Cover Photo: The map summarizes the results of the phylogeographic and dating analyses for *Mycobacterium tuberculosis* Complex (Source: *Nature Genetics*; doi: 10.1038/ng.2744)

Acknowledgement

This summary was compiled from individual and team reports by Tewodros Tariku with editorial support from Rawleigh Howe and Abraham Aseffa. AHRI research staff, team leaders and students are acknowledged for their input.
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Scientific Advisory Board

AHRI acknowledges the invaluable contribution of the AHRI Scientific Advisory Board members to the continued development of research at the Institute. The Annual Scientific Advisory Board meeting in 2012 took place at AHRI on 26-30 November 2013.
Obituary

HAIMANOT G/EGZIABHER (BSc, MSc) (1959 - 2013): TO A VERY SPECIAL PERSON

From AHRI Staff

Ms. Haimanot G/eqziabher (popularly known as Haimi) died unexpectedly of a subdural haematoma and complications of diabetes and hypertension on July 23, 2013 after she was admitted to Black Lion hospital. Her funeral was held at St. Michael Church (Yeka, Addis Ababa) on 24th of July 2013 at 3:00 pm.

Haimi was born in 1959 in Addis Ababa and studied her elementary and high school education at Lyce Gebremariam. She then joined University of Surrey Guildford in England and did her BSc in Microbiology. Thereafter, she moved then to Belgium and received a rich experience in tropical infectious diseases for 4 years. Upon her return to Ethiopia, she was imprisoned by the former Derg regime for her perceived political views.

In 2010-2011, she accomplished her MSc in Clinical Trials at the KCMC, Tanzania, and her thesis described the etiology of pediatric scepticemia at Black Lion Hospital in Addis Ababa.

In 1990, she joined AHRI as a research assistant. Haimonot was instrumental in the development of the first TB lab at AHRI in 1993, the first of its kind in Ethiopia. Instrumental in contributing expertise and training of students in virtually all of the studies in TB at AHRI since 1993, she has in addition been responsible for the training, either directly or indirectly, of a large portion of the lab personnel in Ethiopia in TB culture and diagnosis. More recently, she has helped to pioneer AHRI’s expansion into applied bacteriology. For the last 23 years, she served AHRI and ALERT and Ethiopia in her capacity as Research Assistant, Senior Researcher and finally as Chief Health Science Professional; a role that has improved the lives of many people. "I love AHRI", she said so many times, good times or bad; as such, her dedication will always represent one of the cornerstones of this institution.

The AHRI staff remembers Haimanot always for her hard work, love and honesty. May her soul rest in peace!
## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>ALERT</td>
<td>All Africa Leprosy, Tuberculosis and Rehabilitation Training (ALERT) Center</td>
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<tr>
<td>BCG</td>
<td>Bacillus Calmette-Guerin</td>
</tr>
<tr>
<td>BE</td>
<td>Bio-equivalence</td>
</tr>
<tr>
<td>BTB</td>
<td>Bovine tuberculosis</td>
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<tr>
<td>CL</td>
<td>Cutaneous Leishmaniasis</td>
</tr>
<tr>
<td>EDCTP</td>
<td>European and Developing Countries Clinical Trials Partnership</td>
</tr>
<tr>
<td>EHNRI</td>
<td>Ethiopian Health and Nutrition Research Institute</td>
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<tr>
<td>ENL</td>
<td>Erythema nodosum leprosum</td>
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<tr>
<td>EPTB</td>
<td>Extra Pulmonary TB</td>
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<tr>
<td>FMoH</td>
<td>Federal Ministry of Health</td>
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<tr>
<td>FNAC</td>
<td>Fine Needle Aspirate Cytology</td>
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<tr>
<td>GCLP</td>
<td>Good Clinical Laboratory Practice</td>
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<tr>
<td>GCP</td>
<td>Good Clinical Practice</td>
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<tr>
<td>INH</td>
<td>Isoniazid</td>
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<td>IVI</td>
<td>International Vaccine Institute</td>
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<td>LTBI</td>
<td>Latent TB infection</td>
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<tr>
<td>M. tuberculosis</td>
<td><em>Mycobacterium tuberculosis</em></td>
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<tr>
<td>MDR-TB</td>
<td>Multidrug-Resistant TB</td>
</tr>
<tr>
<td>MPIIB</td>
<td>Max Planck Institute for Infection Biology</td>
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<tr>
<td>SATVI</td>
<td>South African Tuberculosis Vaccine Initiative</td>
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<td>TB</td>
<td>Tuberculosis</td>
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<tr>
<td>TF</td>
<td>Typhoid Fever</td>
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<tr>
<td>TSAP</td>
<td>Typhoid Fever Surveillance in Africa Program</td>
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<tr>
<td>TST</td>
<td>Tuberculin Skin Test</td>
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<td>WHO</td>
<td>World Health Organization</td>
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Executive Summary

The year 2013 stands out as a year of review and planning in AHRI. It is marked by implementation of the Balanced Score Card (BSC) system and further revision of the AHRI Strategic Plan. AHRI staff spent a significant proportion of the year training on, discussing, formulating and testing a revised workflow process aligned with the Health Development Army policy of the Government. Although work is still going on to optimize BSC with management structure and harmonize processes, the AHRI experience has so far been positive.

The drive for change has been energized by the promise of H.E. the Minister of Health, Dr Kesetebirhan Admasu, to upgrade AHRI with infrastructure and mandate. Practical steps have been taken since. A senior team of MoH architects was greatly inspired by a visit to the Karolinska Institute where "building for the future" is going at full speed in earnest. AHRI has been instructed to commission an assessment of the national health research landscape and its optimal placement to best serve the goals of the sector. It is hoped that these developments will lead to practical changes in 2014-2015 and mark a new era for AHRI.

The research output in 2013 is evidenced by 36 publications, the largest number in a year so far! The proportion of AHRI first authors is 75%. Most of the journals are in the medium impact factor range while some are of low impact. The proportion of articles in local and regional journals has doubled from last year reaching 20%. Strain data set collected by AHRI in Ethiopia was part of the global sample pool used to confirm the out-of-Africa migration of TB with humans which placed the unique Ethiopian Lineage 7 at having diverged from the ancient lineages about 64 k years ago. A number of articles have provided important evidence for practical use in disease control. One example is the woreda level national risk map of visceral leishmaniasis which for the first time provides information on where VL is endemic or is likely to be present in the country.

The clinical trial work at AHRI maintained a good balance between planning and implementation. The data analysis of three clinical trials were completed in 2013: the 4 FDC, the phase I TB vaccine trial (ThyB 03) and phase IV cholera vaccine bridging trial. Dissemination of results will be carried out in 2014. Another clinical trial, evaluation of an ointment against Ethiopian cutaneous leishmaniasis completed enrolment while the STREAM trial assessing an improved regimen for MDR TB is progressing well. The plans for an outer membrane based meningitis vaccine trial are underway for possible launch at the end of 2014.

Nine postgraduate students (4 PhD, 5 MSc) completed their studies in 2013 and 28 others (11 MSc and 17 PhD) are at various stages of thesis work supported by the Institute. The selection committee is reviewing the applications of the next series of postgraduate students at AHRI.

AHRI’s support for postgraduate training was boosted by the success of two collaborative training grants, a grant from NIH to Emory University in collaboration with AHRI, Addis Ababa University (AAU) and the Ethiopian Health and Nutrition Research Institute (EHNRI) and another grant to AHRI
in collaboration with AAU and Swedish Universities. Both grants will provide funding for postgraduate student support with a focus on high quality training of competitively selected future research leaders in biomedical sciences. A third grant to Sussex University in collaboration with institutions in Cameroun and Sudan will target postgraduate training in genetics and bioinformatics.

Five large projects funded by the European and Developing Countries Clinical Trials Partnership (EDCTP) will end this year. This will present challenges for AHRI to transit research staff to new tasks. Although the number of collaborative applications submitted for new grants was relatively higher than in previous years (29), the proportion of success was lower: with 9 rejected, 6 granted and 14 still pending. AHRI staff are working on concepts for grant applications for the coming EDCTP 2 and Horizon 2020 calls.

Core funding was provided to AHRI by Sida in 2013 and assistance is expected to continue. The request for resumption of NORAD support is still being processed in Oslo. Ernst and Young was commissioned by NORAD to undertake a whole system review of AHRI as part of the process. The outcome is expected soon. Infrastructure support has been received from TBCARE/USAID for the expansion of the TB lab at AHRI. The contributions of EDCTP to AHRI's capacity over the last several years has been tremendous and further use of the emerging opportunities in EDCTP-2 would be vital.

Collaboration with ALERT hospital and Training Unit was significant in 2013. In addition to the close interaction through the BSC process, ALERT staff have benefited from postgraduate training support at AHRI. The clinical laboratory was assisted by AHRI in its bid for accreditation. The clinical facility at AHRI for the East African Regional Bioequivalence Center was established in an ALERT building renovated for the purpose. ALERT senior clinicians are increasingly involved in major roles of collaborative research (TB/HIV research, clinical trials). The success of AHRI in 2013 would not have been possible without the administrative support of ALERT.

AHRI is in the process of building its own Finance and Procurement offices directly accountable to the Scientific Director. It is hoped that the challenges with delayed purchase and reporting will be minimized as a result. In addition, the ALERT Board of Management will be meeting regularly and will monitor the efficiency of the work process and good governance at AHRI.

The guidance of the Scientific Advisory Board of AHRI through the sometimes very difficult periods at the Institute has kept the motivation high. Its regular consultation with the Ministry of Health was pivotal in aligning AHRI with the national system. This has continued through 2013.

Overall, AHRI remained vibrant in 2013 and is further posed to take a leap into a new era in the next years thanks to the bold initiatives taken by the Ethiopian Government and the generous support of the partners, Sida and NORAD. AHRI is particularly grateful to the Ministry of Health and the very strong commitment, constructive engagement and generous support of Sida in 2013. The next year will mark an exciting period of transition for the Institute.
Highlights 2012/2013

New *Mycobacterium tuberculosis* lineage is found in Ethiopia

Strains causing tuberculosis (TB) are genetically diverse. This affects transmission, disease severity, response to vaccination and treatment efficacy. For example, modern lineage "Beijing strains" are known to be more frequently drug resistant. Ancient strains tend to prefer latency than rapid progression to disease, a characteristic of adaptation to human population density.

AHRI researchers, in collaboration with European scientists, have identified a new lineage of *Mycobacterium tuberculosis* (*M. tuberculosis*) restricted to Ethiopia (or the Horn of Africa). This is now known as Lineage 7 and appears to have emerged about 60-70,000 years ago around the period of human migration out of Africa (see cover photo).

The identification and reporting of Lineage 7 has enabled researchers to confirm that TB originated in East Africa and migrated with early humans to the different corners of the world. There is close geographical association of mycobacterial lineages with human population groups.

The close co-evolution of humans and mycobacteria means that the study of immune responses to TB should consider genetic diversity of both humans and strains. This includes vaccine development efforts. The findings indicate that Ethiopia is an exceptionally well suited country for the investigation of TB immune response in humans.

References:

- Nat Genet. 2013 Oct;45(10):1176-82. doi: 10.1038/ng.2744

News coverage includes

- www.abc.net.au/science/articles/2013/09/02/3839130.htm
- www.sciencedaily.com/releases/2013/09/130901154024.htm

Inauguration of Bioequivalence Center

A regional bioequivalence center was inaugurated at ALERT center on September 22, 2013 in the presence of representatives of the Ministry of Health (MoH), Ministry of Industry and other invited guests. The center was established to conduct bioequivalence tests at reasonable cost and support registration of generic drugs by regulatory authorities in the eastern African region. The Center is housed in a building donated by ALERT for the purpose and renovated with AHRI core funds.
STREAM trial Investigators Meeting

On June 24-25, principal investigators from STREAM sites in Ethiopia, South Africa and Vietnam as well as experts from the International Union Against Tuberculosis, the Medical Research Council of the United Kingdom’s Clinical Trials Unit (MRC-CTU), Institute for Tropical Medicine in Belgium, the Liverpool School of Tropical Medicine, and the U.S. Agency for International Development (USAID) met at AHRI to discuss challenges and experiences in implementing the STREAM trial so far. Participants observed that the trial has made considerable progress since its launch in 2012 and has enrolled more than 100 patients to date. AHRI’s clinical trial team, the host of this first Investigators Meeting, has been involved with the STREAM trial since the early stages of its development and recruiting patients since early 2013.

Award

Dr Abraham Aseffa was one of the awardees this year at the 15th Annual Review Meeting of the health sector held in Mekelle on 19-23 October 2013. The award was the first to honor research contributions in the Forum and consisted of a glass plate, a medal and certificate.

Three young Ethiopian researchers awarded the 12th AHRI Tore Godal prize

Three young Ethiopian researchers (Tewodros Tariku, Agerie Tadele and Girmay Desalegn) were awarded the 12th AHRI Tore Godal prize on November 30, 2012 in the presence of his Excellency, the Minister of Health, Dr Kesetebirhan Admasu. The researchers were awarded for their work on host immune response to tuberculosis and improving TB diagnostic methods. Each of the awardees received a certificate, medal and a cash prize of 10,000 ETB.

The AHRI Tore Godal prize is given yearly to deserving young candidates who have carried out outstanding research in the biomedical sciences. The award is named after a Norwegian scientist, Dr Tore Godal, the second AHRI director in the early 1970s.

National Conference on Hepatitis

A national conference on hepatitis was co-organized with Prof Bjorn Myrvang of the University of Oslo and Dr Nega Berhe of the AAU Aklilu Lemma Institute of Pathobiology on 23-25 September 2013 at Ghion Hotel. The conference highlighted the need to boost hepatitis research in Ethiopia. A coordinating team was established to stimulate collaboration on hepatitis research between Ethiopian and Scandinavian clinicians.
Research Team Reports
Tuberculosis Team

Tuberculosis (TB) is a major public health problem in the developing countries. Nearly one-third of the world’s population is infected with the causative microorganism, *M. tuberculosis*. TB control in Ethiopia dates back to more than half a century. According to World Health Organization (WHO), Ethiopia stands eighth globally and third in Africa among the 22 high TB burden countries. The incidence of TB in Ethiopia is estimated at 155 and 356 per 100,000 individuals for new smear positive pulmonary and all forms of TB, respectively.

Research is an essential component of TB control program. Enabling and promoting research is among the six key elements of the global stop TB strategy; research is needed for the development of new drugs, diagnostics and vaccines as well as for improving program performance. Accordingly, the AHRI TB team is conducting research aiming to understand clinical, epidemiological, behavioral, immunological, and molecular aspects of host-pathogen interactions.

Team Members

- Dr. Markos Abebe, TB Team Head and Post-doctoral Scientist
- Dr. Adane Mihret, Post-doctoral Scientist
- Dr Liya Wassie, Post-doctoral Scientist
- Dr Abebe Habte, Post-doctoral Scientist
- Dr Ketema Tafesse, Researcher
- Tewodros Tariku, Research Assistant
- Shiferaw Bekele, Lab technologist and TB lab Head
- Bamlak Tesemma, Research Nurse
- Nahome Getachew, Lab technician
- Azeb Tarekegn, Lab technician
- Alemayehu Kifle, Lab technician
- Desalegn Addise, Lab technologist
- Marechign Yimer, Lab technician
- Aboma Zewdu, Animal Health Assistant
- Martha Zewdie, PhD Student
- Semegn Tesfaye, Research Nurse
- Elena Hailu, Assistant Researcher
- Fikirte Melaku, Lab technologist
Establishment of a natural transmission model in cattle to validate the BCG challenge model and to enable assessment of TB vaccine to prevent TB transmission

- PI: Gobena Ameni
- Co-investigators: Ketema Tafess, Aboma Zewude, Melaku Tilahun, Tsegaye Hailu, Abraham Aseffa, Stefan Berg, Glyn Hewinson, Martin Vordermeier

Bovine tuberculosis (BTB) is a zoonotic disease transmitted to humans through consumption of contaminated animal products and inhalation of cough droplets from cattle infected with *Mycobacterium bovis*. The disease is endemic to Ethiopia but occurs in high frequency in commercial dairy farms. Despite the wide use of test and slaughter control policy in western countries, Ethiopia cannot adopt this approach for economic reasons. Instead, vaccination could be an appropriate and a better control option. Presently, *Mycobacterium bovis* bacillus Calmette-Guerin (BCG) is the only vaccine that is being used for the control of TB. The potential application of this vaccine for the control of BTB has been evaluated in different regions of the world and is shown to confer various levels of protection. In this study, a natural transmission challenge model will be used to evaluate the efficacy of BCG against BTB. Young calves will be administered BCG or placebo, and introduced into a herd with a very high natural TB prevalence. Protection from subsequent progression to disease will be assessed by tuberculin skin testing, *in vitro* TB antigen IFN-γ production and post-mortem histological and pathological evaluation of multiple tissues.

**Funding Source:** DFID and Gates foundation  
**Collaborating Institution(s):** Animal Health Veterinary Laboratory Agency (AHVLA), UK  
**Contract Period:** January 2012- December 2014  
**Current status:** On-going

**AETBC: The evaluation of *M. tuberculosis* specific host cytokine signatures in whole blood culture supernatants as diagnostic biomarkers for active TB infection**

- Co-investigators: Adane Mihret, Lawrence Yamuah, Abraham Aseffa, Rawleigh Howe  
- Project Members: Yonas Bekele, Tigist Shumet, Sefina Juhare, Miliket Aytenew, Semege Berhanu, Bamlak Tessema, Yilikal Aseffa, Etsegenet Assefa, Senait Mabreja

The AETBC consortium project had four overall goals. The first was to evaluate the performance of a novel cytokine biomarker assay in the accurate diagnosis of TB among a cohort of subjects presenting in outpatient primary care clinics with symptoms consistent with TB. This biomarker assay detects IL-1α, MIP-1β and EGF in the supernatants of whole blood supernatants cultured overnight with TB antigens. The second objective was to screen for new candidate biomarker signatures from the same cohort utilizing a number of different sample preparations.
and assay approaches. This involved the collection, in addition to sputum for standard microbiological analysis and whole blood for the first objective, of plasma, serum, urine, saliva and whole blood for additional molecular analysis and in vitro responses to a panel of newly described M. tuberculosis antigens. Assays have primarily focused on detection of IFN-γ and multiple other cytokines, but this sample material can be utilized for many of the molecular approaches defined for the related GC6 project. The third objective was to develop a field friendly approach using lateral flow devices for cytokine detection, and the fourth to promote capacity development through site infrastructure upgrades, training workshops and a number of African student fellowships for M.Sc., PhD and postdoctoral candidates.

**Funding Source:** EDCTP

**Collaborating Institution(s):** The AETBC (African European TB Consortium) is composed of LUMC (Netherlands), LSHTM (UK), MPIIB (Germany), MAK (Uganda), Stellenbosh University, (South Africa), KPS (Malawi), EHNRI (Addis Ababa), MRC Gambia, UNAM (Namibia).

**Contract Period:** June 2010-December 2013

**Current status:** On-going; Recruitment and follow up completed

**GC6-74:** “Biomarkers of Protective Immunity against TB in the Context of HIV/AIDS in Africa”, and **GC62013:** “Systems biology to identify signatures of risk of TB disease in Gates Global Challenge 6-74 cohorts”

- **Co-investigators:** Adane Mihret, Lawrence Yamuah, Abraham Aseffa, Rawleigh Howe
- **Project Members:** Yonas Bekele, Rahel Iwnetu, Tigist Abeje, Miliket Aytenew, Semegne Berhanu, Asfaw H/Selassie, Bamlak Tessema, Yilikal Aseffa, Etsegenet Assefa

The GC6-74 project has the goal to discover biomarker molecules associated with TB disease or risk of developing disease. Although a number of specific projects target different cohorts of individuals, the major thrust has been to identify biomarkers which predict progression to TB among those who have been recently exposed to a confirmed TB case. This involved the recruitment of several thousand subjects at multiple institutional sites, and close follow-up over two years, with multiple sample collection and clinical evaluations. From these sites approximately 70 subjects progressed to disease and samples from these and a set of matched controls have been identified and comprehensive molecular analysis will be performed for biomarker signatures. Biomarker or biomarker combinations predicting disease progression will be used to screen and enrich for candidates in future phase II and phase III vaccine trials which will greatly simplify and reduce operating costs.

**Funding Source:** BMGF

**Collaborating Institution(s):** LUMC (Netherlands), LSHTM (UK), MPIIB (Germany), CWU (US), Stanford (US), University of Utrecht (Netherlands), MAK (Uganda), Stellenbosh University, (South Africa), KPS (Malawi), EHNRI (Addis Ababa), SATVI (S. Africa), MRC, Gambia.

**Contract Period:** June, 2005 to December, 2012

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**Current status:** GC6-74 project is completed, the follow-up project GC62013 has been ongoing for nearly a year. Samples from participating institutions have been shipped to South African Tuberculosis Vaccine Initiative (SATVI), South Africa and have been subject to quality control analysis. Future plans include RNA sequencing (Seattle Biomed) and metabolomic analysis (MPIIB) which will begin shortly.

**Characterization of innate and memory phenotypes to TB and hormone modulations in apparently healthy children and adolescents across age:**

Collaboration and integration of Tuberculosis Vaccine Trials in Europe and Africa (TBTEA)

- **PI:** Liya Wassie
- **Co-investigators:** Rawleigh Howe, Soren Hoff, Abraham Aseffa, Markos Abebe
- **Project Members:** Nahom Getachew, Azeb Tarekgne, Semegne Tesfaye, Mesert Gebre

The underlying basis of the current study is our earlier observation conducted on apparently healthy school-age children and adolescents, which showed a significant disparity in the age-specific incidence of TB infection as assessed by the tuberculin skin test (TST) and QuantiFERON (QFT) TB Gold assay (Liya Wassie et al., Manuscript In preparation). Whereas significantly higher fraction of older adolescents reacted in the QFT assay, there was no appreciable difference across age in TST reactivity. This discrepancy raises the possibility that the age related effects reflect changes in the underlying immune system such as that regulated by sex/puberty hormones rather than simply differences in exposure to TB. Apart from standard TB specific quantiferon assays, flow cytometric analysis defining multiple lymphocyte and antigen presenting cell subsets, Th1 and Th2 signature cytokines among mitogen reactive memory T cells, Toll like receptors (TLR) by RT-PCR and TLR induced monokine responses will be among the many immune assays employed. These responses in turn will be correlated with plasma sex and mineralocorticoid hormone levels as well as clinical signs pre and post puberty.

**Funding Source:** EDCTP
**Contract Period:** January 2012-December 2013
**Current status:** On-going

**Evolution of Immune Response during TB treatment (EVO-TB)**

- **PI:** Markos Abebe
- **Co-investigators:** Abraham Aseffa, Liya Wassie, Martha Zewdie, Rawleigh Howe, Adane Mihret, Lawrence Yamuah

Comparing immune responses of TB patients with defined, sputum positive *M. tuberculosis*, versus those from uninfected or latently-infected controls will serve as a marker for ineffective immunity. In the study, patients are followed through the course of their TB treatment and their IFN-γ, TNF and IL2 cytokine response, as well as the memory cell subsets, will be analyzed by flow cytometry. Correlation between immune response, clinical status and conversion of sputum positivity will also be done. The difference between the two states (and between those states and
those of the healthy community controls) would tell us a great deal about control of
*M. tuberculosis* infection and will help to identify surrogate markers for vaccine
evaluation. Thus far, fifty-six blood samples are collected from TB patients, contacts
and healthy controls. Flow cytometry optimization has been completed and the
analysis will start shortly.

**Funding Source:** EDCTP  
**Contract Period:** March 2011-March 2014  
**Current status:** Ongoing

### Improving the Sensitivity of QFT- TB Gold Assay using T cell blast and cell death
inhibiting factor (ISQA)

- **PI:** Markos Abebe
- **Co-investigators:** Abraham Aseffa, Tewodros Tariku, Adane Mihret, Liya Wassie, Martha Zewdie, Rawleigh Howe, Milikit Aytenew

Over the years, different immune based TB diagnostic tests have been developed.
However these tests have limited utility in TB endemic areas due to low sensitivity
and/or specificity. The QFT-TB Gold is one of such assays which uses *M. tuberculosis*
specific antigens, ESAT-6 and CFP-10. Though the incorporation of these antigens
into the assay resulted in more than 97% specificity, the sensitivity is still suboptimal
(<60%) in TB endemic countries. The goal of this project is to identify additional
molecules or mechanisms that could increase the sensitivity of QFT test. In
particular we will explore the hypothesis that reversal of antigen stimulated
apoptosis with inhibitory antibodies will increase detectable TB specific IFN-γ
production. Enhancing the sensitivity of this assay will enable the use of the kit in
immuno-compromised individuals such as HIV-TB co-infected patients facilitating
early diagnosis and treatment.

**Funding:** AHRI Core budget  
**Contract Period:** September 2013-June 2013  
**Status:** On-going

### Implementation & evaluation of task shifting to mid-level health workers, FNA
cytology technique in Ethiopia: A pilot project

- **Investigators:** Abraham Aseffa, Nigatu Endalafer, Biruck Kebede, Dawit Assefa, Ezra Shimelis, Adugna ABERA, Daniel Fiseha, Fasil Tsegaye

The current national practice of performing Fine Needle Aspirate Cytology (FNAC)
to diagnose TB lymphadenitis is entirely dependent on highly trained pathologists.
The number and distribution of these health professionals in the country is not
sufficient to make the service widely accessible to the general population. This pilot
program is intended to task-shift FNAC diagnostic method to middle-level health
professional. By doing this, the test can be used in areas where an enormous burden
of Extra Pulmonary TB (EPTB) cases are found. Training modules and Standard
Operating Procedures (SOPs) related to FNAC technique and result interpretation
has been prepared and 17 trainees (laboratory technologist, health officers and
nurses) from Oromia, Amhara, Tigray and SNNPR were given a 3 week theoretical
and practical training.
Multi-Drug Resistance (MDR) TB Patients` Cost Tool study

- **PI**: David Collins, Management Sciences for Health, USA
- **Co-investigator**: Demissew Beyene

Providing TB treatment is complicated by the occurrence of multidrug-resistant TB (MDR-TB) strains that respond only to second-line drugs. Since treatment centers for patients infected with such strains are not widely available in the country, receiving appropriate medical care can be difficult and this poses serious problem to control TB. This study estimated the costs incurred by patients with MDR-TB. The study found that costs for diagnosis and treatment of MDR-TB were significant. The largest share of these costs was incurred during the intensive treatment phase when patients are hospitalized. The financial burden was exacerbated by patients’ inability to work during treatment.

**Funding Source**: MSH, USA
**Collaborating Institutions**: MSH, USA
**Contract Period**: 2012-2013
**Current status**: Completed

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**Completed PhD studies**

**TB-deworming**

- **PI**: Ebba Abate
- **Supervisors**: Abraham Aseffa, Thomas Schön
- **Co-investigator(s)**: Olle Stendahl, Daniel Elias, Assefa Getachew, Shitaye Alemu, Ermias Diro, Sven Britton

Helminth infection in the setting of other infectious diseases has recently received a great deal of attention because of the widespread prevalence in developing countries and the observations that de-worming therapies can significantly modulate immune responses to unrelated organisms and vaccines. In the present investigation, we explored the hypothesis that treatment of helminth infections in patients with newly diagnosed TB could modulate immunity and thereby contribute to an enhanced response to TB chemotherapy, potentially leading to more efficacious or shorter duration protocols in the future. Of 140 patients, 24% of whom were HIV positive, were randomized to groups receiving either albendazole or placebo, and then assessed for clinical and immunological parameters after two months of TB therapy. Clinical outcomes, as assessed by TB score, smear conversion or radiological findings, did not differ between the control and albendazole de-wormed group. However, albendazole significantly affected several immunological outcomes, including lowering eosinophil counts, decreasing the Th2 signature cytokines IL-5 and IL-10, and lowering the percentages of T regulatory cells. In conclusion, de-worming did not influence the response of patients to
standard TB chemotherapy, but did significantly impact immune system parameters.

**Funding Source:** AHRI Core budget, The Swedish Research Council, The Swedish Heart and Lung Foundation, King Oscar II Jubilee Foundation, SIDA/SAREC and European and Developing Countries Clinical Trials Partnership (EDCTP), Swedish Medical Association (SLS), The Groschinsky Memorial Foundation and the Marianne and Marcus Wallenberg foundation

**Collaborating Institutions:** University of Gonder, Linköping University

**Contract Period:** March 2009 - January 2013

**Current status:** Completed

**Gene Expression and Cytokine Pattern of Pulmonary Tuberculosis Patients and their Contacts in Ethiopia**

- **PI:** Adane Mihret
- **Supervisors:** Abraham Aseffa, Rawleigh Howe, Gerhard Walzl
- **Co-investigators:** Yonas Bekele

Identification of infection-stage specific biomarkers are critical to allow the development of better tools for combating TB. In an attempt to identify such biomarkers, we studied pulmonary TB patients and their contacts in Addis Ababa, Ethiopia. A total of 45 genes were analyzed using the Multiplex Ligation Dependent Probe Amplification (MLPA) technique. We found a number of genes which alone, or in combination, gave a promising discriminatory power to differentiate between TB cases and their contacts and latently infected versus uninfected individuals. Similarly, analysis of cytokines and chemokines showed that single or combination of plasma cytokines and chemokines can discriminate the different clinical groups of TB. These markers may be suitable for the development of clinically useful tools but require further validation and qualification in different populations and in larger studies.

**Funding Source:** BMGF and EDCTP

**Collaborating Institution(s):** Stellenbosch University

**Contract Period:** March 2009 - March 2014

**Current status:** Completed

**On-going PhD studies**

**Analysis of regulation of immune response in Tuberculosis (IRTB)**

- **PI:** Martha Zewdie
- **Co-investigators:** Soren Hoff, Abraham Aseffa, Åse Andersen, Peter Anderson, Rawleigh Howe, Markos Abebe, K. Yamuah, Markos Abebe

One of the target goals to control TB is development of a vaccine that has better efficacy than the currently used BCG vaccine. Previous studies have shown that vaccine induced Th1 response alone does not correlate with protection. One possible explanation is that an excess of regulatory cells plays a negative immune-regulatory function that hamper the development of strong Th1 immunity; or that
insufficient regulatory cells or function results in an inappropriately exuberant Th1 response which wanes prematurely.

Though the role of regulatory T cells, including their activation and functionality, has been investigated during TB infection, their contribution is not adequately understood. It is not known if these cells influence the potential ability to mount a protective immune response during a TB exposure, infection or after vaccination. It is also not known whether the appearance of these cells is a cause or consequence of M. tuberculosis infections.

The overall aim of this study is to investigate the expression of the different subsets of regulatory T cells as well as Th1 immune responses in individuals that are given the H1 TB vaccine, in TB patients at diagnosis and after completion of therapy, and in healthy individual controls. In addition, "quality" of the memory immune response in these groups will be assessed thus allowing us to compare memory in a failed natural immune response (TB disease) with a protective natural immune response (control of infection leading to latency) with the immune response generated by vaccination.

**Funding:** EDCTP
**Collaborating Institutions:** 2011-2014
**Contract Period:**
**Current Status:** Ongoing

**Molecular Epidemiology and Drug Resistance of Mycobacterium tuberculosis Among New Smear Positive Pulmonary Tuberculosis Patients in Eastern Ethiopia**

- **PI:** Berhanu Seyoum
- **Supervisors:** Meaza Demissie, Alemayehu Worku, Abraham Aseffa
- **Co-investigators:** Shiferaw Bekele, Elena Hailu,

Periodic surveillance and monitoring of anti-TB drug resistance is vital element in the control of drug resistant TB. However, there is no adequate data that describe the level of drug resistance, genetic diversity of M. tuberculosis and treatment outcome in the country in general & in particular eastern Ethiopia. Thus, the current study is designed to fill the existing gaps to further strengthen the existing control programme. A health facility based cross-sectional study was conducted between December 2011 and March 2013 in selected health facilities found in Dire - Dawa, Harara ang Jigiga towns, eastern Ethiopia. The preliminary results show that the highest rate of mono drug resistance was associated with INH (12.3%); the proportion of MDR-TB is (1.3%). Periodic surveillance of drug resistance is essential to limit the spread of drug resistant TB strains.

**Funding Source:** Haramaya University and AHRI Core budget
**Collaborating Institutions:** Haramaya University
**Contract Period:** 2012-2015
**Current status:** On-going
Validation of Tuberculosis Diagnostic Algorithm and Newly Emerging Tests for the Diagnosis Childhood Tuberculosis in Ethiopia

- **PI:** Ibrahim Ali
- **Supervisors:** Abraham Aseffa, Markos Abebe, Yimtubeznash Woldeamanuel

Pediatric TB remains a diagnostic challenge. This study was conducted in Addis Ababa to evaluate the current diagnostic algorithm and the performance of the various currently available tests in the diagnosis of childhood tuberculosis using specimens collected from health facilities.

The role of Cattle in transmitting the causative agent of tuberculosis in two Zones of Amhara region

- **PI:** Araya Mengistu
- **Supervisors:** Abraham Aseffa, Demissew Beyene

A close intimacy between cattle and humans in developing countries creates a conducive environment for Zoonotic transmission of M. tuberculosis. However, despite the isolation of M. tuberculosis from cattle, the role of animals in the maintenance and transmission of this pathogen has not been studied in depth in Ethiopia. The aim of this study is to determine the role of cattle in the maintenance and transmission of *Mycobacterium tuberculosis* complex (MTBC). Using molecular and epidemiological approaches, we will identify M. tuberculosis lineages that are circulating in the region and understand the possible risk factors for transmission of MTBC. Findings from this study will enable TB control authorities to design new and improved intervention strategies. The study will be conducted in the rural areas of North Wollo and Gondar. Ethical approvals have been obtained and field work is underway.

**Completed MSc Studies**

Prevalence of Endometrial Tuberculosis among Patients Undergoing Endometrial Biopsy at Tikur Anbesa Specialized Hospital, Addis Ababa, Ethiopia

- **PI:** Sileshi Abdissa
- **Supervisors:** Adane Mihiret, Gobena Ameni, Markos Abebe, Tamrat Abebe
- **Co-investigator:** Sisay Teklu, Yohannes Derese, Yonas Bekuretson, Abraham Aseffa

Female genital tuberculosis (FGTB) is known to cause severe tubal disease leading to infertility and its incidence parallels closely with the overall prevalence of TB in a community. Its magnitude is underreported because diagnosis is difficult and requires invasive techniques. Investigation with advanced microbiological techniques may allow for easier, fast and correct diagnosis and treatment that may help to prevent complications. The aim was to determine the prevalence of endometrial TB among women who underwent endometrial biopsy for evaluation of various conditions at a referral hospital and characterize the isolates. A cross-
Sectional study was conducted at Tikur Anbessa Specialized Hospital (TASH), Gynecology Outpatient Department (OPD). TB isolates from leftover biopsy samples were cultured; species identification and genus typing were performed using deletion typing and multiplex PCR respectively. Histopathological examination was also performed in the samples. IS1081-PCR identified 7/152 (4.6%) biopsies as endometrial TB. Only four of the seven (4/152, or 2.6%) were positive by culture. The prevalence of endometrial TB was thus 2.6% (4/152) but 4.6% (7/152) with IS1081-PCR. Histological examination, however, identified only 2/152 (1.3%) as suggestive of endometrial TB. Only one of these samples was positive with both IS1081-PCR and culture. All of the four isolates were M. tuberculosis. The agreement between the clinical diagnosis and IS1081-PCR and/or culture, was found to be 0.28. Taking culture as gold standard, the sensitivity and specificity of IS1081-PCR and histology were 100% and 98%, and 25% and 50% respectively. The study found that M. tuberculosis is relatively frequently encountered in endometrial biopsy but the true magnitude of endometrial TB requires thorough investigation and may be missed with histopathological examination alone.

Active Case Finding for Pulmonary TB and Detection of Drug resistance among HIV-infected patients in Gondar, Ethiopia

- **PI:** Martha Alemayehu
- **Supervisor:** Baye Gelaw, Ebba Abate, Abraham Aseffa, Liya Wassie, Yeshambel Belyhun, Russell R. Kempker, Henry M. Blumberg
- **Co-investigator:** Shiferaw Bekele

Patients co-infected with HIV and TB often lacks the classic symptoms of pulmonary TB thus making TB diagnosis difficult. The aim of this study was to determine, through active case finding of HIV-infected patients, the prevalence of undiagnosed pulmonary TB cases including MDR-TB. A cross sectional study was conducted from February 2012-November 2012 among HIV-infected patients attending the ART clinic of the University of Gonder (UOG) hospital. Our results showed that out of 250 HIV-infected participants, screened for TB through active case finding, 9 (3.6%) were smear +ve/culture +ve and 6 (2.4%) were smear -ve/culture +ve. RD9 typing showed that out of 15 isolates 10 (66.6%) were M. tuberculosis species, 1 (6.7%) belonged to Mycobacterium genus and four isolates were non Mycobacteria. Mono-drug resistance was identified only for streptomycin in one newly diagnosed TB patient and MDR-TB was not observed. Therefore, the prevalence of undiagnosed PTB infection among HIV-infected patients in Gondar was 4.4%. Active screening of known HIV-infected individuals for TB, with at least one TB symptom should be considered.

**Funding Source:** AHRI core budget,
**Collaborating Institutions:** University of Gonder, Emory University
**Contract Period:** 2012-2013
**Current status:** Completed
**On-going MSc Studies**

*Mycobacterium tuberculosis* specific immune response among HIV infected pregnant women

- **Investigators:** Mahlet Biruk
- **Supervisor:** Markos Abebe, Aster Tsegaye, Rawleigh Howe, Nebiat Gebreselassie
- **Project Member:** Nahom Getachew, Azeb Tarekegn

Pregnant women with HIV infection who harbor *M. tuberculosis* are at about 10 times at increased risk of developing active tuberculosis compared to their HIV negative counterparts. WHO recommends that this group of population should be screened for latent TB infection (LTBI) and receive prophylaxis treatment to prevent reactivated TB. However, there is no reliable method of LTBI diagnosis in pregnant women, necessitating alternative approaches such as immunoassays for these individuals.

Although some studies have attempted to compare the efficacy of cell mediated immune responses in LTBI detection in these group of populations, these studies only assessed TB specific IFN-γ production, and did not evaluate other cytokine responses, nor were humoral immune responses addressed. Moreover, to our knowledge, no studies of HIV infected pregnant women have been conducted in Africa where the risk groups are predominantly represented. This study will determine multiple cytokine and antibody responses in vitro to *M. tuberculosis* among HIV infected pregnant women, and compare these responses with other standardized tests including the Tuberculin Skin Test (TST) and IFN-γ Release assay (IGRA).

**Funding Source:** AHRI core budget  
**Collaborating Institutions:** Addis Ababa City Administration Health Centers  
**Contract Period:** 2012-2014  
**Current status:** On-going

**Comparison of apoptosis related molecules and mechanisms functioning at immunological synpse of macrophage and T-cells from peripheral blood and lymph node of TB lymphadenitis patients**

- **PI:** Nejat Juhar  
- **Supervisor:** Markos Abebe and Abraham Aseffa, Anne Spurkland, Beyene Wondafrash and Lule Teshager

Apoptosis is an essential process in the growth and maintenance of the immune system. It is also one of host defense mechanism to kill intracellular pathogens. Many studies showed that it plays an important role in the host response against TB. The majority of these studies are conducted from peripheral blood samples, and do not necessarily reflect the local immune response where the immune response occurs. The study aims to compare the expression of apoptosis related molecules on macrophage and T-cells from peripheral blood and diseased lymph node of TB.
lymphadenitis patients. Understanding the difference might help us to better define the immunopathogenesis of TB and contribute to the framework of information needed for the design and development of improved TB vaccines.

**Funding Source:** AHRI Core budget and Jimma University  
**Collaborating Institutions:** University of Oslo, Jimma University  
**Contract Period:** 2012 – 2014  
**Current status:** Ongoing; Ethical clearance obtained

**Phenotypic and genotypic assessment of mycobacteria isolates in Dessie and surrounding, North East Ethiopia**

- **PI:** Minwuyelet Maru  
- **Supervisors:** Solomon H/Mariam, Endalamaw Gadissa, Abraham Aseffa

The burden of TB is aggravated by the emergence and expansion of drug resistance TB. As Ethiopia is one of the 22 countries with MDR-TB burden, a continuous surveillance program to determine the TB strains that are circulating in the county provides useful information for effective control strategies. This study will assess genotypes and drug resistance pattern of *M. tuberculosis* complex species in South Wollo Zone of Amhara regional State. Thus far, we have isolated and characterized strains cultivated from 92 sputum samples with the remaining 50 collected samples to be evaluated within the next few months.

**Epidemiology and drug resistance pattern of mycobacterium tuberculosis in Northwest Ethiopia: resource limited region**

- **PI:** Tekle Airgecho  
- **Co-investigators:** Yimtubezinash Woldeamanuel, Demissew Beyene, Abraham Aseffa, Daniel Asrat

Despite the availability of short course regimens of first line anti-tuberculosis drugs, emergence of drug resistant *M. tuberculosis* strains still pose a major challenge to TB prevention and control efforts. The burden and fate pattern of TB drug resistance in developing countries, including Ethiopia, remain largely unexplored, mainly due to unavailability of laboratory tests beyond the century old microscopy. Moreover, remote areas that are far away from urban medical centers lacks these tests and the circulating TB strains in such areas are not known. This study is being conducted in the Benishangul-Gumuz region and its surroundings, an area bordering Sudan, to determine the drug resistance pattern and diversity of *M. tuberculosis* strains circulating among pulmonary TB patients. This will add information to the national database and contribute to the evidence based TB control strategy in the region as well as the whole country.

**Funding Source:** AHRI core budget and AAU  
**Collaborating Institutions:**  
**Contract Period:** 2012–2014  
**Current status:** In progress
Bacteriology Team

Research in bacteriology team includes understanding epidemiological and molecular mechanisms of bacterial diseases including meningitis, pneumonia, typhoid fever, and diarrhea elicited by non-typhoidal salmonella. Together with its partners, the team has found a previously unreported circulating strain within the W135 serogroup of Neisseria meningitidis, a major contributor of meningitis epidemics in Africa. This strain was responsible for a major outbreak in Burkina Faso in 2000 and required a change of the vaccine in use for epidemic control. The presence of W135 in Ethiopia means that future outbreaks have to be closely monitored so that epidemics due to W135 are managed through a trivalent vaccine containing not only the antigens produced by common strains A and C present in bivalent vaccine stocks, but also that of W135.

Team Members

- Wude Mihret, Senior Researcher and team head
- Dr. Demissew Beyene, Post-doctoral Scientist
- Dr. Oumer Ali, Research Assistant
- Tsehaynesh Lemma, Medical Microbiologist
- Dr Mekonnen Teferi, Research Assistant
- Elena Hailu, Research Assistant
- Biruk Yeshitela, Research Assistant
- Emawayish Andargie, Laboratory Technologist
- Fikirete Mulatu, Laboratory Technologist
- Mahelet Tadesse, Laboratory Technologist
- Tesfaye Moti, Laboratory Technologist
- Wondale Mekonnen, Laboratory Technologist
- Melaku Yiedenekachew, Biologist
- Wondewosen Tsegaye, PhD student
- Nigus Zegeye, MSc student
Research

Surveillance of bacterial meningitis in Ethiopia and examining factors affecting meningococcal disease severity

- **PI:** Professor Dominique Caugant and Dr Abraham Aseffa
- **Co-investigators:** Wude Mihret, Tsehaynesh Lemma Afework Kassu, Beyene Moges, Yared Merid, Fitsum Woldegebriel, Workebeba Abebe Taye, Admasu Tenna Mamuye, Arslan Ahmed, Einar Rosenqvist.

Ethiopia is one of the countries in the African meningitis belt region, an area affected repeatedly with meningitis epidemics. This study is designed to investigate the burden and etiology of bacterial meningitis from selected hospitals (Tikur Anbessa Specialized, Hawassa and Gonder) over a one-year period in a non-epidemic period. Microbiological culture studies indicated that more than 50% of cerebrospinal fluid (CSF) samples showed bacterial growth. Of these, 11 were confirmed to be *S. pneumoniae*, 8 *N. meningitides*, and 1 *H. influenzae* using conventional PCR techniques. Conversely, analysis of selected CSF sample (n=65) with nested PCR indicate 24 positive strains of *N. meningitidis*.

**Funding Source:** Norwegian Research Council (grant no. 192477)

**Collaborating Institution(s):** Norwegian Institute of Public Health (Oslo, Norway), University of Gondar Medical Hospital (Gonder, Ethiopia), Black Lion Hospital (Addis Ababa, Ethiopia), Hawassa University Referral Hospital (Hwassa, Ethiopia), SNNPR Regional Health Bureau (Hawassa, Ethiopia)

**Contract Period:**

**Current status:** On-going

**Typhoid Fever Surveillance in Africa Program (TSAP)**

- **PI:** Dr Florian Marks, Dr Abraham Aseffa
- **Co-investigators:** Dr Mekonen Teferi, Biruk Yeshitila, Yohannes Derese, Dr Alemayehu Worku, Dr Fuad Ibrahim, Florian Marks, Ursula Panzner, Thomas Weziba

Typhoid Fever Surveillance in Africa Program (TSAP) is a collaborative project with the primary objective of estimating the incidence of typhoid fever (TF) in Africa using a standardized surveillance method. The second aim is to determine the healthcare-seeking behavior of the catchment population through administration of a health care utilization survey (HCUS) which enables the denominator in incidence calculation.

The Ethiopian project was launched in March 2012 and recruitment will continue until March 2014. Febrile patients are being recruited from four clinical sites in and around Butajira by taking 10 Kebeles under a Demographic surveillance site (DSS) as
a sentinel population. Up to now, more than 800 patients have been recruited and all relevant lab and clinical data are collected and double entered into a database. Data is not yet analyzed.

**Funding Source:** International Vaccine Institute  
**Collaborating Institution(s):** International Vaccine Institute, Butajira Hospital and Addis Ababa University.  
**Contract Period:** 2012-2014  
**Current status:** On-going

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**MenAfriCar: Studies on the epidemiology of meningococci in five countries of the African meningitis belt**

- **PI:** Brian Greenwood, Abraham Aseffa  
- **Co-investigators and study team members:** Oumer Ali, Lawrence Yamuah, Adane Mihret, Rawleigh Howe, Ahmed Bedru, Wude Mihret, Tsehaynesh Lemma, Alemayehu Worku, Hiwot Mamo, Yenenesh Kelile, Fantanesh Melese, Tesfaye Moti, Hiwot Tilahun, Genet Amare, Wondu Wagaye, Tsegaye Hailu, Samuel Ayele, Biruk Yeshitela, Selfu Girma

The primary objective of the MenAfriCar study is to determine the epidemiology of meningococci carriage in five African meningitis belt countries (Chad, Ghana, Ethiopia, Nigeria and Senegal) prior to the introduction of new meningococcal conjugate vaccines. A multicentre study is needed because the prevalence of carriage and the importance of individual risk factors for carriage are likely to vary across the meningitis belt. It is an observational study with three main components in each of the five target countries. These are

- Cross-sectional surveys of an age-stratified population of 2,000 subjects conducted once during the dry season and once during the rainy season  
- A study of risk factors for carriage of serogroup A meningococci and for carriage with meningococci belonging to other serogroups.  
- A study of the rates of acquisition and loss of carriage of serogroup A meningococci in households of carriers and of the factors that determine this including bactericidal antibody concentrations.

The study was undertaken in Meskan and Mareko Districts, Gurage Zone, in the Southern Nations, Nationalities and Peoples Regional State in Ethiopia. The result of cross-sectional studies is described in the table below. Data from the cross-sectional survey and the household survey is currently under analysis. ELISA determination of serum antibodies and PCR in the laboratory arm of the study is being performed.
Characterization and antimicrobial susceptibility patterns (CASP) of blood culture isolates from septicemic patients at St Paul’s hospital, Addis Ababa, Ethiopia

- **PI**: Adugna Nigussei
- **Co-investigators**: Mekonnen Teferi, Biruk Yeshitila, Gesite, Tsehay

CASP was initiated in December 2012 with the objective to describe the prevalence of bacterial species and their antimicrobial sensitivity pattern from blood culture isolates among septicemia suspected patients in St Paul’s hospital, Addis Ababa. Blood culture samples (n=185) were analyzed and 23% of them were found positive for bacteria. More than 10 types of bacteria were identified. Bacterial typing and drug sensitivity results were communicated with health centers to assist in clinical management of the patient. Recruitment is continuing and the project is expected to be complete in March 2014.

**Funding Source**: AHRI core budget
**Collaborating Institution(s)**: St. Paul Hospital
**Contract Period**: 2012-2014
**Current status**: On-going

Impact of meningococcal conjugate vaccines on serogroup A transmission in Ethiopia – mechanism and dynamics of clearance of asymptomatic carriage - The Ethiopian carriage study

- **PI**: Dominique A Cougant, Abraham Aseffa
Disease caused by *Neisseria meningitides* (*N. meningitides*) is a significant cause of morbidity and mortality in the African meningitis belt. Serogroup A *N. meningitidis* disease occurs as devastating epidemics of meningitis, resulting in tens of thousands of cases and thousands of deaths. To eliminate this epidemic, a new serogroup A meningococcal conjugate vaccine, MenAfriVac, was developed by the Meningitis Vaccine Project (MVP). The vaccine was introduced in mass vaccination campaigns in Burkina Faso and parts of Mali and Niger in December 2010. Roll-out of MenAfriVac is planned to encompass all 25 countries of the African meningitis belt by 2016.

The aim of the project is to demonstrate the ability of MenAfriVac and other conjugate vaccines to reduce pharyngeal carriage, and thus, transmission of the pathogen. The study will investigate the dynamics of carriage clearance in correlation with vaccine-induced antibody responses in serum and saliva. The study may thus provide further knowledge on the mechanism of action of conjugate vaccines and determine an antibody threshold necessary to prevent carriage.

The project has already obtained ethical clearance from Norway and Norway.

**Funding Source:** NIPH  
**Collaborating Institution(s):** The Norwegian Institute of Public Health (NIPH), WHO-Geneva, CDC Atlanta, Addis Ababa University, Gondar University, Arba Minch University, Arba Minch General Hospital, SNNR health bureau, Amhara Regional Health bureau, The Federal Ministry of Health of Ethiopia, EHNRI  
**Contract Period:** 2013-2016  
**Current status:** On-going

**On-going PhD studies**

The impact of Ten-valent pneumococcal conjugate vaccine (PCV10) on *Streptococcus pneumoniae* nasopharyngeal carriage rate, and on phenotypic and genetic diversity of isolates in Addis Ababa, Ethiopia

- **PI:** Wondewosen Tsegaye  
- **Supervisors:** Abraham Aseffa, Yimtubezenash W/Amanueal  
- **Co-investigator(s):** Oumer Ali, Teshaynesh Lemma

*Streptococcus pneumoniae* (Pneumococcus) represents one of the most important human pathogens, with high morbidity and mortality rates. Nasopharyngeal (NP) carriage in children plays a major role in its spread within the family, school, day-care center, kindergarten and orphanage populations, and hence represents as one step in the pathogenesis of associated Invasive pneumococcal Disease (IPD) and non-
invasive diseases. Since October 2011, the Ethiopian government introduced the ten-valent pneumococcal conjugate vaccine (PCV110) into the routine vaccination programme. There is nevertheless lack of adequate baseline information on epidemiological factors (such as the rate of carriage and transmission, serotypes, genetic relatedness of isolates, antibiotic susceptibility profile for commonly used antibiotics) for subsequent impact assessment. The study is being conducted in seven health centers of Addis Ababa city administration. Thus far, 619 nasopharyngeal samples were collected from newborns (< 45 days old) and the following species were identified: 194 Streptococcus pneumoniae, 87 Moraxella catarrhalis, 28 Haemophilus Influenzae, 145 Staphylococcus aureus and 2 Streptococcus pyogenes. Demographic and risk factors data, serotyping and molecular characterization of the isolates will be done in the coming year.

**Funding Source:** AHRI core budget  
**Collaborating Institution(s):** Addis Ababa University  
**Contract Period:** 2012-2015  
**Current status:** On-going

**On-going MSc Studies**

**Throat carriage rate and antibiotic susceptibility pattern of group A streptococcus in children with rheumatic fever on secondary antibiotic prophylaxis in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia**

- **PI:** Nigus Zegeye
- **Supervisors:** Abraham Asseffa, Abebe Habte, Daniel Asrat, Yimtubezinash W/Amanuel, Etsegenet Gedlu

Rheumatic fever is caused by Group A, beta-hemolytic streptococcus also known as *S. pyogenes*. It is the cause of rheumatic heart disease in children. The profile of this pathogen among children who are on secondary rheumatic fever antibiotic prophylaxis has not been studied well in Ethiopia. This study is being carried out at Tikur Anbessa hospital. Throat culture and biochemical tests are done to isolate beta-hemolytic streptococci. The isolated strains will be then identified by serogrouping and emm typing. Antistreptolysin O (ASO) titer will be measured from serum sample to differentiate streptococcal colonization from streptococcal throat infection. Risk factors associated with streptococcal throat infection will also be studied. Sample collection has been completed and the serotyping and other lab tests will be done in the next few months.

**Funding Source:** AHRI core budget  
**Collaborating Institution(s):** Addis Ababa University  
**Contract Period:** 2012-2014  
**Current status:** On-going
Clinical Trial Team

Since its first GCP trial in 2001, the AHRI clinical trial team has been engaged primarily in a wide spectrum of capacity building activities, including development of clinical sites, human capital, laboratory facilities, etc.

Clinical trials are demanding by resource and standards that could only be met through time, experience and partnership. The number of trials is now growing and the nature and standards from different partners are getting diverse. Accordingly, the team is striving to meet the required standards proactively as a clinical site despite prevailing constraints. This year five active projects have been handled with improved performance in terms of required standards in all aspects. Recruitment and follow-up for the cholera vaccine trial was completed successfully. Additional facilities and standards have also been set for the conduct of bioequivalence studies at the campus. Therefore, the team will keep on restructuring itself to remain competent in the field and to accommodate the growing demand and standards.

Team Members

- Dr Tesfamariam Mebrahtu, MD, MPH, Clinical Trial Team Head and Principal Investigator
- Dr Mekonnen Teferi, DVM, MSc, Assistant Researcher
- Dr Zenebe Akalu, MD, Principal Investigator
- Dr Oumer Ali, MD, MSc, Principal Investigator
- Dr Nebiat Gebregzehber, PhD, Post-Doctoral Scientist
- Chalachew Misganaw, HO, MPH, Clinical QA Officer
- Hawult Taye, HO, MPH, Study Physician
- Kalehiwot Mekonnen, Nurse, MPH, Clinical Coordinator
- Fantanesh Melese, HO, Study Physician
- Yemiserach Zewdei, Nurse, MSc, Study coordinator
- Sr Helen Teklu, Research Nurse
- Sr Roman Sahelu, Research Nurse
- Sr Sefinat Juhar, Research Nurse
- Sr. Helina Seid, Research Nurse
- Sr. Haimanot Agize, Research Nurse
- Sr. Bilcha Tadesse, Research Nurse
- Ermias Hundito, Field nurse
- Meseret Habtamu, MSc, Clinical Laboratory Coordinator
- Fekadu Zenebe, Lab Technologist
- Yilkal Aseffa, Lab Technologist
- Lensa Abera, Lab Technologist
- Emawayish Tsegaye, Study Facilitator
- Sr. Haimanot Agize, Research Nurse
- Sr. Bilcha Tadesse, Research Nurse
- Ermias Hundito, Field nurse
- Meseret Habtamu, MSc, Clinical Laboratory Coordinator
- Fekadu Zenebe, Lab Technologist
- Yilkal Aseffa, Lab Technologist
- Lensa Abera, Lab Technologist
- Emawayish Tsegaye, Study Facilitator
Research

4 FDC (2002-2013): (A two-arm single-blinded, randomised comparison of four fixed-dose drug combination (4FDCs) (intervention group) versus standard treatment with separate TB drugs (comparator group)


The trial data analysis was completed and Clinical Study Report developed. A manuscript writing meeting was held in Lagos, Nigeria and one article submitted for publication. Final Clinical Study report is under review by the study team.

Report back meetings will be carried out in 2014

Funding: WHO/TDR
Collaborating Institutions: St Peter’s hospital, Bole Health Center, Adama Hospital
Contract Period: 2002-2012
Current status: Closed

The Evaluation of a Standardized Treatment Regimen of Anti-Tuberculosis Drugs for Patients with MDR-TB (STREAM)

- Local PIs: Dr Tesfamariam Mebrahtu (AHRI) and Dr Daniel Meresa (St Peter’s hospital)

The emergence and spread of MDR-TB is a big hurdle to TB control worldwide. Currently, treatment can take as long as 24 months and due to this many patients do not comply with the standard treatment period. To avoid this problem, new drugs or combination of drugs that can be taken in shorter period are needed urgently. The current study is a non-inferior multi-center, international parallel group, randomized controlled trial primarily aimed to assess whether outcomes of a novel regimen is not inferior to a WHO approved MDR-TB regimen. The study regimen consists of moxifloxacin, clofazimine, ethambutol and pyrazinamide (supplemented by kanamycin, isoniazid and prothionamide in the four months of the intensive phase) that will be given for 9 months. A total of 100 patients are expected to be recruited from AHRI/ALERT and St Peter’s Hospital in Ethiopia. At AHRI’s site, approximately 50% of participants have been recruited since the trial has started in February 2013.

Funding: the Union and Medical Research Council, United Kingdom (MRC-UK)
Collaborating Institutions: St Peter’s hospital
Contract Period: 2012-2015
Current status: Recruiting
A Randomized, Double-blind, Controlled Trial to Evaluate the Safety and Immunogenicity of a Killed Oral Cholera Vaccine (Shanchol®) in Healthy Individuals in Ethiopia (Shanchol trial)

- PI: Abraham Aseffa
- Co-PI: Zenebe Akalau

WHO has recently prequalified a killed whole cell oral cholera vaccine (OCV), facilitating its use to cholera epidemic affected areas. The current study serves as a bridging trial to assess the safety and immunogenicity of a two dose regimen of the OCV in the Ethiopian population. Previously, the vaccine has been evaluated in a large number of human subjects in India, Vietnam, and Bangladesh, where its safety immunogenicity, and clinical protective efficacy has been demonstrated. We aim to confirm our presumptive understanding that two doses of OCV is safe and immunogenic in healthy individuals aged 1 year and above. The trial was an individually randomized, controlled, double blinded, placebo controlled conducted in 216 subjects, equally divided into two arms consisting of healthy children and adults. Recruitment and follow-up have been completed and we have observed that the vaccine is generally safe. Upon completion of all vibriocidal assays, vaccine and control cohorts will be will be compared. If safety and immunogenicity of the vaccine is proven, mass vaccination will be given in the Shashemene area, Ethiopia.

Funding Source: IVI
Collaborating Institutions: -
Contract Period: 2012-2013
Current status: Completed

Double Blinded, Randomized, Placebo Controlled, phase II trial of Shiunko Ointment in Ethiopian patients with localized Cutaneous Leishmaniasis lesions (Shiunko trial)

- PI: Omer Ali
- Co-investigator (s): Abraham Aseffa, Endalamaw Gadissa, Mohammed Beyan, Elisabet Bezabih, Kenji Hirayama, Juntra Karbwang
- Project Member (s): Yemisirach Zewdie, Lensa Abera, Fantanesh Melese, Fikerte Mulat, Haimanot Agize

Cutaneous leishmaniasis (CL) is a major tropical skin disease which represents a public health and social problem in many developing countries, including Ethiopia. None of the treatments currently used in Ethiopia have solid evidence to support the national treatment guidelines for CL. Research into safe and efficacious treatment options through the conduct of standard clinical studies/trials is needed. One such new
candidate is Shiunko, a Chinese medicinal ointment that was formulated by Japanese surgeon Seishu Hanaoka.

The current trial is a single-center study undertaken at Ankober Health Center, North Shewa Zone of the Amhara Regional state, Ethiopia. As a phase II trial, its primary objective is to assess the efficacy of 4 weeks Shiunko Ointment for the treatment of uncomplicated localized Cutaneous Leishmaniasis (CL) by taking clinical improvement and parasitological clearance as end point measurements. The trial planned to enroll a total of 40 patients in both the study and control arms. Recruitment is complete and 34 of the patients are on follow up. The overall performance of the trial was very encouraging and both Nagasaki University and the manufacturer of the drug have shown interest to proceed to a phase III trial.

**Funding:** AHRI core budget and University of Nagasaki  
**Collaborating Institution (s):** Nagasaki University  
**Contract Period:** 2013-2014  
**Status:** On-going

### Bioequivalence (BE) Clinical Studies

- **PI:** Mekonnen Teferi

New pharmaceutical companies are flourishing in Africa. Most of such plants produce generic drugs which are commonly required to undergo clinical testing for their bioequivalence (BE) before market authorization. Thus establishment of a BE center with standard clinical facilities will help to foster the production and utilization of generic drugs that could be produced by local pharmaceutical industries and beyond. In line with this, a regional bioequivalence center (RBEC), which will serve the Eastern Africa region, has been recently inaugurated at Addis Ababa University, School of Pharmacy. AHRI was one of the key partners that assist from the initial idea to project maturation.

A clinical trial of bioequivalence studies will be done at AHRI. In line with this, AHRI has invested more than 1 million Ethiopian birr to prepare its site to meet international standards as clinical site for the conduct of BE studies. A dedicated & fully furnished 12 bed capacity BE study ward with a framework of the necessary documents (i.e. Standard Operating Procedures and Case Record Forms) was recently inaugurated in the presence of government officials and different partners. A study protocol on 'ciprofloxacin' was submitted for ethical review and received approval. The project aims to conduct at least 10 studies per year and obtain WHO qualification to meet its regional scope.
Funding: AHRI Core budget

Immune reconstitution in TB and HIV disease using antimicrobial treatment with vitamin D and phenylbutyrate (VitD/PBA trial)

- **Post-doctoral Scientist:** Nebiat Gebreegziabher
- **Principal Investigators in Ethiopia:** Amsalu Bekele, Senait Ashenafi, Betemariam, Getachew Aderaye, Endale Kassa, Wondwossen Amogne, Getachew Aseffa, Alemayehu Worku, Abraham Aseffa
- **Principal Investigators in Sweden:** Susanna Brighenti, Jan Andersson and Peter Bergman

VitD3 and PBA enhance mucosal immune responses to infections whilst simultaneously limiting over-exuberant inflammatory responses. In this study, the effects of vitD3/PBA treatment supplementation will be investigated in active pulmonary TB and in Highly Active Anti-Retroviral Treatment (HAART)-naïve HIV-positive individuals in Ethiopia. These are vulnerable groups of patients who would benefit tremendously from a safe and effective immunotherapy that would enhance their probability to control microbial infection, shorten the duration of standard drug treatment thus limiting potential side-effects that are normally associated with long term therapy. The study is a randomized, double-blinded, placebo-controlled, phase-II clinical trial. It is 40% complete after eight months. Average recruitment is 4-5 patients per week for both the TB and HIV arm of the study.

**Funding** Source: Karolinska Institute  
**Collaborating Institutions:** Black Lion Hospital  
**Contract Period:** 2012-2015  
**Current status:** Recruiting
Leishmania, Malaria and Neglected Tropical Diseases Team

The team currently conducts research in basic and translational aspects of leishmania, malaria, and other neglected tropical diseases including filariasis and podoconiosis. The team is also actively involved in disease mapping projects where possible disease occurring sites are identified using statistical and geographic information system (GIS) technology. This approach is proved to be cost effective and has helped FMoH and other institutions to do preventive work early before the disease occurs.

Basic science aspects include drug resistance in malarial parasite and understanding of host innate immune response to Leishmania. As part of its mission, the team is actively working with the FMoH and is a member of the national neglected tropical disease task force. Similarly, the team is working as a technical working group for the national onchocerciasis elimination guideline. The team members have also actively participated in revising and editing the 2nd edition of guideline for diagnosis, treatment and prevention of leishmaniasis in Ethiopia.

Team Members

- Dr. Endalmaw Gadissa, Team Head and Post-doctoral Scientist
- Ahmed Seid, GIS and Remote Sensing Specialist
- Teshome Tsegaw, GIS and Remote Sensing Specialist
- Sisay Getachew, PhD student
- Lemu Golassa, PhD student
- Memberework Chanyalew, PhD student
- Adugna Abera, research assistant
- Geremew Tasew, PhD student
- Birtukan Endale, Lab technologist
- Menberework Chanyalew, PhD student

Research

Risk Mapping of Cutaneous Leishmaniasis in Ethiopia

- **PI:** Ahmed Seid
- **Co-investigators:** Teshome Tsegaw (AHRI), Endalamaw Gadissa (AHRI), Adugna Abera, Aklilu Teshome, Abate Mulugeta, and Abraham Aseffa
- **Project Member(s):** Merce Herrero, Daniel Argaw, Alvar Jorge

Cutaneous leishmaniasis (CL) is a neglected tropical disease highly associated with poverty. Treatment is still problematic and no vaccine is still available. There is a growing public health challenge with new outbreaks in areas previously not known to be endemic. This is true in areas with high HIV co-infection rates. Moreover, environmental factors play an important role in disease distribution but their effect are still poorly understood. The study aims to develop risk model based on environmental factors...
using GIS and statistical approach. It is a collaborative work with FMoH, WHO Ethiopian country office and WHO Geneva office.

A total of 2512 GPS points of CL presence & absence data in kebele level were collected, and analyzed with major determinant environmental parameters. Data on Cutaneous leishmaniasis were defined by clinical diagnosis, and confirmed by a positive skin test and/or parasitological examinations. The environmental CL risk model provided an overall prediction accuracy of 90.4% with slope, elevation, and annual rainfall as best predictors of CL.

The study revealed that 22.54% of the total area is at high risk for CL mainly the highland Part of Amhara, Oromia, Tigray and SNNPR regions. The study also showed that more than 28 million people at risk of the disease.

This is the first risk map for CL in Ethiopia and the Federal Ministry of Health can use the data to implement evidence based leishmaniasis control program. Similar studies can also be done using approach for other diseases.

**Funding Source:** WHO Geneva Office and WHO Ethiopian Country Office

**Collaborating Institutions:** Disease Prevention and Control Programmes, World Health Organization, Ethiopia Country Office, Addis Ababa, Ethiopia, Department for the Control of Neglected Tropical Diseases, Leishmaniasis Control Programme, World Health Organization, Geneva, Switzerland

**Contract Period:** June, 2010 - June, 2013

**Sentinel Site Survey for Lymphatic Filariasis Elimination Programme in Ethiopia**

- **PI:** Endalamaw Gadisa, Ahmed Seid, Teshome Tsegaw, Adugna Abera, Lensa Abra

Lymphatic filariasis (LF) is a major cause of permanent long-term disability affecting 120 million people in Asia, Africa, the Western Pacific & some parts of Americas. Sub-Saharan Africa, and accounts for 40% of the global burden with an estimated 394 million people at risk, of which 30 million are from Ethiopia. The disease is identified by the Ethiopian Neglected Tropical Diseases strategic plan as one of the diseases targeted for elimination. Sentinel site & spot-check sites are required to effectively monitor & evaluate the progress of the program in each implementation unit. The objective of the study is to determine baseline prevalence in Sherkole, Mao-komo & Sirba-abay districts. A rapid immunochromatographic Test (ICT-cards) was employed to detect circulating *Wuchereria bancrofti* antigen from fingerpicks blood samples. The overall
antigenemia was 10.56% (95/900), with wide district to district variation: the least (1%) in Mao Komo and the highest in Sirba Abay (24.33). The finding was communicated with the ministry of health for the planned start of Mass drug administration contributing for the control program.

**Funding Source:** Liverpool school of tropical medicine
**Collaborating Institutions:** FMoH, EHRI
**Contract Period:** 2012-2013
**Current status:** Completed

**On-going PhD studies**

Innate immunity to visceral and cutaneous leishmaniasis: German African collaborative project

- **PI:** Menberework Chanyalew and Geremew Tasew
- **Supervisors:** Ger van Zandbergen, Abraham Aseffa, Tamas Laskay, Uwe Ritter, Endalamaw Gadisa, Markos Abebe
- **Co-investigator(s):** Birtukan Endale, Selfu Girma, Geremew Tassew, Adugna Abera, Lenesa Abera

Leishmaniasis is a neglected tropical disease with an estimated incidence of 1.6 million new cases per year. The available drugs are toxic and/or expensive for the most affected. Moreover, most diagnostic methods not only involve invasive procedures but also need well-trained medical personnel and equipment. Of the infected only a small proportion develop clinical symptoms while most control the infection. Considerable progress has been made in understanding the adaptive immunity conferring protection but little is known about the innate immune responses against Leishmania parasites. Innate immune responses are not only essential for effective early defense, but also shape the development and type of adaptive immune responses as well. Therefore, understanding the pathogen-induced innate immune dysfunctions could shed light for the effort to develop immune intervention strategies and/or develop better tools for early detection of infection. The objective of this study is to identify innate immune mechanisms that are targeted by Leishmania for evasion to obtain new insights into the role of cellular mechanisms linking innate and adaptive immune responses. Since its start, 6 VL and 22 patients have been enrolled in the study. Advanced immunological techniques including FACS based whole blood assays, phagocytosis assays, reactive oxygen release assays, analysis of cellular activation and determination of dendritic and macrophage cell subtypes, ELISA for assessing cytokine secretion and single cell analysis of skin lesions have been employed or are planned.

**Funding Source:** DFG
**Collaborating Institution(s):** University of Lubeck, University of Regensburg, Paul Elrich Institute
**Contract Period:** 2011-2016
**Current status:** Protocols optimized, field laboratory arrangement completed and sample collection started.
Clinical and molecular assessment of *Plasmodium vivax* chloroquine resistance and population genetic diversity in South Nations, Nationalities and Peoples Regional State (SNNPR), Ethiopia

- PI: Sisay Getachew
- Co-investigator(s): Beyene Petros, Abraham Aseffa, Rice. N. Price, Sarah Auburn

Despite the global effort to reduce death by plasmodium parasite, malaria continues to kill nearly a million individuals per year. The parasite is increasingly resistant to many of the commercially available drugs including chloroquine (CQ), which is used as the first line drug to treat *P. vivax* in Ethiopia. Treatment of *P. vivax* patients is further complicated by the parasite’s ability to live in dormant stages in liver (hypnozoites). Thus, distinguishing true CQ resistant *P. vivax* cases from those associated with re-infection or relapse cases by genotypic analysis will clarify the extent of true CQ resistance and help guide needed changes in treatment policy and other actions. The study is being conducted in Southern Ethiopia in areas where malaria incidence is high. More than 300 patients [Ziway, (N=57), Guba/Halaba (N=87), Shoine (N=87) and Kolla Shele (N=82)] were followed for over 28 days and blood samples were taken every 7 days after 3 days of treatment with CQ. 150 samples were also collected from nearby areas [Hawassa and Wondogenet] to determine *P. vivax* population diversity. Genotyping will be done by the PhD candidate at the Menzies School of Health Research, Australia, in November and December, 2013.

**Funding Source:** AHRI Core Budget, Addis Ababa University and Menzies school of Health Research  
**Collaborating Institution(s):** Addis Ababa University and Menzies school of Health Research, Australia  
**Contract Period:** 2012 -2014  
**Current status:** On-going

Ecology of Plasmodial infections in selected regions of Oromia, Ethiopia: Clonal diversity, prevalence of antimalarial drug resistance-conferring mutations & host genetic characterization

- PhD candidates: Lemu Golassa  
- Supervisors: Nizar Enweji, Berhanu Erko, Abraham Aseffa, Göte Swedberg

Prompt and effective malaria diagnosis not only alleviates individual suffering, but also decreases malaria transmission at the community level. The commonly used diagnostic methods, microscopy and rapid diagnostic tests, are usually insensitive at very low-density parasitaemia. Molecular techniques, on the other hand, allow the detection of
low-level, sub-microscopic parasitaemia. This study aimed to explore the presence of sub-microscopic Plasmodium falciparum infections using PCR technique.

PCR-based parasite prevalence was compared against microscopy and the rapid diagnostic test (RDT). The prevalence of sub-microscopic P. falciparum carriage was 19.2% (77/400) (95% CI = 15.4–23.1). Microscopy-based prevalence of P. falciparum infection was 3.7% (54/1,453) while the prevalence was 6.9% (100/1,453) using RDT alone. Using microscopy and PCR, the estimated parasite prevalence was 20.6% if PCR were performed in 1,453 blood samples. The prevalence was estimated to be 22.7% if RDT and PCR were used. Of 54 microscopically confirmed P. falciparum-infected subjects, PCR detected 90.7% (49/54). Out of 100 RDT-confirmed P. falciparum infections; PCR detected 80.0% (80/100). The sensitivity of PCR relative to microscopy and RDT was, therefore, 90.7% and 80%, respectively. The sensitivity of microscopy and RDT relative to PCR was 16.5 (49/299) and 24.2% (80/330), respectively. The overall PCR-based prevalence of P. falciparum infection was 5.6- and 3.3 fold higher than that determined by microscopy and RDT, respectively.

The study is the first in Ethiopia to uncover the presence of sub-microscopic malaria carriages given that malaria transmission is seasonal and unstable in the country.

Funding Source: AHRI Core budget and AAU graduate program
Collaborating Institutions: AHRI, AAU graduate program and Uppsala University
Contract Period: 10/2012-10/2014
Current status: Completed and manuscript is published

Therapeutic Efficacy of Artemether-lumefantrine for the treatment of uncomplicated Plasmodium falciparum Malaria in South Ethiopia

- PI: Seleshi Kebede
- Supervisors: Abraham Aseffa, Nega Berhe, Girmay Medhin, Peter G Kremsner, Thirumalaisamy P Velavan

With 75% of the Ethiopian population at risk of malaria, accurate diagnosis is crucial for malaria treatment in endemic areas where P. falciparum and P. vivax co-exist. The present study evaluated the positive predictive value of regular malaria microscopy using nested PCR as a reference in febrile patients. Positive P. falciparum slides from 314 febrile malaria patients were reevaluated for their infection status by nested PCR. Of these, seven patients (2%) were negative for any of the plasmodium species. Moreover, a high frequency of P. falciparum and P. vivax mixed infections was observed using nested PCR. Among 180 microscopically confirmed P. falciparum cases, 111 (62%) were diagnosed as P. falciparum and 44 (24%) were diagnosed as P. vivax. Of 131 microscopically confirmed P. vivax cases, 110 (84%) were diagnosed as P. vivax and 14 (11%) were diagnosed as P. falciparum. Plasmodium malariae were detected as 2 mono and 2 mixed infections in four individuals. Our finding indicated that there were
high numbers of misdiagnosis, false positivity and under report of mixed infections by 
regular microscopy which needs consideration by the responsible bodies.

**Funding Source:** AHRI Core Budget, Addis Ababa University  
**Collaborating Institutions:** University of Tuebingen  
**Contract Period:** 2011 - 2014  
**Current status:** On-going

### On-going MSc Studies

**The New Micro-culture Method (MCM) for the diagnosis of Cutaneous Leishmaniasis in Ethiopia**

- **PI:** Lensa Aberra  
- **Supervisors:** Endalemaw Gadisa, Geremew Tasew, Tariku Belay, Jemal Hussen, Mesefen Hunegnaw  
- **Project members:** Adugna Aberra, Haregewen Yetasha, Genet Amare

Despite the high burden of CL in Ethiopia, the exact magnitude of the disease is not well known. This is due to unavailability of health facilities with effective diagnostic capabilities and recording system at district level where many cases are found. Due to this, large numbers of cases are either undiagnosed or misdiagnosed. Currently available diagnostic methods are very expensive and difficult and thus cannot be used in the field settings. Recently, a newly method called the Micro-Culture method (MCM) has been developed in Turkey and Peru and was shown to be sensitive, rapid and cost effective to diagnosis CL caused *Leishmania tropica* and *L. major*. This study aims to evaluate the applicability of MCM for the diagnosis of CL caused by *L. aethiopica*.  
Cutaneous lesion samples were collected from 124 participants who came to the leishmania clinic of AHRI/ALERT and health centres of Ankober, Silti and Kella districts found in Ethiopia. The sensitivity and specificity of MCM was compared with other conventional diagnostic methods and the result shows that MCM is significantly more sensitive (95.8%) than the traditional culture method (72.9%) and smear microscopy (70.8%). In addition, the incubation period in MCM is reduced by 2 days compared to traditional culture. Moreover, there is a 76% cost reduction when using MCM. In general, in this study MCM was demonstrated to be a more sensitive, rapid and cost effective diagnostic techniques for CL caused by *L. aethiopica*. Thus, we recommend further detailed study involving a larger group of study subjects in the other parts of the country so that MCM can be seriously considered as an alternative diagnostic approach at national level.

**Funding Source:** AHRI core budget  
**Collaborating Institution(s):** Ethiopian Health and Nutrition Research Institute (EHNRI) and Jimma University (JU)  
**Contract Period:** 2012-2013  
**Current status:** Completed; Thesis will be defended soon.
Leprosy Team

In spite of therapeutic success achieved with multidrug therapy (MDT), still more work is needed to significantly decrease new leprosy cases. The team is currently working on different research projects with the aim to develop new and improved diagnostic tests, investigate transmission, immunopathology and genetic susceptibility.

Together with Leishmania, Malaria and Neglected tropical disease (NTD) team members, who have experience in disease mapping, the team is intending to work on mapping hot spot leprosy areas in Ethiopia, alongside with other priority research areas, to generate evidence based findings which can be transformed into practice to assist the existing leprosy control strategy.

Team Members

- Dr. Abraham Aseffa, Scientific Director and Senior Scientist
- Dr. Demissew Beyene, Postdoctoral Scientist and Training Coordinator
- Mrs Kidist Bobosha, PhD candidate
- Dr. Markos Abebe, Postdoctoral Scientist and TB team coordinator
- Mrs. Martha Zewdie, PhD candidate
- Yonas Bekele, Assistant Researcher
- Tadeye Abeje, Assistant Researcher
- Mrs. Tsehaynesh Lemma, Researcher
- Edessa Negera, PhD candidate
- Nigussie Seboka, M.Sc student

Research

Assessment of the Performance of general health workers in leprosy control activities at public health facilities, in Amhara and Oromiya regions, Ethiopia

- PI: Tadeye Abeje
- Co-investigators: Eshetu Kebede, Kidist Bobosha, Ismaile Hassen, Tsehaynesh Lema, Lawrence Yamuah, Birru Shiguti, Melkamu Fenta, Megersa Negasa, Demissew Beyene, Tsegaye Hailu, Abraham Aseffa

Despite the availability of drugs to treat leprosy and curb its transmission, the prevalence and annual incidence of new cases is persistently high for the past 10 years in Ethiopia. More than 80% of the reported new cases were from Oromia and Amhara regional states. This study is designed to assess the knowledge, skill and attitude towards leprosy of general health workers at public health facilities in these two regions. The study showed that the majority of health workers had poor knowledge in recognition of the early signs and symptoms of leprosy, reaction and its management. The attitude of health workers was also found to be unfavorable towards leprosy suspects and people affected by leprosy. The skill of general health workers was also found to unsatisfactory; the majority of them were unable to perform sensation testing and voluntary muscle testing. The performance of health workers is strongly associated
with the level of qualification, in-service trainings and previous exposure to leprosy work. In order to improve the skill, knowledge and attitude of health workers, continuous training and health education on leprosy should be emphasized at pre-service and in-service levels.

**Funding Source:** AHRI core budget  
**Collaborating Institutions:** -  
**Contract Period:** 2011-2013  
**Current status:** Manuscript is prepared to disseminate the finding from this study but it is not yet submitted to a selected journal for publication.

**On-going PhD Studies**

Development of novel tools for early detection of *M. leprae* infection and Leprosy reaction

- **PI:** Kidist Bobosha  
- **Supervisors:** Annemieke Geluk, Abraham Aseffa, Tom Ottenhoff  
- **Co-investigators:** Yonas Bekele, J.J van_der_Ploeg van_Schip, Louis Wilson, Krista Meigaarden, Markos Abebe, Martha Zewdie

Leprosy is still a challenging disease as the current diagnostic techniques and tools are not able to detect the disease at an early stage. The availability of whole genome sequence of *M. leprae* has brought better opportunity in leprosy diagnostic research and development. In this study, several recombinant *M. leprae* specific proteins and peptides were tested for their immunogenicity and ability in detecting highly exposed individuals. Among the identified biomarkers, IP-10 was further tested in Up converting Phosphor based lateral Flow assay (UCP-LF) in dry preparation at Leiden University Medical Center (LUMC) and AHRI and the results in both settings were comparable. In addition, the results from the UCP-LF and ELISA assays showed good correlation indicating the potential of the IP-10 based UCP-LF assay for larger field applications.

**Funding Source:** NLR/ Leiden University Medical Center, WHO/TDR, IDEAL and AHRI core budget  
**Collaborating Institutions:** LUMC  
**Contract Period:** 2009-2013  
**Current status:** Writing up of the PhD thesis is completed and submitted for the faculty to be approved for defense

**The Immuno-pathology of Erythema Nodusoma Leprosoma**

- **PI:** Edesa Negera  
- **Co-investigators:** Diana Lockwood

Type 1 (T1R) and type 2 (erythema nodosum leprosum or ENL) leprosy reactions occur in 20-30% of leprosy patients. In spite of a substantial body of detailed descriptive information, factors which precipitate these reactions are poorly understood.
ENL is an inflammatory complication with fever, malaise, and crops of painful erythematous nodules. Though there is evidence which supports cell mediated immunity playing an important role in the pathogenesis of ENL, no circulating or fixed immune-complexes have been demonstrated as a sole cause of ENL. Hence, investigating mechanisms of immunopathology in ENL is essential to understand the development of the disease and to improve immunotherapy. We hypothesize that ENL initiated by activated T cells following decreased frequency of regulatory T cells and perpetuated by immune-complex formation and deposition in skin tissues. This is a case-control study will be done and phenotypic properties of cellular immunity will be investigated from blood samples.

**Funding Source:** London School of Hygiene & Tropical Medicine (LSTHM)

**Collaborating Institutions:** LSTHM

**Contract Period:** 2012-2015

**Current status:** The project has obtained ethical approval from AHRI/ALERT ethical review committee and is now submitted to the national ethical committee

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**On-going MSc Studies**

**Haptoglobin gene polymorphism amongst patients with leprosy in Ethiopia**

- **PI:** Nigussie Seboka
- **Supervisors:** Endashaw Bekele, Demissew Beyene
- **Co-investigators:** Yonas Bekele, Shimelis Nigussie

Haptoglobin (Hp), which is encoded by the Hp gene, located on chromosome 16q22, is a hemoglobin-binding protein. It has antioxidant and immune-modulatory properties which are crucial for innate immune response. There are clear functional differences between the genotypes which include differences in modulation of oxidant stress, recycling of hem-iron, and immune function. The immune-modulatory activity of haptoglobin during infection prevents Th1-Th2 imbalance due to the development of various pathologic conditions which has been seen in different infectious diseases. The aim of this study is to assess the Hp gene allele frequency relationships with leprosy disease among leprosy patients at ALERT hospital.

**Funding Source:** AHRI core budget

**Collaborating Institutions:** ALERT hospital

**Contract Period:** 2012-2013

**Current status:** On-going
HIV and Sexual Transmitted Diseases Team

The HIV team has been established in AHRI since mid-2000, where research on HIV, STI and other viral infections are embraced. The team was re-established again early this year with aim the aim of engaging researchers working in the area of HIV research and other sexually transmitted infections. Since ALERT Hospital is also one of the centers that provide clinical care and services for HIV and STD, the team has envisaged its research activities by engaging physicians working in the Hospital. Research in the team includes immune-pathogenesis, epidemiology and patients care.

Team Members

- Dr. Rawleigh Howe, Senior Scientist
- Dr. Adane Mihret, Post-doctoral scientist
- Dr. Liya Wassie, Post-doctoral scientist
- Yonas Bekele, Researcher
- Tadeye Abeje, Researcher
- Milikit Aytenew, Lab technologist
- Kassu Alemayehu, Lab technologist
- Melaku Adal, PhD student
- Melat Tsegaye, Master’s student
- Mikias Negash, Master’s student

Research

On-going PhD Studies

Role of HLA polymorphism in driving HIV variation and influencing disease progression in HIV infected individuals in four hospitals in Addis Ababa, Ethiopia

- PI: Melaku Adal
- Supervisors: Dr. Rawleigh Howe with technical assistants from Milikit Aytenew and Kassu Alemayehu

The overall aim of this study is to assess the different HLA polymorphisms during HIV infection that have role in HIV disease progression. Gag, nef and pol genes of HIV isolated from HIV positive individuals prior to therapy will be sequenced and compared with high resolution HLA typing to identify putative HIV escape gene mutations associated with distinct HLA allelic polymorphisms within the peptide binding pocket. In parallel, peptides corresponding to candidate gene regions of interest will be assessed for CD8 T cell stimulatory properties in vitro. The study is a collaborative study between Oxford University, London and AHRI. Thus far, about 600 blood specimens have been collected several local hospitals.

Funding Source: AHRI core budget and Oxford University
Collaborating Institution(s): Oxford University, London
Contract Period: 2012-2016
Current status: Sample collection completed; viral sequencing of isolates from these samples in the upcoming year.
Immunological Response to HBV Vaccine in Children: The Impact of HIV infection in the vaccine response in Addis Ababa, Ethiopia

- **PI**: Yonas Bekele
- **Supervisors**: Rawleigh Howe, Abraham Aseffa, Francesca Chiodi, Anna Nilsson
- **Collaborators**: Meseret Gebre and Kidist Bobosha

The prevalence of Hepatitis B virus (HBV) infection in Ethiopia and other sub-Saharan African countries often approaches 50%, and this underscores the importance of the HBV vaccine. However, this and other vaccines are known to elicit suboptimal immune responses in HIV patients, indicating that either improved vaccination scheduling or improved vaccines are needed in this population of individuals. Most studies documenting HBV vaccine responses among HIV patients have been in adults; few have been performed in children. The overall aim of this study is to evaluate serological response to HBV vaccine in HIV positive and negative children, aged between 3 and 8 years who have no prior exposure to HBV vaccine or infection and further assess the functional and phenotypic properties of memory B cells to HBV vaccine.

**Funding Source**: KI and Swedish Medical Research Council.
**Collaborating Institution(s)**: Karolinska Institute (KI), Sweden
**Contract Period**: 2013-2015
**Current status**: On-going

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Immunological response to rotavirus vaccine in HIV-1 infected infants in Addis Ababa, Ethiopia

- **PI**: Yonas Bekele
- **Supervisors**: Rawleigh Howe, Abraham Aseffa, Francesca Chiodi, Anna Nilsson
- **Collaborators**: Meseret Gebre and Kidist Bobosha

Diarrheal diseases are the common cause of considerable morbidity and mortality worldwide especially in HIV-1 infected children in Africa. Rotavirus is recognized as one of the most frequent causes of severe diarrheal disease especially in infants and young children, though a significant disease burden can be reduced by vaccination. However, impaired responses to childhood vaccinations have been reported in HIV-1-infected children despite successful antiretroviral therapy. The aims of the current study are to assess the antibody response at 1, 6 and 12 months after Rotavirus vaccination in HIV positive and negative infants, to compare the impact of HIV on the Rotavirus vaccine efficacy with that of other childhood vaccines (measles, HBV) previously studied in HIV positive infants; and to assess the cell surface expression of molecules involved in B cell survival and apoptosis in HIV positive and HIV negative infants both pre and post rotavirus vaccination.

**Funding Source**: KI and Swedish Medical Research Council
**Collaborating Institution(s)**: Karolinska Institute (KI)
**Contract Period**: 2014-2016
**Current status**: On-going
Evaluation of multiple micronutrients and aloe inner leaf gel extracts in a pediatric HIV population in Addis Ababa, Ethiopia

- **PI:** Mary van der Wal
- **Co-advisors:** Rawleigh Howe, Solomie Derebesa, Meseret Gebre, Vilma Yuzbasiyan-Gurkan, Linda Mansfield, James Resau

HIV is a complex disease characterized by chronic immune activation, chronic inflammation, increased oxidative stress and immune dysfunction. Gut associated lymphoid tissues (GALT) lining the entire intestinal tract is a major region of HIV replication and associated damage. While HAART is of benefit in reducing viral titers in the periphery and slowly restoring lymphocyte numbers, immune function remains compromised for some time in many individuals, and increased markers of oxidation stress and inflammation only slowly normalize and rarely return to baseline levels. Persistent viral replication within the gut of patients on HAART has been described. Children in the developing world have additional burdens placed on their immune function by endemic intestinal helminthes, exposure to increased numbers of pathogens and chronic malnutrition. Malnutrition can suppress thymic function, further impacting immune restoration. These additional burdens result in broader support needs that are not addressed by HAART. Little research is conducted in developing countries so the impact of these and measures to address them have not been thoroughly explored. The proposed clinical trial with HIV+ children in Ethiopia will seek to evaluate the impact on intestinal mucosal integrity, immune activation, immune restoration, and clinical outcomes following supplementation with a multiple micronutrient blend and processed aloe gel (PAG) supplementation. The addition of these simple and inexpensive measures to the treatment regimens of children in developing countries warrants further investigation.

**Collaborating Institution (s):** AHRI

**Completed MSc studies**

T cell activation, Proliferation and Memory Differentiation in Ethiopian HIV Patients

- **PI:** Mekdes Meaza
- **Supervisors:** Samual Kinde, Markos Abebe, Abraham Aseffa and Rawleigh Howe

Enhanced immune induction is a hallmark of HIV pathogenesis. It is elicited in response to HIV itself, and indirectly by opportunistic infections or as a consequence of intestinal inflammation and mucosal disruption. The vast majority of work has defined induction processes before ART or following successful ART, but our understanding of induction processes in patients experiencing treatment failure (TxF) is limited. In order to explore induction parameters, flow cytometric approach was used to evaluate populations of activated (HLA-DR+CD38+T cells), proliferating (Ki-67+ T cells) and naïve and memory subsets of T cells (defined by expression of CD62L and CD45RO) from HIV+ subjects.
with low CD4 counts, HIV+ individuals with high CD4 counts, HIV+ TxF subjects, and HIV negative control subjects. Our result indicated that individuals with treatment failure appear to have a unique induction parameter phenotype which allows discrimination between other groups of HIV positive and HIV negative individuals. We recommend future studies with larger samples sizes of a prospective design to confirm and extend these findings.

**Funding Source:** AHRI core budget  
**Collaborating Institution (s):** ALERT hospital and St. Paul Millennium College ART centers  
**Contract Period:** July 2011 - March 2013  
**Current status:** Completed

### On-going MSc studies

**HIV-1 Gag specific poly-functional, proliferative and cytolytic CD8 T-cells response in elite controllers and long term non-progressors in Addis Ababa, Ethiopia**

- PI: Melat Tsegaye  
- Supervisors: Nebiat Gebreselassie, Rawleigh Howe, Beyene Petros, Dawit Wolday

Current vaccine strategies for protection against HIV infection are focused on comparisons of cohorts with or without disease progression. A small percentage of individuals (1%), so called “Elite Controllers (ECs)” are able to contain the virus without any medication. Though these individuals are tested positive by standard HIV antibody tests, they lack measurable virus in plasma by standard clinical assays (i.e., plasma viral loads are consistently below 50–75 RNA copies/mL) and have CD4 count at least above 500 cells/ul. One of the immune system features exhibited by elite controllers is the presence of high frequencies HIV specific of poly-functional CD8+ T-cells, which display properties of both conventional CD8 CTL as well as CD4 helper T cells. In this study, we propose to confirm and extend previous findings by evaluating HIV gag peptide specific IFN-γ, IL-2 and TNF-α and IL-21 cytokine production, surrogates of cytotoxic T cell function (evaluation of CD107 and de novo synthesized perforin) in relation to in vivo proliferation of CD8+ T-cells from elite controllers, ART naïve HIV chronic progressors with CD4 count less than 500 cells/ul, and HIV chronic progressors on ART.

**Funding Source:** AHRI core budget  
**Collaborating Institution (s):**  
**Contract Period:** 2012-2014  
**Current status:** Ethically approved; sample collection on the way
Analysis of co-receptors and innate immune markers in HIV-1-exposed seronegative subjects (HESNs)

- **PI**: Markos Negash
- **Supervisors**: Afework Kassu, Beyene Moges, Liya Wassie

Serodiscordance of HIV, whereby sexual partners of HIV positive individuals remain HIV seronegative, occurs in a small fraction of couples. Although the role of genetic and adaptive immune factors in this protection have been well studied, fewer studies have explored innate immune function in HIV exposed seronegative. In this study, we hypothesize that expression and function of innate immune cell markers, in particular TLR 7, known to be an innate receptor for HIV, alleles of KIR gene products on the surface of NK cells, as well as NK lytic function, are significant factors contributing to protection in HIV-exposed seronegative individuals. Using RT-PCR and ELISPOT approaches we will evaluate these markers in both partners of discordant couples as well as healthy individuals,

**Funding Source**: AHRI core budget
**Collaborating Institution (s)**: University of Gonder
**Contract Period**: 2012-2013
**Current status**: Ethically approved; sample collection on the way

Assessment of peripheral γδ T cells: phenotypic and functional heterogeneity in singly and dually infected HIV-TB patients in Addis Ababa, Ethiopia

- **PI**: Mikias Negash
- **Supervisors**: Rawleigh Howe, Liya Wassie

γδ T cells comprises minor subsets (<5%) of the circulating CD3+ T- lymphocytes. An increase in relative and absolute number of γδ T cells, however, has been described in peripheral blood of HIV-1 seropositive individuals as well as in HIV patients co-infected with *Mycobacterium tuberculosis*. Different studies indicate that the increase in γδ T cells in HIV patients is mainly attributed by the Vδ1 subset, thought to be expanded in response to HIV antigens; rather such cells may be redistributed from mucosal areas. The predominant Vγ2Vδ9 subset in healthy individuals is found to be quantitatively and qualitatively defective in HIV infection, and inconsistent results have been reported in HIV/Mtb co-infection. This study is aimed to analyze the profile of subsets of γδ T cells with respect to expression of activation (CD38), proliferation (Ki67), adhesion (α E β7, CD56), and exhaustion (PD1) markers, and functional cytokine production in HIV positive patients with and without Mtb disease.

**Funding Source**: AHRI core budget
**Collaborating Institution (s)**: -
**Contract Period**: 2012-2014
**Current status**: Ethically approved; sample collection is underway
New MSc studies

Seroprevalence of Cytomegalovirus and Hepatitis E Virus among Pregnant Women in Ghandi Memorial and Yekatit 12 hospitals, Addis Ababa, Ethiopia

- PI: Meseret Abebe
- Supervisors: Ibrahim Ali, Adane Mihret, Abraham Aseffa, Rawleigh Howe

Hepatitis E is a common cause of pregnancy related hepatitis and is associated with significant morbidity and mortality. Cytomegalovirus infection, while mild or asymptomatic in most individuals can have devastating consequences on fetal development during the first trimester of pregnancy. The overall aim of this study is to determine the seroprevalence of CMV and HEV among pregnant mothers in Addis Ababa. The study is a collaborative study between AAU and AHRI, where the funding is covered by AHRI core budget. The study has been initiated in the middle of the year and is expected to end next year.

Funding Source: AHRI Core budget
Collaborating Institution (s): -
Current status: Starting
Support Units

Biostatistics Unit

The Biostatistics unit makes an effort to provide answers to statistical inquiries from AHRI staffs and students starting from survey design (sample size determination, choosing appropriate study design, data entry...etc) to data analysis and interpretation of results. The unit offers trainings and consultations in statistical methods and applications and strives to introduce different methods and applications in line with the demand of study objectives. Legese Negash, who joined AHRI in 2013 has replaced Yoseph Kana as team leader.

Data Management Unit (DMU)

The mission of the Data Management Case Team is to contribute quality data management and statistical analysis for researchers and students.

Since December 2003 (the time the Data Manager was employed), there has been a gradual transformation from no proper back-ups of the units data, no archiving, no dedicated person for the unit’s data and no proper filing and documentation system to well established Data Management Centre that is operating according to acceptable practice for both generalized and clinical trials data management procedures.

He has been supported by a team of dedicated data management staff who have worked tirelessly to establish good and implemented procedures for questionnaire or CRF and database design, double data entry with good verification and validation, data analysis, good back-up, filing and archiving system all of which have greatly enhanced the security and confidentiality of the unit’s and collaborator’s data.

Team Members

- Dr. Lawrence Yamuah, DM Case Team Leader and Senior Scientist / Data Manager
- Tsegaye Hailu, Interface Leader and Assistant Data Manager
- Hiwot Tilahun, Biostatistician
- Wondu Wagaye, Data Entry Clerk
- Samuel Ayele, Data Entry Clerk
- Hilina Tadious, Data Entry Clerk
- Meseret Tilahun, Data Entry Clerk
List of Projects actively supported by the unit

- AETBC with EDCTP
- Cholera Vaccine Trial
- STREAM Project
- Leishmaniasis Project
- GC6
- BTB Vaccine Trial
- Cancer Project
- Bio-Equivalence Project
- Capstone Student Project
- Knowledge and self-care practice of leprosy patients and factors associated to self-care in ALERT Addis Ababa:
- Hospital Service Satisfaction in ALERT Addis Ababa
- Cyclosporine study
- Surveillance of Bacterial Meningitis in Ethiopia

Laboratory Unit

The laboratory management team is responsible in the overall organization of AHRIs’ laboratory. It works to create conducive research environment to all end users including research staffs, students and visitor. In the past year, different activities were performed including preparing new SOPs (n=80), up-dating existing SOPs (n=20), and organizing safety and GCLP training.

The laboratory is comprised of 8 units (see below) each of which managed by responsible person with the overall coordination by the lab manager, Nigatu Endalafir.

- Clinical trial
- Containment-3 TB Laboratory
- Immunology
- Molecular Biology
- Bacteriology
- Pathology
- Engineering
- Support staff

The lab owns real-time PCR, conventional PCR, FACScanto, Luminex e, Elispot reader, ELISA washer and reader, clinical chemistry analyzer and Hematology analyzer Machines.

Project Management Office (PMO)

The project management office (PMO) oversees more than 60 projects including masters and PhD research works. The office has recently been set up in a new way and constitutes project managers, researchers, and finance and procurement staff members. The unit primarily is established to:

- Follow project operations
- Ensure effective use of funding
- Collate and report project status to senior management and collaborators
- Manage project documentation
- Compile and update on project status
- Monitor projects achievement
- Search and distribute grant calls
- Provide technical review of grants and initiate submissions

In the future, the office aims to use standard project management practices throughout the organization by employing automated project management system which will facilitate monitoring, easy retrieval and communication of project related information.

**AHRI/ALERT Ethics Review Committee**

**Mission:** Facilitate ethical review processes at AHRI and ALERT for study protocols conducted at AHRI and ALERT Hospital  

**Number of members:** 12  

**Secretariat:** Dr. Liya Wassie, Prof. Getachew Tilahun, Kalehiwot Mekonnen and Hirut Solomon

**Accomplished tasks:**

- Number of execute meeting held: 11 regular and 15 expedited  
- Protocols reviewed: 56 [30 full board and 26 expedited]  
- Status of protocol applications: 39 approved, 9 resubmitted, 7 resubmitted and approved; 8 pending  
- Training: Supported two postgraduate diploma training on bioethics  
- Developed institutional guideline and SOP on bio-banking and use of stored specimen and assessment tool to review social and behavioral sciences  
- Hosted a workshop for 25 participants coming from different Institutional Review Boards (IRBs)
Initiatives

One Health Group

The majority (60%) of all infectious diseases is of zoonotic nature, and of these over two thirds have a wildlife reservoir. Diseases in animals threaten public health, ecosystem health, biodiversity and can have severe economic burden at individual and societal level. Since pathogens are shared by people, animals (domestic and wild) and the environment, their control has to include a holistic approach, hence the One-Health concept. The positive impact on public health is often highest when the disease is controlled in the animal reservoir (e.g Brucellosis, Bovine tuberculosis, rabies).

This new research group started in 2011, with the aim at doing One-Health research in zoonoses that include rabies, BTB, Brucellosis. The group intends also be involved in pastoral health in Ethiopia at the human-animal-ecosystem interface.

The first phase of the One-Health project in Awash, funded by AHRI and investigating the epidemiology of BTB, brucellosis and rabies around Awash National Park was finished.

This year’s priority was less in field work and more in writing grants to secure funding for future projects so that post-graduate students and collaborators can join the team. The group was also involved in several One Health meetings in Ethiopia to share their expertise (Universities, FAO, SNV, DFID, IMC, SDC). Networking, synergistic activities with among others EWCA, FAO, WHO and publishing manuscripts were further priorities.

The One Health activities at AHRI are coordinated by Dr Rea Tschopp who leads the initiative.

Capacity Strengthening for Operational Research (OR) in Tuberculosis

Objective: Strengthen problem solving operational research within the health services

Background: A TB Research Advisory Committee (TRAC) was established under the chairmanship of AHRI in 2001 to coordinate research support to the Ministry of Health TB program. It has conducted national TB conferences and funded research methodology courses since. The function was integrated into the Ministry of Health Stop TB Partnership in 2009 and is now a mechanism within the MoH.

Current status: The TB Research Advisory Committee (TRAC) chaired by AHRI has been leading capacity building efforts on operational research (OR) on TB in Ethiopia. In 2012, TRAC facilitated the development and endorsement of an OR Roadmap for Ethiopia defining research priorities. A first activity under the road map was the development of the capacity building for operational research on TB in Ethiopia (CORE-TB) initiative in collaboration with the IUATLD, KNCV and USAID TBCARE-I hosted at AHRI. The project will run for 3 yrs and is expected to generate policy relevant data for improvement of national TB control. In 2013, the project strengthened its Secretariat at AHRI and launched training for regional health workers. Regional teams have developed project proposals in two separate cohorts so far. A second major milestone was the
call for proposals to be funded by TRAC to which Letters of Intent have been received and proposals to be funded selected. The preparations for the 9th Annual TB Research Conference are underway with the SNNPR and Hawassa University, this year’s hosts. Fasil Tsegaye and Dr Daniel Fisseha lead the TRAC Secretariat hosted at AHRI funded by TBCARE/USAID.

AHRI-AAU Biomedical Science Postgraduate Training Partnership Program (BSPP)

The dramatic expansion of postgraduate intake at Addis Ababa University runs the risk of compromising quality in biomedical research and training unless it is supported by targeted development of selected research leaders in universities to serve as nuclei for building a critical mass of scientists. The Armauer Hansen Research Institute (AHRI) has a strong track record of postgraduate student training in biomedical sciences for Addis Ababa University by exposing them to its own and partner laboratories at international Centers of Excellence and supporting high quality research by the candidates.

Objective: A pilot biomedical science postgraduate program is proposed to train research leaders for biomedical departments of regional universities in collaboration with Addis Ababa University.

Activities: Research support and training awards will be given to the best 10 PhD students in medical microbiology, genetics and biotechnology registered at AAU. A bridging course in research leadership and laboratory training at AHRI and collaborative partner institutions in Sweden will be supported. Each PhD candidate will conduct research over 4 years and participate in training of Masters and undergraduate students meantime. Upon graduation, the young scientist will be provided with a small grant to start his/her own research at the Department. The project will support Sabbaticals for AAU Professors and short term exposure of postdoctoral scientists of the relevant departments at the AAU to collaborating Swedish laboratories. AHRI will provide laboratory access and thesis supervision as well as project management. The estimated cost to support 10 PhD theses, 10 postdoctoral fellowships and 10 sabbaticals in five years is 1.6 million USD (about 320,000 USD/year). At least 5 Biomedical Departments in the regional universities and 5 Departments in AAU will have strengthened their Biomedical Science training quality with highly qualified young scientists and research leaders in the pilot project.

Expected outcome: The core capacity will have a ripple effect on quality education in biomedical research.

Current status: Grant obtained from Sida. Discussions underway with the Addis Ababa University Office of the Vice President for implementation.

Risks and mitigation:

- Possible lack of continued support for the project by partners. Will need additional funders to join the program. Effort underway with NORAD.
- Possible lack of acceptability by students and faculty - negative attitude to "double standards": Establish a transparent competitive recruitment based on merit using an independent body of reviewers and advisory board.
Ethiopia-Emory TB Research Training Program (EETB-RTP) (text taken directly from the application now funded)

The Ethiopia-Emory TB Research Training Program (EETB-RTP) represents a partnership between Emory University in Atlanta (USA) and three Ethiopian institutions in Addis Ababa including the Armauer Hansen Research Institute (AHRI), an internationally respected research institute focused on TB investigation; Addis Ababa University (AAU), a degree granting university which is the oldest and largest university in Ethiopia; and the Ethiopian Health and Nutrition Institute (EHNRI), a national public health institution that is part of the Ethiopian Federal Ministry of Health. The EETB-RTP is focused on providing didactic and mentored TB research training for promising Ethiopian investigators; the goal is to provide trainees and their institutions with the skills and capacity to carry out internationally relevant TB-related research (e.g., clinical and/or translational research, epidemiologic research, implementation science [sometimes also called operational research], behavioral/social sciences research, and laboratory based research). The EETB-RTP is funded by a Global Infectious Diseases grant from the U.S. National Institutes of Health (NIH) Fogarty International Center.

Specific Aims of the program include:

1. **To build human resource capacity and enhance the research infrastructure for high quality TB-related research in Ethiopia** by providing research training and research opportunities in TB to a diverse group of Ethiopian researchers with outstanding potential. This includes providing opportunities for research training in relevant laboratory, clinical, translational, epidemiologic, implementation science and behavioral/social science related research. Didactic research training occurring in Ethiopia through Master and PhD-degree programs at AAU will be augmented through the EETB-RTP using high quality, semester long, distance learning courses delivered by faculty at Emory University (Atlanta, USA) via real-time web-based videoconferencing as well as through intensive short courses carried out in Ethiopia. A comprehensive mentoring program for trainees, which includes both Ethiopian and internationally based mentors, will also be an important program component.

2. **To build sustainable research capacity in Ethiopia in order to enhance prevention, detection, treatment, and control of TB, and the evidence-based translation of research to improve public health practice and strengthen the public health infrastructure.** This requires the development and mentoring of a critical mass of scientists and health professionals with in-depth scientific expertise and complementary skills that enhance the capacity of collaborating institutions to conduct internationally-recognized research that is relevant to Ethiopia.

3. **To enhance opportunities for multidisciplinary TB-related research and collaboration.** Many trainees may elect to focus on a theme for research training that is tied to a major health priority in Ethiopia, namely enhancing the TB case detection rate and detection and treatment of drug resistant TB including multidrug resistant (MDR) and extensively resistant (XDR)-TB.

4. **To enhance in-country research ethics training in Ethiopia** for TB-related trainees and investigators, collaborators, and members of Institutional Review Boards (IRBs).
**Long-Term Training Activities**: Long-term training is the most important component and focus of the EETB-RTP given the program’s goal to develop a cadre of multidisciplinary researchers who are successful and funded investigators that carry out internationally recognized TB-related research and translate research findings into practice and public health policy (Specific Aim 1). There will be 3 options or tracks for long-term training:

1. **PhD graduate degree program/pre-doctoral research training**: PhD graduate students at AAU (in the Biomedical Sciences, Behavioral/Social Sciences, Public Health or Patho-biology) who are committed to a research career that encompasses TB-related investigation will be eligible to apply to the program. In general, PhD students will have completed their core course work before they are accepted into the EETB-RTP. These students at AAU will generally be entering the thesis stage of their PhD degree program at the time of acceptance to our program. The EETB-RTP will provide didactic and mentored research training for long-term trainees including PhD students with the expectation that their thesis is focused on TB-related hypothesis-driven research. Didactic training provided by the EETB-RTP (at a minimum) will include the three Emory University graduate school distance learning courses (Scientific and Grant Writing, Biostatistics, and Data Management). In addition to the program for training graduate students in their last two years of their PhD degree program, support will also be provided to selected current EHNRI staff (who have a Master degree) for support for the entire 4-year PhD program given the limited number of PhD level scientists with research expertise at that institution.

2. **Postdoctoral research training with opportunities through the EETB-RTP for didactic training including graduate degree programs (e.g., MPH or MSc degree)**: Postdoctoral trainees, including junior faculty members at AAU (MD or PhD), postdocs (PhD or clinical fellows) or MD or PhD-level scientists at the three Ethiopian institutions (AAU, AHRI, EHNRI), who are interested in obtaining further didactic training to provide a foundation for a career in TB-related research are included in this track. All long-term trainees (in any of the tracks) will have their graduate degree program at AAU supplemented by the three semester long Emory University graduate school distance learning courses as well as short courses and workshops and will have protected time for didactic and mentored research training. A number of postdoctoral trainees in this track will likely focus on clinical and translational research training including Implementation Science research. The new AAU Master of Science in Research Methodology provides an ideal training vehicle for such trainees from any of the three Ethiopian institutions who are interested in careers in clinical investigation.

3. **Postdoctoral research training opportunities through non-degree training**: Training opportunities for long-term trainees includes providing opportunities for research training in relevant laboratory, clinical, translational, epidemiologic, implementation science and social science related research. These trainees will also take the three Emory University distance learning courses but would be in a non-degree program.

**Support for Long Term Trainees**: Those long term candidates accepted into the EETB-RTP will be supported for two years of didactic and mentored research training (EHNRI staff will be eligible to receive up to 4 years of support). The second year of support is dependent upon satisfactory performance in the first year of the program. Long term trainees accepted into the EETB-RTP will receive:
UK-Africa Genomics and Global Health Research Centre -
Wellcome Trust Centre for Global Health Research

The Centre will build capacity for independent research at three LMIC partner institutions, fostering environments that empower scientists to contribute to a wider African research enterprise.

The targets of the Centre are:
1. Generic research skills workshops run annually at each African institution.
2. Four specific skills courses run in African Institutions over the 5 years focusing on specific areas identified as being important by these institutions.
3. Fifteen fellowship applications will be written during the 5 years of this project, recognizing the importance of developing a range of scientists from those needing basic research training to supporting senior fellows as research leaders who can independently sustain the development of future researchers.
4. At least one collaborative grant on global health or genomics obtained by each institution through competitive application in the course of the project: our ability to respond as a network to other grant calls will make this a realistic goal.
5. Genomics research teams established or strengthened at each African institution with competence improved through technology and skills transfer as a result of above training.
6. By the end of the project, at least one summer course on genomics and global health run at each African institution using local expertise, demonstrating competence for possible sustainable regular programmes. This will guarantee that the UK partners have transferred basic lasting competence through the grant.
7. Development of university courses e.g. Masters Courses in Ethics and Genomic Research once institutional capacity has been build.
Post-graduate Training

Training of students (Masters, PhD and summer interns) is one of the key missions of AHRI. Students registered at different Ethiopian Universities are accepted annually to do their thesis work with the supervision of AHRI scientists. The tables below shows list of students that are working at AHRI towards their master’s and PhD degree in 2012/2013.

Masters students

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<th>Name of students</th>
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<tr>
<td>Emebet Mohammed (F)</td>
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<tr>
<td>Lensa Aberra (F)</td>
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</tr>
<tr>
<td>Mahlet Birku (F)</td>
<td>On Progress</td>
</tr>
<tr>
<td>Markos Negash</td>
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</tr>
<tr>
<td>Martha Alemayehu (F)</td>
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<tr>
<td>Mikias Negash</td>
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<td>Minwuyelet Maru</td>
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<tr>
<td>Nejat Juhar (F)</td>
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<tr>
<td>Nigus Zegeye</td>
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<tr>
<td>Nigussie Seboka</td>
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<td>Silenat Biresaw (F)</td>
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<td>Sileshi Abdissa</td>
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<tr>
<td>Tekle Airgecho</td>
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<td>Zerihun Yaregal</td>
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# Doctoral Students

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<td>Ibrahim Ali</td>
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<td>Kidist Bobosha (F)</td>
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<tr>
<td>Lemu Golassa</td>
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<tr>
<td>Martha Zewdie (F)</td>
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<td>Markos Abebe, Gelila Tesfaye</td>
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<td>Selected participants from Ethiopian Universities and research institutes</td>
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<td>Gelila Tesfaye</td>
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Publications – 2012/2013


10. Dakar discussion group on priorities for research on epidemic meningococcal disease in, A., D. Altmann, A. Aseffa, M. Bash, N. Basta, R. Borrow, C. Broome, D. Caugant, T. Clark, J. M.


### ARMAUER HANSEN RESEARCH INSTITUTE (AHRI)

**STATEMENT OF INCOME AND EXPENDITURES**

**FOR THE YEAR ENDED DECEMBER 31, 2012**

<table>
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<tr>
<th>Notes</th>
<th>INCOME</th>
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#### Government

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#### Contract (Full time)

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## Contract (Part time)

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<td>Amha Ademe Tesfaye</td>
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Funders, Partners & Collaborators

Federal Democratic Republic of Ethiopia
Ministry of Health

Norad

Sida

SWEDISH INTERNATIONAL DEVELOPMENT
COOPERATION AGENCY

Addis Ababa University

World Health Organization

Karolinska Institutet

CORDIS

European Commission

TDR

For research on
diseases of poverty
UNICEF • UNDP • World Bank • WHO

Global Health and Vaccination Research (GLOBVAC)

Norwegian Institute of Public Health

EDCTP

menafrican

African Meningococcal Carriage Consortium

wellcome trust

Bill & Melinda Gates Foundation

Swiss TPH

Swiss Tropical and Public Health Institute
Schweizerisches Tropen- und Public Health-Institut
Institut Tropical et de Santé Publique Suisse
Institute Information

Armauer Hansen Research Institute (AHRI)
Jimma Road, ALERT campus
Tel +251-113-483752
Fax +251-113-211563
www.ahri.gov.et