Collaborating Sites with attached laboratories, hospitals and field sites:

Bhubaneswar/Odisha:  Asian Institute of Public Health AIPH Head Quarters with four hospitals and three field sites.

KEM Medical College Mumbai: Collaborating site (multicenter ICMR study of antibiotics resistance)

Government Medical College, Puducherry: Collaborating site (multicenter ICMR study of antibiotics resistance)

All India Institute of Medical Sciences, Delhi: Reference lab

Field Sites (in Odisha) – Each field site has an attached hospital, laboratory, and a data center:

- Sundergarh district (250 villages in Kuarmunda & Lathikata blocks) – rural community includes tribal villages and 31 urban slums around Rourkela.
- Khorda district (154 villages in Jatni and Balianta blocks) – typical rural community, additional 22 urban slums around Bhubaneswar
- Rayagada district (321 villages in Kasipur, Kalyan, Bissam-cuttack, Muniguda, Singhpur, Ramnagguda blocks)

The attached AIPH labs in the hospitals (except Rayagada) in Odisha state have full-fledged microbiology laboratories with Bactec culture machines, API diagnostic system, -80 freezers, PCR machines, gel electrophoresis, DNA isolation, and other ancillary equipment for conducting basic molecular microbiology work. The All India Institute of Medical Sciences serves as the reference microbiology laboratory for all sites and conducts molecular studies on frozen isolates.
**Capital Hospital, Bhubaneswar:** Largest government-run hospital in the capital city of Odisha, serves as the patient receiving site for Khorda district. The microbiology laboratory for the district is housed also here. A level II nursery first established with assistance from U.S.-based AIPH faculty has now become the regional center for training in neonatal care by UNICEF.

**SCB Medical College Hospital, Cuttack:** About 20 Kms from Bhubaneswar serves as the referral hospital for AIPH study patients.

**Ispat General Hospital, Rourkela:** This hospital is the largest tertiary care hospital in western Odisha managed by the Steel Authority of India Ltd. Although we work with the government hospital (Rourkela General Hospital), we made a conscious decision of developing IGH as our hub due to its faculty (offer DNB in several subjects) and staff, and existing research labs well known in India and abroad for malaria research.

**District Head Quarter Hospital, Rayagada:** is the nodal hospital for the six study blocks.

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**Randomized Clinical Trial Sites in the community setting in Odisha**

**Field Operations with a three-tier monitoring system:** AIPH’s well developed community intervention network is represented by the attached schematic diagram. Full time study physicians and officers provide clinical, laboratory, training, monitoring services while we utilize a large group of employees (Anganwadi workers) of the government system. One Anganwadi worker (lady of the same village) acts as the link between. In the event that the AW worker is sick or is on leave, the duties are carried out by the Anganwadi Helper, also an employee of the ICDS system.
Maternal and Child Health Research: Funded by R0-1 and U0-1 grants from the NIH, and additional local support, Dr. Panigrahi has conducted large scale surveillance of morbidity in neonates and children in India. These research efforts span from preterm birth, birth asphyxia, sepsis and pneumonia in children to bacterial vaginosis in women. Intervention studies at these sites include development of training modules and capacity building of physicians and paramedical personnel, other socio-behavioral interventions, and laboratory research.

ANISA (Aetiology of Neonatal Infection in South Asia) Study: Although infection is well known to be a major contributor to morbidity and mortality in neonates and young infants, very few population-based studies have systematically examined the timing and causative agents of infection. Especially, viral agents have not been looked for that could be contributing significantly to this morbidity. Dr. Panigrahi is now conducting a population-based study supported by the Child Health Research Foundation with funding from the Bill and Melinda Gates Foundation in two large cohorts (>400,000 population) in eastern India in collaboration with the Asian Institute of Public Health.

Neonatal and Infant Infections and Probiotics Research: Worldwide, about 4 million neonates die every year; 99% of these die in developing countries. One fourth of these deaths are due to infection including invasive disease (sepsis) and pneumonia. Accomplishing MDG-4 goals are heavily dependent on averting these deaths. Even after the neonatal period, during infancy and early childhood, infections including diarrhea constitute bulk of the morbidity. Lacking Antibiotics are typically used to treat such infections, but the cost and logistics in hard to reach areas pose serious impediments in the delivery of such treatment. This is also confounded by the burgeoning problem of antibiotics resistance worldwide and limits the ability to provide optimal treatment in resource constrained settings.

Dr. Panigrahi’s team has worked on various aspects of these infections and recently completed the largest clinical trial of probiotics in an effort to prevent neonatal infections. This study, funded by an R0-1 grant from NIH enrolled 4556 neonates in India was topped early by the DSMB due to demonstration of unequiovocal efficacy against infections including sepsis, pneumonia, and diarrhea.

IMMENSE Study: In large mother-baby cohorts population with over 10,000 mother-baby dyads, we have launched a new study called IMMENSE (IMPact of Maternal ENvironmental and Socio Economic factors in child health and development) utilizing CGHAD partner sites. This has been made possible with funding from the University of Nebraska Foundation. With the wide spread increase in mining activities in Odisha state, new industries, use of pesticides, and fertilizers, indoor and ambient pollution and many other exposures, and concomitant increase in cancer rates, change in the epidemiology, onset age etc. it is impossible not to put these variables into the equation of public health in transitional economies such as India.

Systematic data collection is ongoing in India including examination of air and water quality and collection and banking of vital biological samples from mothers and babies. These cohorts are being followed over the longer term to examine short and long term impacts of these exposures. Planned analyses include range from epigenetic to phenotypic changes in this population.

Impact of sanitation access and menstrual hygiene management on psychosocial stress, behavior, and health among girls and women in Odisha, India: The United Nation’s World Water Development Report indicates “access to safe water and adequate sanitation services has proved to be one of the most efficient ways of improving human health”. This research study aims to examine how poor water,
sanitation, and hygiene (WASH) conditions impact sanitation and hygiene practices among Indian girls and women (14-45 yrs) during various their life-course. It also explores behavioral and societal conditions that could influence mental, physical, and reproductive health. To address the temporal and contextual complexities between WASH conditions and women's health, three sub-studies have been designed within a broader conceptual framework. A population census is documenting baseline conditions, behaviors, reported stress and urogenital symptoms, and related health-care utilization. CGHAD faculty and students work closely with Indian collaborators at AIPH, India, and several other U.S. and U.K.-based faculty at Emory, Oklahoma University, and London School of Hygiene and Tropical Medicine.

Antimicrobial Drug Resistance; a World-wide Concern: The WHO Director-General's Global Report on Antimicrobial Resistance released in April, 2014 demonstrates a dangerous new epidemiological era characterized by the world-wide increasing prevalence of drug-resistant microbes. According to a CDC report released last year, antibiotic resistance annually causes more than 2 million illnesses and over 23,000 deaths in the United States. Widespread use of antibiotics, not only in hospital settings but also in the general population, agricultural and animal feed practices has increased the rates of bacterial population resistant to multiple drugs. Increasing antibiotic treatment failures is a global public health concern. Dr. Dinesh Chandel and other CGHAD faculty members utilizing laboratory facilities at UNMC and overseas are engaged in tracking antibiotics resistance in different populations.

The developing world, where antibiotic are available without a prescription is now experiencing an acute problem of antimicrobial resistance in populations starting from neonates to adults and the elderly. The frequency and spectrum of antimicrobial-resistant infections has increased in both hospital and the community settings. In an Indo-US collaborative study, CGHAD scientists reported increased rates of neonatal sepsis mainly due to drug-resistant ESBL-positive infections in an Indian setting. Although nosocomial drug-resistance is a burgeoning problem globally, appearance of ESBLs even in the rural population, and so early in life, raises serious concerns. Following these studies, CGHAD faculty in collaboration with major Indian medical institutions and the Asian Institute of Public Health conducted a PCR-based survey of ESBL-gene fecal carriage among infants and found equally high rates of carriage (in stool) of bacteria with ESBL-encoding genes.

In an ongoing research study involving high-throughput DNA sequencing based metagenomics protocols, we are examining the possible impact of early probiotics intervention in changing the gut flora in the developing infants and subsequent change in the acquisition of antibiotic-resistant organisms.
Research on Multidrug Resistant TB in India: CGHAD collaborators at the Asian Institute of Public Health in India have been funded by TB Reach (Stop TB Partnership with a WHO secretariat) to examine MDR TB in a population of over 500,000 that includes migrant and mining workers in Jajpur and Bhubaneswar area. In this innovative initiative, non-formal health care providers including pharmacies that dispense drugs (for fever, cough, and weakness) without a prescription have been brought into the partnership for referral and GenXpert sputum testing. Household contacts of the positive cases, especially the pediatric age group are targeted to provide insights into latent TB.

Infection and Epidemiology of Cancer in South Asia: Utilizing the ongoing collaboration with faculty members at the Asian Institute of Public Health and the Acharya Harihar Regional Cancer Center in Cuttack, resident CGHAD scientists are working on establishing local cancer registries with the aim of identifying the factors leading to the changing epidemiology of different cancers in the Indian subcontinent. Current interests include cervical cancer, breast cancer, and certain lymphomas. Preliminary work has begun to examine specific exposures and risk factors in north India that has recently seen an exponential rise in the incidence of this cancer. CGHAD laboratory scientists are also exploring any possible relationship with Salmonella infection in the development of gall stones and subsequent metaplasia.

A STEP on Health (A Study of Traffic and Environmental Pollution on Health)

Air pollution from road traffic has been linked to a variety of negative health effects. Studies have shown that people who live/ work, near major traffic sources have an increased incidence and severity of health problems that may be related to air pollution from roadway traffic. Health effects linked to traffic pollution exposures include reduced lung function and impaired lung development in children, asthma, cardiovascular disease, low birth weight, pre-term newborns, and premature death. Additional research is needed to learn more about pollutants near roadways, how and to what extent people are exposed to them, and the type and severity of associated health effects in Indian context. CoPH students and collaborating faculty at AIPH, India have completed a pilot study and plan to continue the work over the longer term.

The current research objectives are to:

- Identify and define different sources of emissions through direct measurements
- Assess the health effects from traffic pollution exposures
- Development of suitable biomarkers for human exposure assessments.
Environmental Health Impact of House-hold Energy Choices in India

The disease burden from household air pollution (HAP) is a consequence of exposure to the extremely toxic pollutants produced by solid fuels burned in open fires or stoves in the home for cooking or heating. Nearly two million people a year die prematurely from illness attributable to HAP as a result of solid fuel use (WHO 2009). There is emerging evidence that HAP increases the risk of other child and adult health problems, including low birth-weight, perinatal mortality, asthma, tuberculosis, nasopharyngeal cancer, cataracts, blindness, and cardiovascular disease. Despite the high burden of disease from HAP, it has not received the same attention as other diseases in India. This collaborative research project utilizes two large mother-child cohorts in two districts to follow infants and adults prospectively for quantification of exposure and establishment of any relationship with morbidity and mortality.

A Study on assessment of health effects due to agricultural exposure

Global pesticide exposures are reported to be responsible for over 3 million acute poisonings each year, with the majority in developing countries.

There have been significant collaborative efforts to estimate risks associated with pesticides, with strategies ranging from:

- desktop evaluations (of properties of chemicals, the quantities used, and the likely pathways for uptake)
- to environmental sampling
- quantitation of potential absorption
- to personal monitoring and sampling to establish individual dose.
Exposure Assessment of Microbial Components in Indoor Environment

Each day we are exposed to a complex mixture of microbial agents and components in indoor environments. However, the sources of the microbial communities and the processes that affect them are not well understood. Exposure to bio-aerosols, including fungal ones, has been linked to a range of detrimental health effects. Understanding the source populations and processes that suspend and disseminate microbes and microbial products in indoor air remains a central focus of our research. The impact between those microbial agents in the home environment in relation to respiratory health is still a major issue in research.

Microbial Source Tracking and WASH practice in India: Dr. Pinaki Panigrahi and collaborators at U.C. Davis have recently completed a project in eastern rural India identifying the source of fecal contamination, where outdoor defecation by humans and animals is common practice. These studies were supported by the London School of Hygiene and Tropical Medicine with funding from the Bill and Melinda Gates Foundation.