

Emerging MDR tuberculosis across the US/Mexico border: NIAID R21 A1056207

University of Texas, School of Public Health-Brownsville
 80 Fort Brown, University of Texas Brownsville, SPH Building, 2nd floor
 Friday, November 14, 2003

Meeting Minutes

Attendees

Institution:

Name:

UTHSPH-Brownsville

Joseph McCormick
 Sue Fisher-Hoch
 Adriana Pérez
 Armando Salinas
 Belinda Reininger
 Blanca Restrepo
 Christina Villarreal
 Jaymie Estrella
 Diana Gomez

TDH Region 11

Brian Smith
 Cynthia Tafolla

SouthTexas HealthCare System

Aurora Martinez
 Ernestina Lopez
 José Aguilera
 Mary Díaz

TDH- Austin

Dr. Ramamurthy

UTHSCSA

Denise Dunbar

Baylor College of Medicine, Houston

Teresa Quitugua

Cameron County Health Dept.

Edward Graviss

City of Laredo Health Dept.

Lourdes Pena

UT Pan Am

Hector Gonzalez

Jose Flores

Charles Harlow

Zhixiang Chen

Richard Fowler

Steve Crown

México- Cd. Victoria

Francisco López-Leal

Jesús Gonzalo Crespo

México- Matamoros

Francisco Mora

José Luis Robles

Horacio Ramírez

México-Valle Hermoso

José Borrego

México – Nuevo Laredo

Víctor Javier Solalinde

México-Monterrey

Hugo Barrera

Anna Rivas

Adrian Rendon

Carmen Molina

Absent:

UTHSPH- Brownsville

Elma Garza

TDH Region 11
TDH Austin
Cameron County Health Dept.
Hidalgo Health Dept.
Jurisdicción Sanitaria III-Matamoros
Jurisdicción Sanitaria IV-Reynosa

Richard Wing
Ken Jost
Yvette Salinas
Rosa Morales
Ernesto Chanes
Magín Pereda

Registration: 9:30am – 10 am

The meeting began at 10:10 A.M. Dr. Joseph McCormick greeted everyone and explained the purpose of the meeting which is to develop a working consortium to perform research designed to fight tuberculosis on both sides of the Lower Rio Grande River. TB is a shared problem. The main aim of this grant is to set the background and infrastructure as a platform for preliminary studies, to demonstrate we can work together as a team, and make ourselves eligible for further funding.

Then Dr. Brian Smith, Director of the Texas Department of Health Region 11, indicated the public health sector gathers a considerable amount of data, however there is rarely enough time, funds and/or enough depth of knowledge to analyze adequately, and even less time to publish the findings. It is therefore very important for the public health sector to work closely with the academic sector. The public health sector has few funds and rarely has time to think about what is new. The academic sector should come to the public health sector so that academics can do something practical to promote the understanding and implementation of public health.

Dr. Francisco Lopez-Leal from the Secretaria de Salud de Tamaulipas-México described their interest in participating in this research project, but wanted to make sure that it transcends pure research so that it has a measurable impact on their patients. They need to understand all the studies thoroughly and want to be sure the rights of their patients and the Mexican health system will be respected. The political will to work with this project has been clearly expressed by Dr. Hector Lopez, El Secretario General de Salud Del Estado de Tamaulipas. He stressed the importance of communication between the academic and the Mexican officials.

Dr. Hugo Barrera described the technology available at the Universidad Autonoma de Nuevo Leon available to this project. This includes advanced molecular biology techniques that could be made available for ongoing TB projects for the consortium.

Dr. Adrian Rendon from the same institution showed pictures of the recently funded center – Centro de Investigacion, Prevencion, y Tratamiento de Infecciones Respiratorias (CIPTIR), geared to study respiratory infections. He received a \$500,000 dollar grant from Club Rotarios. They also have access to modern molecular biology technology and clinical labs so they can do a whole range of activities for this project if necessary.

Dr. Gonzalo Crespo, TB program director for Tamaulipas, presented the statistics for the state of TB in Tamaulipas. They have the 3rd best program in the country and have efficiently implemented the TAES (DOTS) program. One of their greatest challenges is the premature termination of treatment by drug addicts particularly in Nuevo Laredo and Reynosa. Despite the improvements in their state they acknowledge there is much to do and expressed their enthusiasm for working on this project.

We then proceeded to the composition of the consortium. Each consortium member introduced themselves and their institution briefly.

Consortium structure:

Dr. Blanca I. Restrepo presented an Excel spreadsheet with a draft structure for the group to develop. The overall director is Dr. McCormick who is the principal investigator of the grant and the project coordinator is Dr. Restrepo.

Aim 1: Texas side leader was agreed to be Dr. Brian Smith. The Mexican leader will be Dr. Francisco Lopez Leal.

We then looked at to each region and chose a leader for Aims 1 and 2 of the project. During the course of the day this chart was further developed, and the final version is attached to this memorandum.

Some members of the consortium expressed concern about involvement without fully understanding what the studies were all about. These issues were discussed at this point and throughout the meeting, and most participants seemed satisfied with their understanding and participation by the end of the day.

Dr. McCormick briefly outlined the budget. He explained that this is a pilot grant with limited funds but sufficient to allow the consortium to meet annually, subcommittees to meet as needed, and to gather some preliminary data. There are funds for some training of Mexican colleagues to standardize techniques, and in the process generate data and perform some preliminary analyses. The funds will also allow creation of the infrastructure to gather future data. This will be the basis for proposing additional studies where more funds can be provided.

The project timeline was postponed till later in the day to give the participants more time to understand the projects and their contributions. Dr. Restrepo therefore proceeded to review the specific aims of the grants and their implications for the consortium. She clarified the inclusion criteria for consortium members, the study sites, and the benefits to everyone of working in this consortium. The outcome should be that we can work together to understand how TB is transmitted in our two countries, and between them over our common border. The last two aims of the project were discussed: i) understanding the dynamics of transmission between the US and Mexico and, ii) understanding the extent of recent transmission vs. reactivation of tuberculosis in the study area.

Dr. Adriana Perez presented in more detail Aim 2- Strategies to track TB transmission across the Texas- Mexico border, presenting examples of how data will be geocoded and then gathered from various sources, merged and analyzed. The analysis should demonstrate how to find clusters in terms of geography and strain genotypes.

Dr. Susan Fisher-Hoch briefly outlined the principles of the training plan for Mexican sites which has several objectives;

- 1) Collection and characterization of strains
- 2) Training of Mexican colleagues in isolation and drug susceptibility testing techniques at one level, and genotyping at the other.
- 3) Standardization of techniques between the sites.

At the more sophisticated level of training genotyping of *M. tuberculosis* strains will be performed in Dr. Ed Graviss' Lab in Houston. The plan is for Mexican colleagues to collect their own strains and be trained to perform the assays in Houston. The goal is to allow the Mexican centers to establish their own genotyping using techniques comparable to those in Houston so that future data will be consistent between the sites.

Sustainability and quality control are major objectives. The suggestion was made that Dr. Teresa Quitugua will oversee this part of the project, visiting laboratories and providing ongoing advice and further training as needed.

Aim 4 was presented by Dr. Belinda Reininger - The use of social networking to improve tracking of MDR TB transmission. This part of the project is also a pilot study and the aim is to improve to tracking of contact investigations. It goes beyond the customary contact investigations. In addition to asking the patient for the people they know and are in contact with, we now obtain more detailed information about the places visited and frequency of visiting and time spent in various locations. The hypothesis is that TB is not necessarily obtained from someone you know. Frequently contacts may be casual, and the patient may not know the name of the person. The pilot study site will be Hidalgo County/Reynosa. It is planned to conduct 100 interviews, theoretically 50 from Reynosa, 50 from McAllen. (in a later discussion it was proposed to actually analyze the total number of cases: 70 cases from McAllen and 200 from Reynosa will need to be interviewed).

After a working lunch the group broke up into two teams charged with working out how we would collect and analyze information. One group discussed databases and geocoding, the other concentrated on strain collection and characterization.

Addendum:

Dr. Graviss: summary of strain collection and characterization.

Strain collection breakout group: Most *M. tuberculosis* (MTB) isolates from the key surveillance areas have already been acquired through several methods, including: the Binational program, (Reynosa/McAllen, and Brownsville/Matamoros), the following information on strain collection and genotyping was gathered:

- **Laredo/Nuevo Laredo** isolates go to TDH in Austin, but it is not possible at this time to differentiate isolate is from Laredo or Nuevo Laredo in the TDH laboratory.
- **Monterrey** has most of its isolates frozen. Monterrey normally cultures only smear positive patients. Thus isolates are only from the most progressive pulmonary tuberculosis patients.
- Houston has characterized most of Peter Barnes (**Brownsville/Matamoros**) isolates from 2001 to date--a large majority of which are from Matamoros.
- San Antonio has characterized isolates from **Hidalgo and Cameron** counties for the time period of 1998-2002.

For the pilot social network subproject, we need to obtain isolates from all Reynosa and McAllen patients. The South Texas Laboratory has identified 200 TB cases from Reynosa and 70 TB cases from McAllen in 2002, so we assume there will be around 300 isolates to obtain during the study period, and the suggested timetable for this portion of the project is from 1/1/2004-

12/31/2004. Because this is nearly 3 times the number of interviews originally discussed in the grant, a re-evaluation of the monies available for the social network field work will need to be conducted. To offset the cost of the additional isolates- needing genotyping and the additional questionnaires Dr. Graviss suggested that it would be acceptable to perform only MIRU-VNTR and spoligotyping characterization and omit IS6110 characterization since this is very expensive and does not add significantly to the discrimination of strains. The CDC as of 1/2004 will be utilizing MIRU-VNTR and spoligotyping characterization as their primary fingerprinting methods. Some of the previous RFLP data obtained by Houston and San Antonio on Valley/Mexico isolates could possibly be merged with BioNumerics programming by San Antonio, but the timing of this action will need to wait since this software is complicated. Houston can accommodate 2 trainees at a time and training cannot occur until after February 1, 2003. We need to review our plans and budgets before proposing the final arrangements.

Dr. Perez: summary of databases and geocoding:

TEAM 1: TRACKING TB TRANSMISSION: Databases and Geocoding

The team discussed the data presented in two excel files sent to everyone before the meeting occurred. The names of the files are MDR.XLS and VARIABLES02.XLS. Variables02.XLS provides the proposed codes for labeling the data from each one of the USA and Mexican sites.

Mexican databases:

- The Mexican members have information for the following cities on the border: Matamoros, Valle Hermoso, Rio Bravo, Reynosa, Diaz-Ordaz, Camargo, Miguel Aleman, Mier, Guerrero and Nuevo Laredo.
- Their databases have information on 66 variables from years 1998-2003 and 44 variables from years 1996 and 1997. The information from years 1998-2003 is available as a computer generated database. The information for 1996 and 1997 is only available in paper and needs to be created on a computer database.
- They have some information missing for some of the variables requested. For example, some of the strains are not known where they were isolated and it is not known if they are even available.
- The Mexican members described the names of the forms used in Mexico for tracking and identifying the TB cases. They are: 1) Cuadernillo de control y seguimiento, 2) Tarjeta de Control y seguimiento (only to track treatment), 3) SUVE2=Sistema Unificado de Información para la Vigilancia Epidemiológica, 4) Expediente – patient's clinical chart. The information obtained in paper from SUVE2 is entered in the TB-EPI program in EPI info 6. The EPI info database and the installation program will be provided by Dr. Gonzalo Crespo to Dr. Perez as well as a copy of the form 1-4.

US databases:

- Dr. Smith mentioned they need to obtain the IRB approval from Austin to get access to the TDH data sets. He will be the sponsor from PHR11 to obtain the necessary IRB approval for Dr. Perez to obtain access to the dataset from TDH in Austin along with the address and names of the patients.
 - Dr. Smith confirmed the data obtained from forms TB400 A and B and Form 340 are not completely entered into a database at TDH Austin and he is not sure which variables are entered.
- Schedule and timing to obtain databases: Drs. Crespo and Smith mentioned that that timing will only be feasible after IRB and protocols are available in Spanish and English for each party.

We gathered at 3:45 p.m. and each team presented their main findings.

We concluded the meeting at 4 p.m.