Pediatric Heart and Lung Transplant Study Group
Minutes, 4/2/93

Welcome by Dr. Addonizio

Robert Morrow, M.D.
RE: Pediatric Heart Transplant Study
Prospective multicenter study
Defining risk factors for poor outcome
Survivor analysis

1. Scientific research
2. Institution results
3. Future studies

David Naftel, M.D. UAB Cardiac Transplant Resesarch Database
RE: Proposed timetable
Revised TCRD forms: April 1993
Data collection to begin: Jan. 1,1993
First report: Nov., 1993
Summary of Death, Rejection, and Infection

Dr. Boucek: questioned what measures would be taken to insure the accuracy of data entry
Dr. Naftel: multiple checks during data entry process are present and forms will be returned to institution if inconsistencies are found
Dr. Zales asked about the % participation and its ability to be representative
Dr. Radley-Smith asked if study to be prospective or retrospective
Drs. Morrow and Addonizio stated study will be prospective, patients entered at start of study

Dr. Morrow: 13 centers were asked for input in order to revise TCRD forms for pediatric patients
Forms were distributed to representatives of institutions present
Dr. Morrow wants all comments on forms to be returned by April 15, 1993.
Lesley Early was introduced, data manager at UAB

Dr. Morrow began discussion of individual forms
Forms 1 & 2 to be filled out at the time of transplant
Forms 3-8 are event driven, to be completed if event occurs

Form 1: Initial data entry
"Major DX" should read "Congenital heart disease"
Maternal blood type for recipients < 6 months
UNOS status 1 for all recipients < 6 months
Serology
Dr. Chinnock: what will be considered positive titer for serologies?
Dr. Morrow: clinical decision at institution to be used for entry
Preoperative hemodynamics: the **most recent data** to be used
Interatrial restriction

Dr. Morrow; how will interatrial restriction be defined? Possibilities include clinical decision, sizing, doppler flow

Dr. Cantor: clinical decision best

Dr. Boucek: liked clinical decision with specific data to be included

Immunizations: count to be entered

Dr. George: what about vaccinations within a month of transplant?

Dr. Morrow: live vaccinations within a month post-transplant would be more appropriate if entered on the transplant form

Fetal listing

Dr. Zales: what about listing as a fetus?

Dr. Chinnock: babies listed as fetus will not have as much information

Suggestion: fill out form when child born?

Dr. Morrow: initial date of listing to be used, ie. date of listing as fetus to be used

Patients placed on waiting list

Dr. Addonizio: it would be helpful to keep information on patients listed, not just patients transplanted

Dr. Morrow: this involves extra work to fill out a form on all patients listed, not just those transplanted

Comments: consensus is to include all patients listed, not just patients transplanted

Dr. Morrow: form 1 will need to be split into two forms, one at time of l listing, another at time of transplant. New outcome forms will need to be generated (e.g. died on list, palliative surgery performed)

Anti-viral, anti-bacterial prophylaxis

Dr. Morrow: doses of prophylaxis are difficult to enter, dates alone would be helpful

Immunosuppression (initial)

Start date: might not be helpful, maintenance dose might be useful

Form 2: Donor Characteristics

Tricuspid regurgitation

Dr. George: would like tricuspid regurgitation to be entered

Recipient ischemic time (in addition to donor ischemic time)

Dr. Boucek: data should include circulatory arrest time and bypass time of recipient for neurologic outcome

Dr. Michler: low flow or circulatory arrest both be helpful for outcome

Dr. Morrow would like specific recommendations re: defining low flow and circulatory arrest. Donor ischemic time should remain on this form, recipient ischemic time should go on transplant form

Forms 3-8

Coronary angiography: defining lesions only to apply if selective coronary angiograms performed

Death form (8)

Primary cause of death to be entered

Detailed information should then be supplied to generate list of secondary diagnoses or contributing factors

Retransplantation form

Dr. Michler: are outcome forms to be filled out on patients without initial forms complete, i.e. retransplantation

Drs. Addonizio, Boucek, Fricker: retransplantation can be entered as a new transplant, even if primary transplant was prior to study start date.

Dr. Morrow: is it worth it to enter the few patients who are in this situation?

Dr. Micher: cause of retransplantation may be both rejection and coronary graft atherosclerosis, this should be possible to enter

Feedback

Dr. R. Boucek: Will yearly feedback of individual institutional data compared to shared data be a possibility? In addition, would the group be willing to develop a software program to enable data entry for this study and other forms (such as UNOS)

Dr. Morrow: Possibility of feedback will be discussed with UAB. Dr. Robert Bourge is developing software for the adult patients, and this may be able to be adapted for pediatric patients.

Agreement and Understanding

Dr. Morrow: although the form is not legal, the understanding should be the shared information will be controlled by the group

Dr. Michael Nalesnik, Associate Professor of Pathology: Post-transplant lymphoproliferative disease

Elfi Pahl, Children's Memorial, Northwestern University, IL (312) 880-4553 Transplant Coronary Artery Disease Survey

15 centers, 754 transplants
520 survivors (69%, median 72%)

2-210 tx/center, median 38
8/15 centers used induction prophylaxis with OKT3 or RATG
>3 centers D/C steroids
most centers do yearly angiograms, some only every other year

56 patients with TCAD from angiography or post-mortem
24% all deaths in the pediatric age group

Age at DX 0.25-16 years, mean 8.1
Earliest time TCAD presented 0.12-5 years post-TX, mean 1.7 years
retransplant 19
6 survivors
noncompliant >7

Speculation about causes of TCAD (by asking centers)

CMV	5
Hyperlipidemia	2
Cellular rejection	10
Vascular rejection	11
Steroid use	3

HLA mismatch 5

Difficulties with survey
Definition of coronary artery disease was unclear
Difficult to grade, some were seen on post-mortem, others by angiography
Could make two groups: any abnormalities vs. >50% stenosis
Should it be presented at AHA? needs info re: method of DX/ cause of death, age at death, time of diagnosis after transplant,
histologic information from autopsy, eg. cellular rejection,
fibrosis, % narrowing of coronaries (mild, moderate, severe)
Dr. Pahl will ask for further info to complete data for the AHA

Dr. Dan Bernstein, Stanford University, Stanford, CA is interested in a multicenter study of diltiazem, interested centers should contact him (he could not attend the meeting)

Dr. Debra Dodd, Vanderbilt University, Nashville, TN (615)322-7447: Vaccination protocol in infants transplanted < 2 months of age, vaccinated < 4 months
Faxes sent asking for participation
7 centers returned responses saying they were interested
Study ongoing at Vanderbilt and Loma Linda, 8 active patients
Hoping to finish study in 6-12 months
Copy of IRB enclosed in packet for participating centers
Once patient identified, Dr. Dodd's nurse coordinator will send packet of forms:
Enrollment form: Patient information (exclusion on top of form)
Vaccination Form: for each vaccine with stickers
Bloods (4 samples):
Baseline - before vaccination series begins
Prior to each vaccination
1 month after vaccinations completed
Assays to be performed
2 Ab to pertussis
2 functional assays for pertussis
2 assays for HiB
1 assay for polio
Assay for diptheria and tetanus
Reasons hepatitis B excluded from study
1. Hep B not recommended because low-risk and unknown efficacy
2. Administration of Hep B may decrease reactivity to other vaccines
3. It would be preferable to not administer Hep B with study vaccines
Laboratory studies are being performed via NIH funded lab at Vanderbilt, controls to be from that lab

Drs. Boucek and Fricker would like to study live virus vaccines: varicella, MMR

Dr. Robert Michler, Columbia University, New York, NY: Retransplantation

Data has been acquired retrospectively from five centers, others are welcome to participate

17 patients, mean age at first transplant 12 years, age at reTX 16 years
Outcome variables: rejection, infection, early mortality (< 30 days), actuarial survival, transplant CAD
Actuarial survival 1 year 65%, 3 year 42%

Plan is to fax info regarding study to PHLTS group members requesting participation and enter patients retrospectively and prospectively

Dr. Susan Winter, Medical Director, Medical Genetics/Metabolism, Valley Children's Hospital, CA (209) 255-3000 x1620 or (209) 225-8660: Carnitine and Cardiomyopathy Study

Study Title: A multi-center, partially randomized, parallel arm, double-blind, placebo controlled investigation of the safety and efficacy of parenterally and orally administered L-carnitine in the treatment of pediatric cardiomyopathy

Packets were distributed with study design, more available by request
Study is funded by Sigma Tau Pharmaceuticals

Lesley Early: PHTS forms.

Comments to be sent by 4/15/93
Forms returned to participating center 5/15/93 to begin patient entry
Attention should be paid to order of information, so that it will be easier to obtain data from patient charts
Quarterly patient update records will be completed for each patient, kept in patient charts and completed forms and quarterly patient update record should be sent to UAB every quarter (not as they are filled out).
Patient will be assigned code number at beginning of study and will keep that number throughout study

Next meeting AHA, Atlanta, GA.