2) With respect to **form completion information** [initials, certification number(s), and signature(s) of persons completing the form; and the form completion date], please provide answers that indicate when the information was actually recorded on the form, and who actually recorded it, even if it is hours or days after the patient had surgery.

## **6. Enrolled but not Randomized Patients (Protocol for data submission)**

**First**, what is the difference between Enrolled and Randomized? A patient is enrolled in the IHAST2 study when the telephone call or "enrollment call" is made to the computerized system, located at the DMC. Although a patient is assigned a patient ID number at enrollment, and also has a temperature

group (randomly) assigned, the patient is still not yet **officially randomized** into the study. The patient becomes officially randomized into the study only when the RANDOMIZATION ENVELOPE (which contains the assigned TEMPERATURE form) is opened by the anesthesiologist; and this does not occur until just after anesthesia is induced. In other words, only after the RANDOMIZATION ENVELOPE is opened, is the patient randomized into the study. If the RANDOMIZATION ENVELOPE is not opened - the patient is enrolled but not randomized.

To confirm that the RANDOMIZATION ENVELOPE was opened, and that the patient was, in fact, randomized into the IHAST2 study, a second telephone call or “confirmation call” must be made. This telephone call is, once again, to the computerized system located at the DMC. Only after you call does the computer know that the patient was randomized. Therefore, the sooner this call can be made after the RANDOMIZATION ENVELOPE is opened, the better. However, the confirmation call must take place within 24 hours after the enrollment call.

In the event that the patient was enrolled but was not randomized into the study (i.e., the RANDOMIZATION ENVELOPE was not opened), a “confirmation call” must still be made. However, in this case, the caller must select the option indicating that the patient was not randomized. Again, the sooner this call can be made, the better, but this call must be made within 24 hours of the “enrollment call”. In addition to this phone call, the following procedures must be carried out:

- 1) Ensure that the SCREENING and ELIGIBILITY forms are complete.
- 2) Complete the header and footer information on pages 1 and 6 of the ANESTHESIOLOGIST Form. On page 1, provide a brief explanation of why the patient was not randomized (*e.g.*, WFNS

worsened to IV, etc.) in the space provided for item #3. If more space is needed for an explanation, check “Yes” for additional comments (the last item on page 6) and enter comments via the web.

3) Within 48 hours of the confirmation call, mail to the DMC the white copies of the SCREENING and ELIGIBILITY forms and pages 1 and 6 of the ANESTHESIOLOGIST Form. Also, return the Study Packet including both of the UNopened RANDOMIZATION ENVELOPES.

4) Place the yellow copies of the SCREENING and ELIGIBILITY Forms and pages 1 and 6 of the ANESTHESIOLOGIST form back into the corresponding Patient CRF Notebook.

5) Neither the Patient ID nor the Study Packet (which contains the RANDOMIZATION ENVELOPES) will ever be used again.

6) You may remove the remaining unused forms from the Patient Notebook. These forms may be used for other patients if needed.

## 7. Temperature-Related Issues

### Study Packets, TEMPERATURE CRFs, and Other Temperature-Related Issues

#### Use Study Packets Sequentially

Thirty sequential sets of Study Packets containing sealed RANDOMIZATION ENVELOPES were sent to each PCC at the beginning of the study. The sequence of the Study Packets matches the sequential ordering of the Patient Identification number (PID) assigned by the telephone enrollment system. Therefore, it is important to use the Study Packets in sequential order so that the correct RANDOMIZATION ENVELOPE is

opened. For example, if the “brown” RANDOMIZATION ENVELOPE was assigned to patient XX-101 by the telephone enrollment system, but the “brown” envelope for patient XX-102 was inadvertently opened, the temperature assignment on the opened TEMPERATURE form may not be correct. Remember that envelope color says nothing about temperature assignments: Hypothermic and Normothermic assignments are distributed randomly between colors. Brown RANDOMIZATION ENVELOPES may contain either a Hypothermia or Normothermia assignment.

Here are a few things to remember about the Study Packets and RANDOMIZATION ENVELOPES to help avoid a potential mis-randomization.

- 1) Make sure the Study Packets are in sequential order and that none are missing.
- 2) Be sure to pull the Study Packet with the PID labeled on the outside that corresponds to the PID assigned by the telephone enrollment system.
- 3) The two RANDOMIZATION ENVELOPES (brown and white) inside the Study Packet must have the same PID as the Study Packet in which they are contained. **If** you are missing a Study Packet, or if the PIDs from the two RANDOMIZATION ENVELOPES don’t match the Study Packet in which they were contained, contact the DMC immediately so we can correct the problem.

What should you do if you open a RANDOMIZATION ENVELOPE for the wrong PID?

First, contact the DMC right away. Depending on the stage of patient care, the DMC will decide whether you will be asked to use the PID assigned by the telephone enrollment system or the PID for the RANDOMIZATION ENVELOPE that was opened. For the PID not used, we will ask that you return both RANDOMIZATION ENVELOPES to

the DMC, and that PID will never be assigned or used again. Once a PID is assigned by the telephone enrollment system, that PID is never used again even if the envelope was never opened.

Please Record Esophageal and Secondary Temperatures on the Anesthesia Record!

Because all individuals at the CCC must remain blinded to the treatment assignment, a knowledgeable physician audits the intraoperative conduct of the study. This is the role of the IHAST2 Physician Protocol Monitor (PPM), David S. Warner, MD, Department of Anesthesia, Duke University Medical Center.

The DMC sends Dr. Warner a copy of the completed TEMPERATURE form, ANESTHESIOLOGIST form, and a copy of your local hospital anesthesia and 0-2 hour postoperative recovery or critical care records for every patient. The OR anesthesia record and the 0-2 hour postoperative recovery/ICU records are the original source document used by the PPM to ensure proper temperature protocol is being followed. The data from these records will be compared to the data found on the ANESTHESIOLOGIST and TEMPERATURE forms and any discrepancies will be noted by the PPM. This anesthesia record must therefore indicate the patient’s intraoperative temperatures. (It’s also a legal record and should be accurate.)

**Yes**, there is potential for unblinding during the handling/copying of these records, or postoperatively. That is why the photocopy of the anesthesia record is to be sealed in the Study Packet before it is returned to the Study Coordinator (see next paragraph). **Yes**, if someone *really* wants to “unblind” themselves, they can go to the anesthesia record and learn the patient’s temperature. So be it. Everyone caring for patients in IHAST2 is “on their honor” not to intentionally “unblind” themselves.

Again, the esophageal and secondary temperatures at definitive clip placement must be recorded on the anesthesia record by the treating

anesthesiologist and these should match the temperatures on the corresponding TEMPERATURE form. After removing all patient identifiers (*e.g.*, patient's name, social security number, etc.) and placing the PID on each page, a copy of the anesthesia record and 0-2 hour postoperative recovery or critical care records are placed in the Study Packet and sealed before returning them to the local study coordinator. Because these records will contain temperature data, the study coordinator should never open the sealed Study Packet (or anyone who must remain blinded to the temperature assignment for a given patient).

What happens to submitted TEMPERATURE forms?

When the Data Management Center (DMC) receives the small white envelope containing the TEMPERATURE form, it is routed to an unblinded individual, Mr. Rick Peters. Mr. Peters will visually check the TEMPERATURE form for completeness of data and, if complete, will send a copy of this form to the PPM (Dr. Warner). If the form is not complete (*e.g.*, the esophageal temperature was left blank), Mr. Peters will contact the PCC study coordinator *via* e-mail (or telephone). The attending local anesthesiologist who completed the form will also be notified that changes are being requested.

Because blinding is an issue for the TEMPERATURE form, the local study coordinator may not make the changes and, therefore, will be asked to follow these steps:

- 1) give the attending local anesthesiologist the envelope that contains the canary-colored copy of the TEMPERATURE form;
- 2) ask the anesthesiologist to make the changes requested to the canary-colored copy, placing his/her initials and the date that the correction(s) were made, next to it;
- 3) instruct the anesthesiologist (or someone for whom unblinding is not an issue) to make a

photocopy of the corrected form and send or FAX the photocopy to Mr. Peters at the DMC;

4) instruct the anesthesiologist to put the corrected canary-colored TEMPERATURE form back in the small white envelope (or a new envelope with the PID written on it), seal it, and return it to the local study coordinator who should place it back into the Patient's Notebook.

In some cases, the DMC computer system will identify other problems with the TEMPERATURE form. In this case, a Data Edit Report (DER) will be produced and sent to the attending anesthesiologist whose certification number is on the form. The anesthesiologist will be responsible for contacting the local study coordinator to obtain the small white envelope containing the canary-colored copy of the TEMPERATURE form. Then steps 2) through 4) in the previous paragraph should be followed.

Contact information for Mr. Peters at the DMC:

Mr. Rick Peters  
Data Management Center  
2220 WL Bldg.  
Dept. of Biostatistics  
University of Iowa  
Iowa City, Iowa 52242

Phone #: 319.335.6872

Fax #: 319.335.6535

Email: richard-peters@uiowa.edu

## 8. INTERCURRENT EVENTS

### Some Help and A Few More Pointers

#### New Pocket-Size Notebook with Intercurrent Events Codes and Definitions

**Although** all Intercurrent Events (IE) codes and definitions are present in the IHAST2 Operations Manual (Chapter IX, Section S, pages IX-85 through IX-105), we know the Manual is not convenient for day-to-day clinical use. Included

with this issue of the *Update* is a new pocket-sized spiral notebook that contains all IHAST2 IE codes and definitions. We think this new notebook will provide a convenient reference that will “travel” well to the operating room, intensive care unit, and the patient’s bedside.

**Some Time-Saving Hints**

When you are preparing an INTERCURRENT EVENTS (IE) form, it will save you time and effort if you will take the following steps.

• **First, before you submit an IE form, quickly review the IHAST2 diagnostic criteria that must be satisfied for each IE.** If we receive an IE form that does not provide sufficient information to confirm that diagnostic criteria are met, we will contact you and ask you to provide the needed information. More likely than not, this will start the process of a PCC Correction Report, which is a time-intensive process. If a given condition does not meet diagnostic criteria, you may not need to complete the IE form at all!

When a given diagnosis (IE) is made by the patient’s doctor(s), but IHAST2 diagnostic criteria do not appear to be satisfied, we suggest you take the following actions. Review the patient’s condition, and review IHAST2 diagnostic criteria, with the doctor(s) who made the diagnosis in question. It is possible the doctor may have other information that will satisfy IHAST2 diagnostic criteria. In this event, you should complete and submit the IE form. If, after review, IHAST2 diagnostic criteria still cannot be satisfied, the local Principal Investigator (PI) or Co-PI should review the matter and decide whether or not to report the IE. After this second review, if the IE is “mild” in severity and does not satisfy IHAST2 diagnostic criteria, your center may elect not to report it at all. (Hence, no IE form!) For IEs that are “moderate” or “severe” in their clinical impact, but do not meet IHAST2 diagnostic criteria, please contact the Clinical Coordinating Center (CCC) before coming to a final decision about whether or not to file an IE form. A short phone call can save you (and us!) a lot of time.

• **Second, please provide sufficient information in the narrative box that will allow us to confirm that diagnostic criteria have been satisfied.** Believe it or not, we actually review every single IE form that is submitted! If there is not sufficient information provided in the narrative box (item #1 of the INTERCURRENT EVENTS form) to permit confirmation that IHAST2 diagnostic criteria have been satisfied, we have no choice but to contact you. As discussed above, this contact from us can only result in more work for you in terms of PCC Correction Reports, *etc.*

**A New IE Code and Diagnosis**

A new IE diagnosis and code has been added—910, “Other Infection.” The Operations Manual will be revised as follows.

Category-9	Code	Event
Other/Unclassified	910	Other Infection

Definition/Criteria: The diagnosis of “Other Infection” may be made whenever the patient has an infectious process with a microbial agent (bacterial, fungal, viral, parasitic, etc.) that is not accurately characterized by any other infection-related IE diagnosis (*i.e.*, the process is NOT any of the following:

- 100-Septic shock;
- 101-Vascular catheter-related infection;
- 102-Bacteremia;
- 103-Non-neurologic wound infection;
- 300-Pneumonia;
- 400-Hepatitis (infectious);
- 600-Craniotomy incision or bone-flap infection;
- 601-Meningitis or ventriculitis;
- 602-Brain abscess, epidural/subdural infection, encephalitis;
- 700-Urinary tract infection).

Examples of “other Infection” include conjunctivitis, sinusitis, tooth abscess, prostatitis. Because of the extremely large number of possible “other infections,” standard diagnostic criteria for all possible conditions in this category cannot be specified in the Operations Manual. Therefore, the only criteria for diagnosis of “other infection”

is a doctor's clinical diagnosis, using whatever criteria he/she considers appropriate. However, the condition must be considered to be on the basis of a specific microbial agent or process, rather than other non-infectious inflammatory state such as rheumatoid arthritis or nonspecific vasculitis. This code has also been added to the pocket-size IE Handbook, and is located on page 24.

### **IE Form Completion and Completion Date**

The IE form is complete only when item #6 (Has primary IE resolved?) is complete. Therefore, the IE form cannot be completed, and the corresponding IE form completion date cannot be recorded, until item #6 is answered either "No" or "Yes." *Practically speaking, what does this mean?*

- **For all IEs with onset prior to discharge**, item #6 must be answered in one of two ways prior to submitting the data set that is required at hospital discharge:

- 1) If the primary IE resolves (symptoms have disappeared or treatment has been completed) prior to discharge, then item #6 can be checked "Yes" on the date of IE resolution, but not earlier. Therefore, the date the IE resolved is the earliest possible form completion date. If you complete the IE form later than the day the IE resolved, record the actual date the form was completed.

- 2) If the primary IE has NOT resolved prior to discharge, then item #6 is checked "No" on the date of discharge. In this case, the date of discharge is the earliest possible form completion date. If you complete the IE form later than the day of discharge, record the actual date the form was completed.

- **For all IEs with their onset after discharge**:

All intercurrent events (IEs) that occur up to the time of the final 3-month outcome assessment are to be reported. After patients are discharged from the hospital, one mechanism by which IEs may be detected is by completion of the CONTACT FOLLOW-UP form at 6-weeks and 3-months after surgery. Items #10-13 of the CONTACT FOLLOW-UP form ask questions which, if

answered "Yes" are likely to be associated with the occurrence of one or more IEs.

The processes and criteria for reporting IEs that occur after discharge are not different from those that occur prior to discharge. Simply check the box on the INTERCURRENT EVENTS form (item #2) that indicates the IE had its onset after discharge. For IEs that have their onset after discharge, it is possible that you may not be able to complete the IE form until the 3-month follow-up evaluation. *Why?* Item #6 of the IE form asks, "for IEs with onset after discharge", whether the IE has resolved by the time of the 3-Month Follow-up? If the post-discharge IE resolves before the 3-Month Follow-up, you can check "Yes" whenever it becomes appropriate, record the form completion date, and the IE form is done. However, if the post-discharge IE does not resolve before the 3-Month Follow-up, you must wait until the final 3-Month Follow-up evaluation to make the final assessment as to whether or not the IE has resolved. Therefore, for some IEs with onset after discharge, it may not be possible to complete the IE form (or record the form completion date) until the final 3-Month assessment has been made.

### **Delayed Ischemic Neurologic Deficit (DIND) [IE Code 620] vs. "Vasospasm"**

A delayed onset of narrowing of the major conducting cerebral arteries ("vasospasm") occurs in 60-70% of SAH patients. Vasospasm can be detected several ways but transcranial Doppler (TCD) and cerebral angiography are the most commonly used methods. Vasospasm may significantly limit cerebral perfusion. In about half of the patients who have vasospasm, reduced cerebral blood flow exacerbates a pre-existing neurologic abnormality or results in new ischemic injury. Collectively, these neurologic abnormalities are called Delayed Ischemic Neurologic Deficits (DIND). In IHAST2, we are following DIND; we are NOT following "vasospasm."

The key distinction is that the diagnosis of DIND requires a new clinical neurological abnormality or substantive worsening of overall neurologic status. For example, if the patient's daily GCS score deteriorates • 2 points, be suspicious of DIND. However, if the patient has no new neurologic abnormality after surgery, the diagnosis of DIND cannot be made, even if the patient has angiographic vasospasm or high TCD velocities. TCD and/or angiographic abnormalities can support the diagnosis of DIND but, in the absence of new neurologic signs or symptoms, they are not sufficient.

*What if the patient has vasospasm (appropriate abnormalities seen on TCD or angiogram) but receives intensive prophylactic therapy to prevent DIND (e.g., hypervolemic, hypertensive, hemodilution, or vasopressors/inotropes to increase perfusion)? Shouldn't that count as DIND?* **Answer:** No. If there are no new neurologic signs or symptoms, DIND does not exist.

*What if the patient has new neurologic symptoms that are consistent with DIND (see the Operations Manual or the new IE pocket notebook) but we don't have TCD or angiography to prove it? Can we make the diagnosis of DIND?* **Answer:** Yes, but... The diagnosis of DIND is primarily based on the time of onset of the deficits (5-10 days after SAH), the nature of the deficits (decreased level of consciousness with or without focal deficits) and the exclusion of other causes of delayed neurologic deterioration (rebleeding, hematoma, hydrocephalus, brain edema, seizures, etc.). Positive TCD or angiographic findings are not required to make the diagnosis. But, the constellation of new signs and symptoms should be consistent with DIND.

*What if the patient has new neurologic symptoms that are consistent with DIND but TCD (or angiogram) indicate that there is no vasospasm? Can we make the diagnosis of DIND?* **Answer:** Probably not. If, using reliable methodology vasospasm is found to be absent, then the cause of

the neurologic deterioration is probably not DIND, but some other condition (see above). If the patient has some form of significant neurologic deterioration that cannot be categorized as DIND or any other neurologic IE (e.g., NOT 601-meningitis; 610-recurrent SAH; 631-seizure; 632-brain swelling; etc.) then IE code 635-Other Significant Neurologic Disorder or Complication should probably be used. When in doubt, discuss with your local PI and/or call the CCC.

**Recurrent Subarachnoid Hemorrhage [IE Code 610] and item #8 in Section H (page 6) of the ANESTHESIOLOGIST form**

Recurrent Subarachnoid Hemorrhage is defined as: EXCEPT for the primary aneurysmal subarachnoid hemorrhage, ANY instance when any subarachnoid hemorrhage occurs for ANY reason, except direct surgical manipulation. *What does this mean?*

If any new subarachnoid hemorrhage occurs before going to surgery, regardless if the bleeding originates from the aneurysm that lead to the patient's presentation (i.e., rebleeding), or from yet another intracranial aneurysm, it should be reported.

If any new subarachnoid hemorrhage occurs after going to surgery, regardless if the bleeding originates from the aneurysm that lead to the patient's presentation, or from yet another intracranial aneurysm, it should be reported.

*What about aneurysmal bleeding that occurs during surgery?* Item #8 of Section H (page 6) of the ANESTHESIOLOGIST form originally asked whether or not the "Patient had a recurrent subarachnoid hemorrhage." **However, this question has been changed**. The new revised ANESTHESIOLOGIST form is dated 040600 (bottom right hand corner) and Item #8 now reads "Patient had a recurrent subarachnoid hemorrhage not due to surgical manipulation." This change was made with the last Operations Manual revisions that were distributed in April (see IHAST2 Operations Manual Chapter IX, page 44,

dated 4/9/00). Thus, item #8 should be checked as occurring by the anesthesiologist only when the aneurysmal rupture was NOT due to surgical manipulation. For example, if the aneurysm rebleeds in the interval between induction of anesthesia and opening dura, then item #8 should be marked as “Occurred in OR”. Likewise, if there is new subarachnoid bleeding in the first 2 hours after surgery (aneurysmal rebleeding or a new aneurysm ruptures), then item #8 should be marked as “Occurred 0-2h after leaving OR”. However, if in the process of surgical dissection and clipping (or other surgical therapy) the aneurysm ruptures, then item #8 should be marked as “Did not occur”. In this latter circumstance the aneurysm rupture will be recorded by the neurosurgeon on the NEUROSURGEON form (page 3). We are not seeking to establish *blame* for aneurysmal bleeding - we are only seeking to establish *cause*. If you still have some of the old ANESTHESIOLOGIST forms, simply change (write in by hand) item #8 to read “...not due to surgical manipulation”.

### 9. Body Mass Index (BMI)

Body Mass Index (BMI) is an index of the patient’s weight relative to their height. Because obese patients do not cool well *via* surface techniques, patients are not eligible for IHAST2 enrollment if their body mass index (BMI) is more than 35.0 kg/m<sup>2</sup>. A patient who has a BMI of 35.1 kg/m<sup>2</sup> is not eligible. For this reason, the patient’s BMI is to be calculated and recorded on the ELIGIBILITY form (Section B, item #2). The patient’s BMI is calculated as follows:

$$\text{BMI} = \frac{\text{Pt Weight (kilograms)}}{\text{Pt Height(meters) x Pt Height(meters)}} = \frac{\text{Weight}}{(\text{Height})^2}$$

A unit conversion table is provided with enrollment materials to aid in this calculation. The left side of the conversion table is for height, converting feet & inches to meters. It also

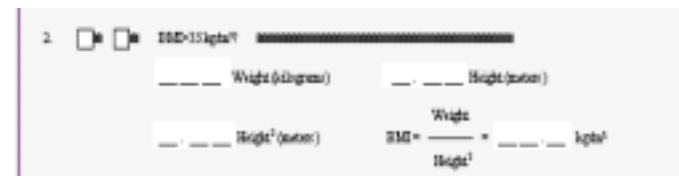
provides the corresponding value for the height multiplied by itself. In other words, height-squared (Height)<sup>2</sup> in (meters)<sup>2</sup>. For example, the table shows a patient height of 5 feet, 4 inches is equivalent to 1.63 meters, and that (1.63 meters)<sup>2</sup> = 2.64 m<sup>2</sup>. The right side of the conversion table is for weight, converting pounds (lbs) to kilograms (kg). For example, the table shows a patient weight of 160 lbs is equivalent to 73 kg. If these height and weight values were to be used to calculate BMI, the resulting BMI would be (73 kg ÷ 2.64 m<sup>2</sup> =) 27.7 kg/m<sup>2</sup>.

We “messed-up” the form initially. The first ELIGIBILITY form (dated 102899 in the bottom right-hand corner of the form) was confusing with regard to what information was being requested in the calculation of BMI. Item #2 looked like this:



It was unclear whether we wanted the patient’s height or (height)<sup>2</sup> to be recorded. What we wanted was the patient’s height (not height<sup>2</sup>) to be recorded in the space provided. Sorry - we apologize that the form was not clear.

Because of this problem we have revised the ELIGIBILITY form. The new ELIGIBILITY form is dated 032400 (in the bottom right hand corner of the form). Item #2 now looks like this:



To avoid confusion, each element required to calculate BMI is recorded separately: Weight (kilograms); Height (meters); and Height<sup>2</sup>. As described above, BMI (kg/m<sup>2</sup>) is Weight ÷ Height<sup>2</sup>.

Finally, we find that patients are often unsure or inaccurate about their height and weight. Patients tend to underestimate their weight, and overestimate their height. Thus, we strongly recommend that you actually measure the patient's height and weight. We routinely use a tape measure to obtain patient height. Many intensive care unit beds have built-in scales. We find this to be a very convenient way to obtain the patient's actual weight at the time of the eligibility determination.

## 10. Making Corrections to the Patient Log

Until now we have not provided directions for making corrections to the Patient Log. If a patient who does not qualify to be screened for the IHAST2 study is mistakenly logged onto the Patient Log, we ask that you make corrections using the following procedure. First draw a single line through the log number and the incorrect entry. In the margin, next to the corrected entry, please write your initials, the date, and a brief explanation of the error. Do not reuse this Patient Log number.

If SCREENING AND ELIGIBILITY forms have been completed for this patient, we suggest that you keep these forms in your Patient Log Binder. If you choose to keep the forms, please draw a diagonal line through the form, date, initial, and provide a brief explanation of the error. Please do not send the forms to the DMC. Retaining these forms in your Patient Log Binder is not required, but we recommend that you do so to help account for the error.

If other errors are made (such as entering an incorrect date under "Screening Form Completion Date") please correct the item by first drawing a line through the incorrect entry. Then write in the correct entry above the incorrect item, initial, and date.

## 11. Wrong Telephone Number!

Please note that the instructions and telephone number printed on the first version of the INTERCURRENT EVENTS (IE) form is **incorrect**. The form states: "All events in these categories must be promptly reported to the CCC at **319-356-0416**". This is **not correct** in two ways. First, the report should be made by faxing the IE form, not by telephoning the CCC. Second, the listed phone number is **NOT** the CCC. The printed number is the phone number for the OR desk at the University of Iowa. It is close to the CCC number, but it is most definitely **NOT** the CCC.

This error was reported in the March 2000 issue of the IHAST2 *Update* (Volume 1, No. 2, page 7). **PLEASE** cross this number out on all your old unused IE forms and write in the correct number 319-384-8072, which is the CCC fax number. All Severe/Indicator IEs or Death events must be faxed to the CCC - you do not need to call the CCC to report these events.

New revised IE forms have been printed - they are dated 042000 (in the bottom right hand corner of the form). If you already have new IE forms, the correct fax number is printed on them.

We are sorry for the inconvenience. If you have any questions, please call the CCC at **319-356-0461** (not 0416!).

## 12. Contact Follow-up

### CONTACT FOLLOW-UP Form Revision (dated 040300)

Item #7 "What is the patient's current work status?" on the CONTACT FOLLOW-UP form has been revised. The skip-out question "Did the patient return to previous occupation and/or same level of performance?" has been changed so that it

is now a separate question (Item #8 on the Updated form of 040300). Previously as a skip-out, this question was to be answered only if the patient was currently (at the time of the follow-up visit) working full- or part-time. The skip-out did NOT, however, apply if the patient was NOT currently working (at the time of the follow-up visit). Since the skip-out did not apply to question #7, option #3 “*Not employed nor working*”, the examiner was unable to describe whether the patient’s employment status had changed prior to the SAH.

To “fix” this, we have changed the skip-out such that it is now Item #8. Item #8 “*Has the patient returned to previous occupation and/or same level of performance?*” will now allow the examiner to indicate a change in work status of patients who are not working at the time of the follow-up visit.

In addition, Items #7 and #8 of the revised CONTACT FOLLOW-UP form may require further clarification. The description “*Employed (or working)*” applies only if the patient is working. It does not apply if the patient is employed but not back to work. In other words, if a patient is employed (at the time of the follow-up visit) but is still taking sick time, please mark option #3 “*Not employed nor working*” for item #7. Item #8 would then be marked “no” since the patient had not yet returned to their previous level of employment. If a patient is not working (at the time of the follow-up visit) and was not working prior to the SAH, please mark option #3 “*Not employed nor working*” for item #7. Item #8 would then be marked “yes” since the patient was not working prior to the SAH event.

The next Operations Manual Update will include revised procedures (chapter IX) that will reflect the change on the CONTACT FOLLOW-UP form.

### 13. Physician Protocol Monitor (PPM)

#### Why, When, and How the Physician Protocol Monitor (PPM) Will Contact You

The job of the PPM is to ensure that intraoperative patient management is conducted according to the assigned protocol, and that major intra- and early post-operative intercurrent events are reported. Photocopies of the local hospital anesthesia record and early (0-2 hour) postoperative recovery or critical care records (e.g. recovery, ICU flowsheets) are considered to be the “source documents.” The Physician Protocol Monitor (PPM) will review these records and compare them with the information provided on the ANESTHESIOLOGIST and TEMPERATURE forms. If there are discrepancies, or if a protocol issue arises, the PPM will contact your center in one of two ways.

#### A. ITEMS WHICH INVOLVE PATIENT TEMPERATURE

Communication regarding patient temperature cannot involve “blinded” personnel. Hence, communication regarding patient temperature issues can occur only among: 1) the PPM; 2) the responsible Local Anesthesiologist; and 3) unblinded Data Management Center (DMC) personnel (Dr. Clarke, Mr. Peters).

The PPM will review the source document (local hospital anesthesia record) and make a judgement as to whether the responsible Local Anesthesiologist managed the patient in a manner consistent with the assigned temperature group. The PPM will also check the TEMPERATURE form to determine whether the temperature recorded is consistent with that on the local hospital anesthesia record.

If a temperature-related discrepancy exists between the source documents and the

ANESTHESIOLOGIST or TEMPERATURE forms, the PPM will contact the Anesthesiologist who was responsible for the patient's care either by telephone or e-mail to resolve the discrepancy. When discussions have concluded, a summary e-mail will be sent to the responsible Anesthesiologist, with a cc: to Dr. Clarke at the DMC. In addition, the PPM will also e-mail the Local P.I. and Study Coordinator notifying them that a temperature-related discrepancy has been identified and that the PPM has communicated with the responsible Anesthesiologist. The nature of the temperature management discrepancy cannot be communicated to the Local P.I. or Study Coordinator. (If either the ANESTHESIOLOGIST or TEMPERATURE forms require modification, Dr. Clarke will forward the e-mail to Mr. Peters at the DMC, who will manage the process of form and database revision).

**B. ITEMS WHICH DO NOT INVOLVE PATIENT TEMPERATURE**

For matters that do not relate to patient temperature, communication among "blinded" IHAST2 personnel (CCC, DMC, Local Study Coordinator, responsible Local Anesthesiologist, *etc.*) is possible with limited restriction. However, if, in the judgement of the PPM, any matter related to these items might reveal patient temperature information, then communication will be restricted as described in section A.

The PPM will review the source documents for: 1) indications that the patient was not eligible for IHAST2 at the time of presentation to the operating room; 2) consistency with IHAST2 anesthesia protocols; and 3) for intercurrent events (IEs). The PPM will focus his review primarily on those IEs which are: 1) "Indicator" IEs (items 1-10 of Section H. of the ANESTHESIOLOGIST form); or 2) IEs that appear to have been severe (items 11-24 of Section H.).

If a discrepancy exists between the source documents and the ANESTHESIOLOGIST form, the PPM will contact the Local Anesthesiologist

who was responsible for the patient's care either by telephone or, preferably, e-mail to resolve the discrepancy. (In some instances, the PPM may elect to first contact the Local Study Coordinator with regard to the discrepancies). When discussions have concluded, a summary e-mail will be sent to the responsible Anesthesiologist with a cc: to 1) the Local Study Coordinator; 2) the Local P.I.; and 3) Ms. Wichman at the DMC. It is anticipated that resolution of discrepancies may require modification of the ANESTHESIOLOGIST form and/or the addition, modification, or deletion of INTERCURRENT EVENTS forms.

**14. Update Newsletters and  
IHAST2 Operations Manual are on the Web!**

The IHAST2 *Update* newsletter and the IHAST2 Operations Manual are fully accessible on the IHAST2 web site. To access the home page for the IHAST2 web site using your favorite web browser, type in the URL:

<http://ctsdmc.public-health.uiowa.edu/ihast2/>

The home page looks like this:

The University of Iowa

**IHAST2**  
INTRAOPERATIVE HYPOTHERMIA  
for  
ANEURYSM SURGERY TRIAL

Today is Wednesday July 19, 2000

- ▶ home
- ▶ background
- ▶ september 1999 conference
- ▶ operations manual
- ▶ comments
- ▶ updates
- ▶ dmc
- ▶ ccc

**Emergency Physician Contact Number**

Welcome to IHAST2!

This is a large multi-center, prospective, randomized, partially blinded clinical trial, designed to determine whether mild intraoperative hypothermia results in improved neurologic outcome in patients with an acute subarachnoid hemorrhage (SAH), undergoing an open craniotomy to clip their aneurysms. To the best of our knowledge, this is the only NIH funded trial to examine the impact of an intraoperative intervention on neurologic outcome following any neurosurgical procedure. It is certainly the largest

The directory is located on the left side where the Operations Manual and the *Update* newsletter are two of the listings. To access either listing, a certification number is required. Below is an example of logging in to access the *Update* newsletter on the web:

**Login for IHAST2 Updates**

Enter your certification number

If you do not yet have a certification number but would like to be able to access the Operations Manual or the *Update* newsletters, you may contact the DMC (ihast2@mail.public-health.uiowa.edu) or CCC (ihast2@uiowa.edu) for a temporary certification number.

Once you have accessed either the *Update newsletters* or the Operations Manual, you will be given the option of looking at it using HTML or PDF formats. The primary advantage of PDF is the ease of printing neatly, formatted pages. The primary advantage of HTML is the linking which allows you to quickly go from the table of contents directly to the chapter or section of your choice, etc. Here is what you will see if you were accessing the *Update* newsletters:

The University of Iowa

**IHAST2**  
INTRAOPERATIVE HYPOTHERMIA  
for  
ANEURYSM SURGERY TRIAL

▶ home  
▶ background  
▶ september 1999 conference  
▶ operations manual  
▶ comments  
▶ updates  
▶ dmc  
▶ ccc

***IHAST2 Update***

**2000**

January, Volume 1, Issue 1 ([HTML](#)) ([PDF](#))

---

March, Volume 1, Issue 2 ([HTML](#)) ([PDF](#))

To view items in PDF format, you will need Acrobat Reader. If you do not already have this software on your computer, we have supplied the web site where you can download it for free. Here is the web site URL:

<http://www.adobe.com/products/acrobat/readstep.html>

Also, the listings on the left side which were viewable on the IHAST2 home page, are still viewable (and accessible) on the *Update* newsletter page. This was designed to make it more convenient to access any of the listings without doing a lot of backtracking. So if you haven't done so already, please visit the IHAST2 web site and let us know what you think.