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CENTRE
FOR HEALTH AND
POPULATION RESEARCH

PHSD 2001

# MEMORANDUM

29 August 2001

To : Professor Lars Ake Persson
Associate Director, Public Health Science Division

From: Professor Mahmudur Rahman
Chairman, Ethical Review Committee (ERC)

Sub : Protocol # 2001-015

Thank you for your memo of 27th August 2001 with the modified copy of the consent form and the questionnaire for your protocol # 2001-015 entitled "Arsenic in tube-well water and health consequences". The modified version of the protocol is hereby approved upon your satisfactory addressing of the issues raised by the ERC in its special meeting held on 16th August 2001.

Thank you.

International Centre for Diarrhoeal Disease Research, Bangladesh
CENTRE FOR HEALTH AND POPULATION RESEARCH
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To: Chairman, ERC

Date: August 29, 2001

From: Dr. Mohammed Abdus Salam

Subject: **Questionnaire and consent forms of the research study entitled "Arsenic in tube well water and health consequences"**

This has reference to the meeting of the ERC where the committee had requested the investigators to modify the questionnaire and the consent forms, and I took the responsibility to help the investigators in doing so. In response, the investigators have modified the questionnaire per my advice, and I would consider the modified versions as satisfying.

I think that the committee may now consider approval of the latest versions of the questionnaire and the consent forms.

Thanks.

**MEMORANDUM**

August 28, 2001

To Professor Mahmudur Rahman
Chairman, Ethical Review Committee (ERC)

From Professor Lars Ake Persson,
Associate Director, Public Health Science Division

Sub: Modified copy of the consent forms and questionnaire

This has reference to your memo of 19th August 2001 communicating me the decision of the ERC on the modified version of the protocol # 2001- 015 entitled *" Arsenic in tube well water and health consequences."* As advised by you, consent forms (both Bangla and English) and questionnaire have been revised in consultation with Dr. M. A. Salam, a Member of the ERC. I would much appreciate if you could kindly approve the protocol.

Thank you

Attachment I

Date: 28/08/2001

(FACE SHEET) **ETHICAL REVIEW COMMITTEE, ICDDR,B.**

Principal Investigator: Professor Lars Ake Persson

Application No. 2001-15

Title of Study: ARSENIC IN TUBE WELL WATER AND HEALTH CONSEQUENCES

Trainee Investigator (if any): _____

Supporting Agency (if Non-ICDDR,B) _____

Project Status: In process

[ ✓ ] New Study

[ ] Continuation with change

[ ] No change (do not fill out rest of the form)

**Circle the appropriate answer to each of the following (If Not Applicable write NA)**

1. Source of Population:
   - (a) Ill subjects — (Yes) No
   - (b) Non-ill subjects — (Yes) No
   - (c) Minor or persons under guardianship — (Yes) No

2. Does the Study Involve:
   - (a) Physical risk to the subjects — Yes (No)
   - (b) Social risk — (Yes) No
   - (c) Psychological risks to subjects — Yes (No)
   - (d) Discomfort to subjects — (Yes) No
   - (e) Invasion of privacy — Yes (No)
   - (f) Disclosure of information damaging to subject or others — Yes (No)

3. Does the Study Involve:
   - (a) Use of records (hospital, medical, death or other) — (Yes) No
   - (b) Use of fetal tissue or abortus — Yes (No)
   - (c) Use of organs or body fluids — (Yes) No

4. Are Subjects Clearly Informed About:
   - (a) Nature and purposes of the study — (Yes) No
   - (b) Procedures to be followed including alternatives used — (Yes) No
   - (c) Physical risk — (Yes) No
   - (d) Sensitive questions NA — Yes No
   - (e) Benefits to be derived — (Yes) No
   - (f) Right to refuse to participate or to withdraw from study — (Yes) No
   - (g) Confidential handling of data — (Yes) No
   - (h) Compensation &/or treatment where there are risks or privacy is involved in any particular procedure — Yes No n/a

5. Will Signed Consent Form be Required:
   - (a) From subjects — (Yes) No
   - (b) From parents or guardian (if subjects are minor) — (Yes) No

6. Will precautions be taken to protect anonymity of subjects — (Yes) No

7. Check documents being submitted herewith to Committee:
   - ____ Umbrella proposal - Initially submit an with overview (all other requirements will be submitted with individual studies
   - ✓ Protocol (Required)
   - ✓ Abstract Summary (Required)
   - ____ Statement given or read to subjects on nature of study, risks, types of questions to be asked, and right to refuse to participate or withdraw) (Required
   - ✓ Informed consent form for subjects
   - ✓ Informed consent form for parent or guardian
   - ✓ Procedure for maintaining confidentiality
   - ✓ Questionnaire or interview schedule*

   * If the final instrument is not completed prior to review, the following information should be included in the abstract summary
   1. A description of the areas to be covered in the questionnaire or interview which could be considered either sensitive or which would constitute an invasion of privacy
   2. Example of the type of specific questions to be asked in the sensitive areas
   3. An indication as to when the questionnaire will be presented to the Committee for review

We agree to obtain approval of the Ethical Review Committee for any changes involving the rights and welfare of subjects before making such change.

_____ Principal Investigator

_____ Trainee

**ICDDRB: Centre for Health & Population Research** **RRC APPLICATION FORM**

# RESEARCH PROTOCOL

**Protocol No.:** 2001-15

**FOR OFFICE USE ONLY**

RRC Approval: Yes/ No Date:

ERC Approval: Yes/No Date:

AEEC Approval: Yes/No Date:

**Project Title:** **Arsenic in tube well water and health consequences**

**(Revised August 28, 2001)**

**Theme:** ***(Check all that apply)***

- [x] Nutrition
- [ ] Emerging and Re-emerging Infectious Diseases
- [ ] Population Dynamics
- [x] Reproductive Health
- [ ] Vaccine evaluation
- [x] Environmental Health
- [ ] Health Services
- [ ] Child Health
- [ ] Clinical Case Management
- [ ] Social and Behavioural Sciences

**Key words:** Arsenic, drinking water, epidemiology, exposure, health effects, skin lesion

**Principal Investigator:** Lars Ake Persson **Division:** PHSD **Phone:** 9885155

**Address:** Public Health Sciences Division
ICDDR,B, Mohakhali, Dhaka

**Email:** persson@icddrb.org

**Co-Principal Investigator(s):** Mahfuzar Rahman

**Co-Investigator(s):**
1.Shams El Arifeen
2. SM Akramuzzaman
3. Abbas Bhuiya
4. Eva-Charlotte Ekström
5. Md. Khalequzzaman
6. Peter Kim Streatfield
7. Nigar Shahid
8. MA Wahed
9. Md Yunus
10. Mushtaque Chowdhury
11. Marie Vahter

**Student Investigator/Intern:**

**Collaborating Institute(s):** Research Division, BRAC and Institute of Environmental Medicine, Division of Metal and Health, Karolinska Institute, Sweden

**Population: Inclusion of special groups** *(Check all that apply)*:

Gender
- [x] Male
- [x] Females

Age
- [ ] 0 – 5 years
- [x] 5 – 9 years
- [x] 10 – 19 years
- [x] 20 +
- [x] > 65

- [ ] Pregnant Women
- [ ] Fetuses
- [ ] Prisoners
- [ ] Destitutes
- [ ] Service providers
- [ ] Cognitively Impaired
- [ ] CSW
- [ ] Others (specify _____)
- [ ] Animal

**Project / study Site** *(Check all the apply)*:
- [ ] Dhaka Hospital
- [ ] Matlab Hospital
- [x] Matlab DSS area
- [ ] Matlab non-DSS area
- [ ] Mirzapur
- [ ] Dhaka Community
- [ ] Chakaria
- [ ] Abhoynagar

- [ ] Mirsarai
- [ ] Patyia
- [ ] Other areas in Bangladesh _____
- [ ] Outside Bangladesh name of country: _____
- [ ] Multi centre trial (Name other countries involved) _____

**Type of Study** *(Check all that apply)*:
- [x] Case Control study
- [x] Community ~~based trial~~ / intervention ✓ up)
- [ ] Program Project (Umbrella)
- [ ] Secondary Data Analysis
- [ ] Clinical Trial (Hospital/Clinic)
- [ ] Family follow-up study

- [x] Cross sectional survey
- [x] Longitudinal Study (cohort or follow-
- [ ] Record Review
- [ ] Prophylactic trial
- [ ] Surveillance / monitoring
- [ ] Others

**Targeted Population** *(Check all that apply)*:
- [x] No ethnic selection (Bangladeshi)
- [ ] Bangalee
- [ ] Tribal groups

- [ ] Expatriates
- [ ] Immigrants
- [ ] Refugee

**Consent Process** *(Check all that apply)*:
- [x] Written
- [x] Oral
- [ ] None

- [ ] Bengali language
- [ ] English language

**Proposed Sample size:** Total sample size: 190,000 ☐

Sub-group 2850 (Case-referent) ☐

1986 (for miscarriages) ; 1653 (for Stillbirth)
2106 (for neonatal deaths) ☐
675,000 (for cohort)

**Determination of Risk: Does the Research Involve** *(Check all that apply)*:

- ☐ Human exposure to radioactive agents?
- ☐ Fetal tissue or abortus?
- ☐ Investigational new device?
- ☐ Human exposure to infectious agents?
- ☐ Investigational new drug
- ☐ Existing data available via public archives/source (specify_____)
- ☐ Pathological or diagnostic clinical specimen only
- ☐ Existing data available from Co-investigator
- ☐ Observation of public behaviour
- ☐ New treatment regime

observational Study: exposure to arsenic in water

**Yes/No**

☒ ☐ Is the information recorded in such a manner that subjects can be identified from information provided directly or through identifiers linked to the subjects?

☐ ☒ Does the research deal with sensitive aspects of the subject's behaviour; sexual behaviour, alcohol use or illegal conduct such as drug use?

Could the information recorded about the individual if it became known outside of the research:

☐ ☒ a. place the subject at risk of criminal or civil liability?

☐ ☒ b. damage the subject's financial standing, reputation or employability; social rejection, lead to stigma, divorce etc.

**Do you consider this research** *(Check one)*:

- ☐ greater than minimal risk
- ☐ no risk
- ☒ no more than minimal risk
- ☐ only part of the diagnostic test

Minimal Risk is "a risk where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical, psychological examinations or tests. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as a part of routine physical examination".

**Yes/No**

☒ ☐ Is the proposal funded?

If yes, sponsor Name: Sida (funding received) and WHO (committed)

Yes/No

☒ ☐ Is the proposal being submitted for funding ?

If yes, name of funding agency: (1) _____ WHO (committed)

(2) _____ USAID

Do any of the participating investigators and/or their immediate families have an equity relationship (e.g. stockholder) with the sponsor of the project or manufacturer and/or owner of the test product or device to be studied or serve as a consultant to any of the above?

***IF YES, submit a written statement of disclosure to the Director.***

| **Dates of Proposed Period of Support** *(Day, Month, Year - DD/MM/YY)* | **Cost Required for the Budget Period ($)** |
|---|---|
| Beginning date 01/07/ 2001 | *a. Ist Year* _____ *2nd Year* _____ *3rd Year* _____ *Other years* |
| End date 30/06/ 2003 | *b. Direct Cost :* **US $ 540253** *Total Cost* **:US $ 789,655** |

**Approval of the Project by the Division Director of the Applicant**

The above-mentioned project has been discussed and reviewed at the Division level as well by the external reviewers.
The protocol has been revised according to the reviewer's comments and is approved.

LA PERSSON — Name of the Division Director

Signature

28.8.2001 — Date of Approval

**Certification by the Principal Investigator**

I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware

**Signature of PI**

**Date:** 28.8.2001

that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.

**Name of Contact Person** (if applicable)

# Table of Contents



[x] Check here if appendix is included

**PROJECT SUMMARY:** Describe in concise terms, the hypothesis, objectives, and the relevant background of the project. Describe concisely the experimental design and research methods for achieving the objectives. This description will serve as a succinct and precise and accurate description of the proposed research is required. This summary must be understandable and interpretable when removed from the main application. **( TYPE TEXT WITHIN THE SPACE PROVIDED).**

Principal Investigator Lars Ake Persson

Project Name **Arsenic in tube well water and health consequences**

Total Budget USD 789,655 Beginning Date July 2001 Ending Date June 2003


The discovery of arsenic in groundwater in Bangladesh has aroused widespread concern. A major proportion of tube wells for drinking water in the country is contaminated with arsenic. Experiences from other countries indicate that the consequences of this exposure will be extensive and include excess incidence and mortality in cancers and cardio-vascular diseases. However, the knowledge base is weak on the weight of this new burden of diseases and on the speed by which it develops. Little is known about the reproductive health consequences, and about the possible aggravating role of the widespread malnutrition in Bangladesh on arsenic-induced health effects.

The overall objective of this project is to establish a strong epidemiologic platform of research on levels of arsenic exposure through drinking water, occurrence of arsenic skin lesions, consequences for reproductive outcome, effect on adult mortality, modifications of effects by the nutritional status, and effects of an intervention with alternative water sources.

ICDDR,B is running a health and demographic surveillance system in 142 villages of the Matlab thana. The surveillance system contains demographic information, reproductive outcomes, health information, nutritional and health data as well as a linked geographic information system. This area is heavily affected by the arsenic contamination of drinking water. We propose screening for skin lesions in the 220,000 population, assessment of arsenic content of the 9000 tube wells of the Matlab surveillance area, and an establishment of a data base for epidemiological studies of levels of arsenic exposure and manifestations of arsenicosis in the population. Immediate analyses will be performed on the risk for arsenic related skin lesions and effects on reproductive outcome and mortality. A village-based arsenic mitigation activity is coordinated with the surveillance, and priority will be given to the areas with the highest exposure. Reversibility of skin changes will be assessed. The consequences of a shift to other water sources will also be evaluated, including monitoring of diarrhoeal diseases through the surveillance system in Matlab.

The mitigation activity is collaborated with BRAC, a major national NGO with the longest experience of arsenic mitigation programmes in Bangladesh. Collaboration is suggested with the Institute of Environmental Medicine, Division of Metals and Health, Karolinska Institutet (professor Marie Vahter) in the area of arsenic biochemistry.

KEY PERSONNEL (List names of all investigators including PI and their respective specialties)

| Name | Professional discipline/speciality | Role in the project |
|---|---|---|
| 1. Lars Åke Persson | Epidemiologist, professor, head of Public Health Sciences Division, ICDDR,B | Principal investigator |
| 2.Shams El Arifeen | Epidemiologist and head, Child Health Programme | Co-investigator |
| 3. SM Akramuzzaman | Senior Medical Officer, Clinical Sciences Division | Co-investigator |
| 4. Abbas Bhuiya | Social scientist, head, Social and Behavioural Sciences Programme | Co-investigator |
| 5. Eva-Charlotte Ekström | Nutrition epidemiologist, Clinical Sciences Division | Co-investigator |
| 6. Md. Khalequzzaman | Epidemiologist, senior physician, Child Health Programme | Co-investigator |
| 7. Mahfuzar Rahman | Environmental epidemiologist, Public Health Sciences Division | Co-investigator |
| 8. Peter Kim Streatfield | Demographer, head of Health and Demographic Surveillance Programme | Co-investigator |
| 9. Nigar Shahid | Senior scientist, Child Health Programme, Public Health Sciences Division | Co-investigator |
| 10. MA Wahed | Head, Nutrition Biochemistry Section, Clinical Sciences Division | Co-investigator |
| 11. Md Yunus | Scientist and head, Matlab Health Research Programme | Co-investigator |
| 12. Mushtaque Chowdhury | Director Research, BRAC | Co-investigator and co-ordinator of mitigation activities |
| 13. Marie Vahter | Professor, Division of Metals and Health, Institute of Environmental Health, Karolinska Institutet, Stockholm | Co-investigator |

# DESCRIPTION OF THE RESEARCH PROJECT

## Hypothesis to be tested:

Concisely list in order, in the space provided, the hypothesis to be tested and the Specific Aims of the proposed study. Provide the scientific basis of the hypothesis, critically examining the observations leading to the formulation of the hypothesis.

The overall objective of this project is to establish a strong epidemiologic platform of research on arsenic toxicity and health effects, intervention with arsenic mitigation, and follow-up to evaluate effects of the intervention, such as reversibility of arsenic-related skin lesions and possible consequences for contamination of drinking water and diarrhoeal disease morbidity.

The primary hypotheses we will test are:

- Although several studies have demonstrated dose-effect relationship between arsenic in drinking water and various health effects, such as skin changes, the knowledge base is weak for assessment of burden of arsenic induced disease and projections into the future in Bangladesh, especially considering the possible influence of wide-spread malnutrition and the general health conditions of the population. *We postulate that the individual susceptibility to develop arsenic-related skin changes (melanosis, keratosis, leucomelanosis and hyperkeratosis) for a given dose and duration of arsenic exposure is a) higher for younger individuals as compared to older, b) higher for boys and men as compared to girls and women, c) higher for those with anthropometric signs of chronic protein energy deficiency as compared to normal anthropometry and d) higher for those with micronutrient deficiencies (especially selenium, zinc and antioxidants) as compared to those without deficiencies.*

- Laboratory-based studies and a few population-based, mainly ecological studies, indicate that arsenic exposure may increase risk for spontaneous abortions and stillbirths. *We postulate that women who have higher arsenic concentrations in their drinking water and report consumption of water from those tube wells during previous pregnancies have a higher rate of negative pregnancy outcome, i.e. miscarriages, stillbirths and early neonatal deaths.*

- Studies from other countries have shown that long-term exposure to arsenic in drinking water increases the mortality risk for cardiovascular diseases and selected cancers. Given the relatively long use of tube-well water in the Matlab area and the arsenic concentration levels measured in pilot studies there may be reasons to anticipate an arsenic-related excess mortality by such causes. *We postulate that individuals with higher dose-time levels of arsenic exposure have a higher mortality in malignant neoplasms and/or cardio-vascular diseases as compared to those with low arsenic concentration in drinking water.*

- There is only anecdotal information about reversibility of skin changes after shift to arsenic-free water. Follow-up of patients with skin changes including monitoring of arsenic concentrations in urine may provide the needed knowledge. *We postulate that a cessation of arsenic intake through drinking water in individuals with arsenicosis of skin will result in some degree of reversibility of these skin changes.*

- An arsenic mitigation programme with a shift to alternative, arsenic-low or arsenic-free water sources might potentially imply an increased exposure to pathogen-contaminated water, e.g. unclean surface water. However, this does not necessarily imply an increased rate of diarrhoeal diseases, for example in children. *We postulate that a shift to alternative, arsenic-low or arsenic-free water sources as part of a mitigation program will not imply an increased incidence of diarrhoeal diseases in children under five years of age in these households.*

In addition, there are other secondary objectives with the proposed activities. The tube wells in the surveillance area are already having their coordinates in the Geographic Information System (GIS), which is part of the Matlab databases. An update of all newly constructed tube wells is under way. The GIS also includes satellite images of the area at different time periods, and this may be expanded in order to characterise the surface (flooding areas, landscape characteristics) and to study these spatial pattern and geographical and seasonal variation of arsenic contamination of ground water. This part of the databases may also offer opportunities for other scientists in hydrology and geochemistry to link their studies to the population and the health effects.

Another obvious secondary objective is to establish a prospective database for studies of arsenic and health based on the Matlab surveillance system, including individual information on water consumption and arsenic concentration in that water, GIS information on the tube wells, presence or absence of skin changes, interventions with arsenic mitigation activities. This information will easily be linked to other types of information (socio-economic conditions, health data) in the system.

# Background of the Project including Preliminary Observations

Describe the relevant background of the proposed study. Discuss the previous related works on the subject by citing specific references. Describe logically how the present hypothesis is supported by the relevant background observations including any preliminary results that may be available. Critically analyze available knowledge in the field of the proposed study and discuss the questions and gaps in the knowledge that need to be fulfilled to achieve the proposed goals. Provide scientific validity of the hypothesis on the basis of background information. If there is no sufficient information on the subject, indicate the need to develop new knowledge. Also include the **significance and rationale** of the proposed work by specifically discussing how these accomplishments will bring benefit to human health in relation to biomedical, social, and environmental perspectives. **(DO NOT EXCEED 5 PAGES, USE CONTINUATION SHEETS).**

## Background and significance

A major proportion of the tube wells in the large delta region of Bangladesh is contaminated with arsenic, showing levels high above the safety limits (WHO permissible limit 10μg/L and Bangladesh limit is 50μg/L) (1-3). This implies that, according to estimates based on nation-wide surveys, more than 20 million people are exposed to arsenic in drinking water above current safety limits (4). Arsenic exposure through drinking water is known to cause a number of serious health consequences. Skin lesions, i.e. diffuse melanosis followed by spotted melanosis, hyperpigmentation, and keratosis are common and the first recognised health effects – and also believed to be a marker for increased risk for other, more serious malignant and non-malignant consequences. In spite of a vast number of studies from other countries there is still lack of knowledge on the dose-effect relationships between arsenic in drinking water and skin lesions and other health effects. Similarly, there is insufficient knowledge on the possible modifications by age, sex, and nutritional status, and on the possible reversibility of some

of the health effects. Epidemiological information of this type is much needed for proper planning of countrywide interventions in Bangladesh.

### *Arsenic in the human body*

Arsenic is absorbed in the gastrointestinal tract in humans. Inorganic arsenic is methylated during metabolism and is excreted mainly as mono-methylarsenic acid (MMA) and dimethylarsenic acid (DMA) in humans, but only as DMA in animals. Trivalent arsenic ($As_{III}$) is most readily methylated, and the reduction of $As_V$ to $As_{III}$ seems to involve oxidation of glutathione (GSH) and has been proposed to be a critical step in arsenic metabolism. Absorbed arsenic interferes with the activity of several enzymes in the heme biosynthesis pathway and modifies urinary excretion of porphyrins in both animals and humans. Chronic occupational exposure to arsenic results in an increase in total coproporhyrin (I+III) in urine. Thus it may be possible to use this parameter, as well as urinary arsenic, MMA, and DMA, as a means of biological monitoring.

### *Rationale for investigating the variation in individual susceptibility to arsenic-related skin lesions*

The latency (i.e. the time from first exposure to manifestation of disease) for arsenic-caused skin lesions, in particular keratosis, is typically of the order of 10 years (5). However, latency much shorter as well as longer than 10 years may occur, and the rapidity of the appearance of skin lesions seems to be dose dependent. In order to assess the burden of arsenic-induced health problems age- and gender-specific information on the occurrence of such effects is needed, as well as an improved understanding of the exposure to arsenic over time.

The ingested arsenic is methylated and excreted in urine. Children have reportedly a lower degree of methylation of arsenic than adults. Anecdotal information from arsenic mitigation activities in affected areas indicates that children are found to have arsenic skin lesions long before expected latency periods. Some studies indicate a lower degree of arsenic methylation in men than in women, especially as compared to pregnant women (6). This may be part of the reason why men are described to show arsenic-related skin lesions more frequently than women, under seemingly equal exposure levels to arsenic in drinking water (5).

Poor nutritional status might increase the health effects of arsenic through variations in the arsenic methylation capability (7-9). Vitamin A status in the population may be related to susceptibility to arsenic related diseases. The risk of skin cancer in arsenic-exposed individuals has been associated to beta-carotene levels (8, 10). Such associations have also been shown for cardio-vascular disease risks (7). The general nutritional status (as expressed by anthropometry), the antioxidant status and other micronutrients such as zinc status may play an important role in modifying the body's response to arsenic exposure. No information is available on the role of general malnutrition in relation to arsenic-related diseases in a society like Bangladesh, where malnutrition is wide-spread (almost half of the births <2500 grams, more than half of the children stunted, wide-

spread malnutrition among adult women, vitamin A deficiency still common in spite of supplementation programmes, iron deficiency in adult women almost fifty per cent).

### *Rationale for investigating effects on reproductive outcome*

Very little is known about the human effects of arsenic contaminated water on foetal growth, miscarriages and stillbirth. Animal experiments have shown that arsenic exposure increases the risk for foetal death and growth retardation (11). Human data are limited to a few ecological studies of populations exposed to arsenic from drinking water or from work near smelters. Associations with spontaneous abortions and stillbirths have been shown, but are difficult to interpret due to multiple chemical exposures in those groups, or due to the weak study design (12, 13).

Even a relatively low excess risk of abortions, stillbirths and early neonatal deaths related to arsenic in drinking water would have a major public health impact in Bangladesh, due to the vast number of pregnant women exposed to the arsenic contaminated water.

### *Rationale for investigating effects on mortality in cancer and cardio-vascular diseases*

Lifetime excess risk of skin cancer if exposed to arsenic in drinking water has been assessed to be 1.3/1000 for men and 0.6/1000 for women per microgram of arsenic per day. In its latest document on arsenic in drinking water, the U.S. National Research Council (NRC) concluded that there is a combined cancer risk of 1 in 100 at the level of 50 µg /L and 1/10 at the level of 500 µg/L (11). If this is true also for the Bangladeshi population the public health consequences are frightening, since more than a 20 million population currently is estimated to be exposed to have arsenic in their drinking water above the level of 50 µg /L (4).

In Matlab more than half the population have got their drinking water from tube wells for almost 20 years, and one quarter of the population had tube wells as their source of drinking water almost 30 years ago (see figure 1 in preliminary results). This implies that a major part of the population has had a sufficiently long period of exposure to cause arsenic-related deaths in cancers and cardio-vascular diseases (given a relatively constant arsenic level in the tube wells over time). Thus, there are reasons to use the health and demographic surveillance system and assess the current and recent mortality in cardio-vascular diseases and cancers in relation to arsenic exposure. Such information may be used for projections of the nation-wide mortality impact of the arsenic exposure.

### *Rationale for investigating the reversibility of skin changes*

The appropriate treatment for arsenic-induced skin changes is a shift to arsenic-free drinking water. However, there is insufficient knowledge to what extent these skin changes disappear when the individual is no longer drinking the contaminated water. There is anecdotal information available that less advanced skin changes are reversible, but unknown if this also is the case for more advanced lesions. Measurements of urine arsenic levels are needed to judge if the exposure has seized. A better understanding of

the potential reversibility is needed from a clinical as well as a public health point of view.

### *Rationale for investigating any change in diarrhoeal disease incidence when implementing arsenic mitigation activities*

A shift to alternative arsenic-free water sources may potentially imply a shift to pathogen-contaminated water. This is especially the case when surface water will be used as the new water source, but may also be the case when harvesting rainwater. In most mitigation projects so far some control of pathogens has taken place, e.g. by cultivating samples from the new drinking water source. This is an important intermediate step, but a monitoring of diarrhoeal diseases in vulnerable groups, i.e. infants and children, is also needed. The Matlab surveillance system has included a monitoring of diarrhoeal diseases in all children below 5 years of age. This information can be used in order to evaluate if the shift to alternative water sources increases the risk for diarrhoea.

## Preliminary results

Matlab, a field research area of ICDDR,B: Centre for Health and Population Research, has been chosen for field activities of this project. It is situated 53 km south east of Dhaka, accessible by road and river transport. The positioning of Matlab is highly affected by the sedimentation process of arsenic laden soil, as it is situated near the Meghna River, where it joins the confluent streams of the Brahmaputra and Ganges rivers. The area is low-lying delta plain intersected by branches of the rivers and numerous canals. During the monsoon essentially all land is flooded, except clusters of houses built on earthen mound. In 1988-89, a 60-km long embankment was built alongside the bank of the Dhonagoda and Meghna rivers. The embankment was built primarily to protect the area from monsoon flooding so that agricultural activities might be carried out throughout the year.

### *Start of use of tube wells as drinking water*

During the latest decades a radical shift in drinking water sources have taken place (Figure 1). In 1974 one quarter of the Matlab population got their drinking water from drilled tube wells, increasing to a bit more than half in 1982 and 95% in 1996. Thus, potential exposure times to arsenic in tube well water may have a median around 15-20 years for the adult population. The tube well water is only to a limited extent used for washing.

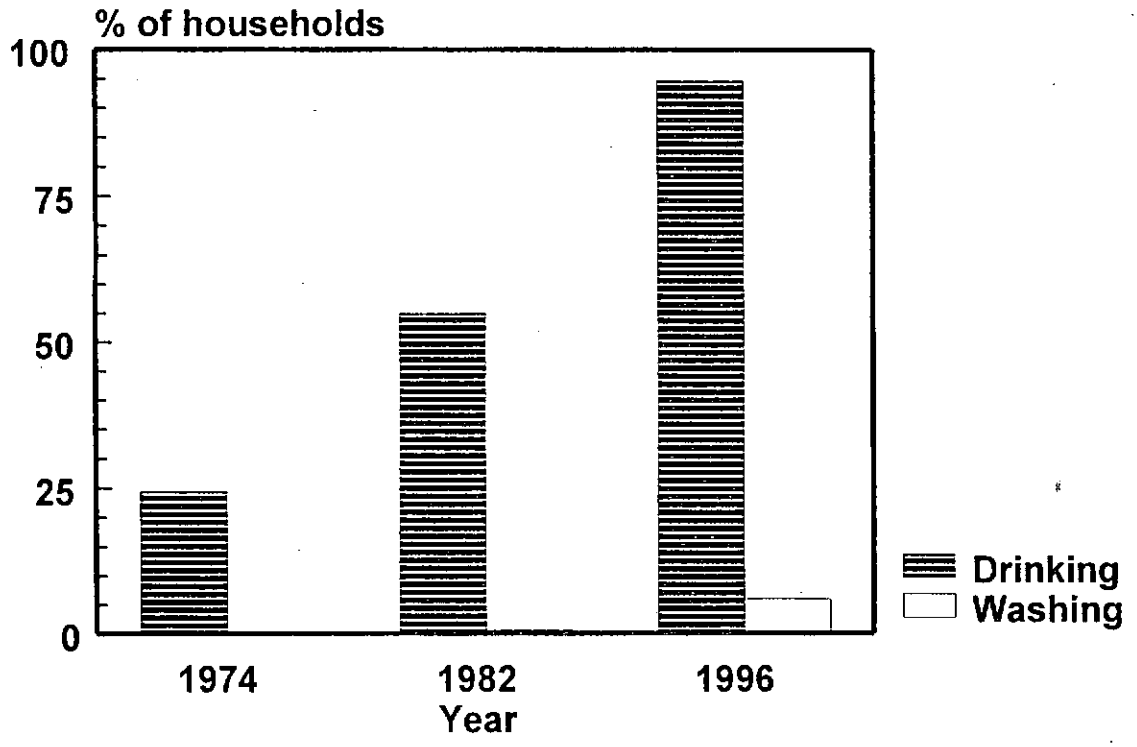


Figure 1. Sources of drinking water in Matlab over time. Based on information from Health and Demographic Surveillance System, Matlab (ICDDR,B. Demographic surveillance system – Matlab. 1996 Socio-economic census. Volume 29. Dhaka, ICDDR,B, 1998).

### *Arsenic concentration*

A pilot study was performed in 1997 with a strategic sample of 60 tube wells from all areas in the Matlab surveillance system. More than three quarters of these samples had total arsenic above the GoB maximum permissible limit of 50 µg/L. In 2001, 20 tubewell water samples were further analyzed and the arsenic concentration was on the same level as in 1997.

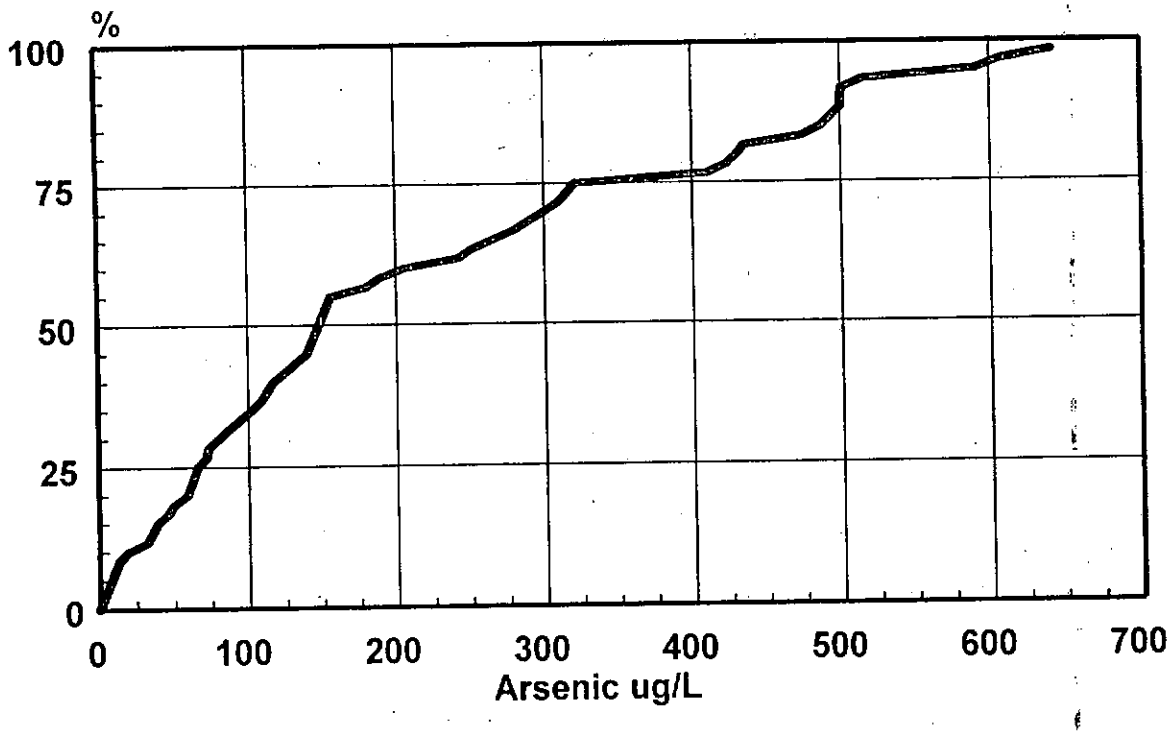


Figure 2. Arsenic concentrations in pilot study of tube wells in Matlab, Bangladesh. Cumulative frequency curve. Median arsenic level 144 ug/L water. Eighty-two per cent of the samples above 50 ug/L.

The Matlab area is located in the central part of the areas in Bangladesh showing the highest arsenic concentrations in tube wells, according to the information provided by the British Geological Survey (4).

### *Skin changes*

No systematic evaluation of the presence of arsenic-related skin changes have so far been performed in Matlab. Linked to the pilot study of tube well water (see above) members of households with a high arsenic content in their water were examined and arsenic-related skin lesions were confirmed in some individuals, and these individuals and households were given appropriate advice. The ICDDR,B staff clinic in Matlab has also diagnosed a number of staff with skin lesions, their tube wells have been tested and appropriate measures have been taken. This more anecdotal information underlines the probability that arsenic-related skin lesions are present in the Matlab area. A survey is needed to assess the prevalence.

### *Reproductive outcomes*

From the information provided by the health and demographic surveillance in Matlab the number and rates of pregnancy outcomes are reported on an annual basis (table 1). Live births constituted 89.1% of the registered pregnancies, miscarriages 8.1% and stillbirths 2.9% (data from 1998).

*Table 1. Number and rates of pregnancy outcomes and early neonatal mortality in Matlab 1998. Data from Health and Demographic Surveillance System – Matlab. Volume 31.*

| *Type of pregnancy outcome* | *Number* | *Rate* |
|---|---|---|
| Total pregnancies | 6486 | 120.1 per 1000 women 15-49 years |
| Live birth pregnancies | 5776 | 89.1 % of pregnancies |
| Total foetal wastage | 710 | 10.0% of pregnancies |
| Early (miscarriages) | 525[1] | 8.1% of pregnancies |
| Late (Stillbirths) | 185 | 2.9% of pregnancies |
| Neonatal deaths (first month) | 236 | 40.5 per 1000 live births |

[1]Out of this 43% reportedly induced.

### *Adult mortality*

Mortality registration is part of the health and demographic surveillance system. A verbal autopsy procedure includes a standardised questionnaire to identify the symptoms preceding death and possible causes. In one year (1998) there were 85 deaths reported due to malignant neoplasms and 160 cardiovascular deaths out of a total of 1111 adult deaths in a population of 134,999 individuals from 15 years an above.

### *Nutritional status*

Malnutrition is widespread in Bangladesh, and Matlab is no exception. Forty-five per cent of the infants are born with a weight below 2.5 kg (in Sweden 5%). Micronutrient malnutrition is common in children as well as in adults. In a recent supplementation trial in pregnant women in another area of Bangladesh 6 out of 10 women had low serum zinc levels (LA Persson, unpublished data). In a recent survey of women in reproductive ages the average weight was 44 kg, and one quarter was below 40 kg. Thus, there are reasons to believe that a relatively high proportion of individuals have protein and energy deficiencies and micronutrient deficiencies that theoretically may be important for the individual susceptibility to arsenic toxicity.

## Research Design and Methods

Describe in detail the methods and procedures that will be used to accomplish the objectives and specific aims of the project. Discuss the alternative methods that are available and justify the use of the method proposed in the study. Justify the scientific validity of the methodological approach (biomedical, social, or environmental) as an investigation tool to achieve the specific aims. Discuss the limitations and difficulties of the proposed procedures and sufficiently justify the use of them. Discuss the ethical issues related to biomedical and social research for employing special procedures, such as invasive procedures in sick children, use of isotopes or any other hazardous materials, or social questionnaires relating to individual privacy. Point out safety procedures to be observed for protection of individuals during any situations or materials that may be injurious to human health. The methodology section should be sufficiently descriptive to allow the reviewers to make valid and unambiguous assessment of the project. **(DO NOT EXCEED TEN PAGES, USE CONTINUATION SHEETS).**

## Methods

### *Study site*

The Matlab study site is briefly described above under preliminary observations. ICDDR,B is running a health and demographic surveillance system in 142 villages of the Matlab thana, encompassing a 220,000 population in 18386 hectares of land. The Matlab health and demographic surveillance system (HDSS) was initiated already in 1963, and records all vital events, as well as in- and out-migration. Births, deaths, marriage, pregnancies and different pregnancy outcomes are registered and up-dated by community health workers on a monthly basis. In addition, selected information on reproductive and child health, socio-economic conditions, and health interventions etc. has been collected cross-sectionally or continuously. A geographic information system (GIS) is an integrated part of the HDSS, and includes spatial information on households, tube wells, health facilities, landscape characteristics etc.

ICDDR,B has a central health facility in Matlab that receives 15,000 patients per year. This facility is equipped to support clinical and public health research in the area. Clinical examinations, laboratory examinations and treatment efforts of patients with arsenic-related diseases may take place in Matlab health facility. Four sub-centres in half of the surveillance area provide primary health care and support to studies. In the other half of the surveillance area the government provides health services to the population.

### *Study procedures*

The shift in drinking water source from surface water to tube well water in the 1970s and 1980s went with some radical changes in perceptions of drinking water quality, taste, relation between water and health etc. Now, a few decades later, a new change in the understanding of drinking water, its qualities and the relation to health is needed. We intend to start the field activities of the proposed studies by an ethnographic study that will focus the following sectors of information: (a) attitudes towards the different drinking water sources, taste of water, practical issues regarding access to water, handling of water and use of drinking water. Who are the decision makers regarding issues of water sources, and use of water for drinking? (b) Perceptions of water and health, water and illnesses and disease. The arsenic-related health effects are often non-visible but some individuals (unknown frequency) have developed arsenic-related skin lesions. Are there any attitudes formed regarding these skin problems and to what extent are those perceived as related to the water? (c) Are there any attitudes formed on arsenic in drinking water? Is there an awareness of the problem, and how is this problem perceived? This research will be conducted in the initial steps of the project, and probably be supplemented by additional fieldwork as the project develops. The initial results of the ethnographic study will be used to finalise questionnaires and procedures used in the project.

The project has two phases: (1) covering the 110,000 population in the part of Matlab, where ICDDR,B is providing health services, and (2) including the remaining part of the

HDSS area – another 110,000 population. Depending upon funding both steps will be taken simultaneously, or following after one another. The first step will enable the creation of a data base that is sufficient for initial answers to the research questions, while the completion of the entire 220,000 population will offer must better power for the analytical work and therefore better precision in the results. See sample size calculations below.

### *Study Design*

- *A retrospective cohort analysis* of current exposure (as a proxy for exposure levels over time) and duration of exposure to the arsenic contaminated water on skin changes will be assessed. Information from testing of all 9000 tube wells (4500 in each step), individual information on water used for drinking, and results of screening for arsenic-related skin lesions in the entire 220,000 population (excluding infants) will be entered into a data base. This will enable us to analyse the doses of arsenic in relation to presence of arsenic skin lesions and will also enable us to evaluate the individual susceptibility to develop arsenic-related skin changes (melanosis, keratosis, leucomelanosis and hyperkeratosis) for a given dose and duration of arsenic exposure.

- A *case-referent* study of the modification by current nutritional status on arsenic-induced skin lesions will be nested into the above cohort study. Individuals with arsenic skin lesions (above 5 years of age) will be selected as cases, and two referents without arsenic skin lesions will be randomly selected from the HDSS databases. Nutritional status of cases and referents will be assessed by anthropometry and blood samples will be taken for nutritional biochemistry. Urine samples will be taken from cases and referents as soon as the cases are identified for analysis of arsenic methylation patterns as well as current exposure levels. This approach will be enabling us for testing the hypotheses that individual susceptibility is higher for those with signs of protein energy malnutrition and micronutrient deficiencies compared to individuals with normal nutritional status.

- *A second retrospective cohort analysis* will be performed to assess current exposure and duration of exposure on reproductive events, such as, spontaneous abortions, still births, and early neonatal deaths during the last three years (1997-2000). The information on reproductive events are available in HDSS database. This approach will enable us to test the hypothesis that women who have higher arsenic concentrations in their drinking water and report consumption of water from arsenic contaminated tube wells during previous pregnancies have a higher rate of negative pregnancy outcome, i.e. miscarriages, stillbirths and early neonatal deaths.

- *A third cohort analysis* will assess the effect of arsenic exposure on overall adult mortality during the last five years (1995-2000). Mortality information including cause of death is available in the HDSS database, specifically cardio-vascular

diseases and cancer mortalities during the last five years. This approach will enable us to test the hypothesis that individuals with higher dose-time levels of arsenic exposure have a higher mortality from malignant neoplasms and/or cardio-vascular diseases as compared to those with low arsenic concentration in drinking water.

BRAC, a Bangladesh NGO, will be responsible for the *arsenic mitigation* component. Initial advice of temporary alternative drinking water sources will be given (arsenic-free tube wells in the neighbourhood). In close collaboration with the concerned people this will be followed by promotion of alternative sources of safe drinking water (rainwater harvesting, treated surface water, and treated arsenic contaminated ground water). The safe water options that BRAC is currently implementing are: rain water harvesting (RWH), treatment of pond water with "pond sand filter" (PSF), treatment of ground water with "Safi" candle filter, and dug well.

- A *follow-up* study will be performed including individuals having skin changes in order to assess the effect of arsenic mitigation on the reduction of arsenic levels in urine (change in exposure), as well as on reversibility of skin lesions, assessed by clinical examination. This will enable us to test the hypothesis that cessation of arsenic intake through drinking water in individuals with arsenicosis of skin will result in some degree of reversibility of these skin changes

- An arsenic mitigation programme with a shift to alternative, arsenic-low or arsenic-free water sources might potentially imply an increased exposure to pathogen-contaminated water, e.g. unclean surface water. Water quality of all alternate safe water options will be monitored and tested by BRAC, especially for diarrhoeal pathogen contamination. This will enable us to test the hypothesis that a shift to alternative, arsenic-low or arsenic-free water sources as part of a mitigation program will not imply an increased contamination of alternate water source.

## Training of field staff

*Training of field team.* Extensive training will be given to the field team on arsenic, its health consequences and skin lesions. The training will be conducted by the staff of ICDDR, B, and assistance will be sought from DCH, NGO- Forum and NIPSOM. The training will especially be focused on how to identify arsenicosis patients.

*Training for FRA and Shastha Sebika (SS, BRAC).* Training will be given about the details of origin and extent of arsenic poisoning in the ground water of Bangladesh. On the second day the FRA and SS will learn about the technique of testing of arsenic in the field using field kit. Later more lessons will be provided on how to collect the water samples, transport and storage.

*Training of Medical Officers.* Training will be given on arsenic and its health consequences at Matlab Training Centre. The training will be conducted by the staff of

ICDDR, B, with assistance from DCH and NGO- Forum. The training will be concentrated on how to identify arsenicosis patients. First, the training will provide details about the origin and extent of arsenic poisoning in the ground water of Bangladesh, health aspects of arsenicosis, and identification of patients. Second, theoretical and practical training will be provided in identifying arsenicosis skin lesions. This training will include patients with different skin manifestation, i.e., keratosis, melanosis and/or leucomelanosis. The participating physicians will examine the identified individuals and classify the skin lesions as arsenic-related lesions, suspected arsenic-related lesions and not arsenic related skin problems. A competent dermatologist will also train the physician in order to have the different diagnoses (DD) for arsenic skin lesions, i.e., Addision's disease, cirrhosis of liver, pellagra, excessive exposure to sun, xeroderma, corns, warts, etc. Later the physicians can train the field teams in order to identify suspected individuals in the field.

*Role of Dermatologist.* A competent dermatologist will be recruited for the study. He will train the study personnel on identification of arsenic related skin lesions and he will also validate randomly selected sub-sample of arsenic lesions, diagnosed by health workers and physicians.

## Skin screening in the field

Trained field teams with male and female field research assistant (FRA) will perform a clinical screening of skin manifestations in the entire study population from 5 years of age and above (approx. 190,000 population, 97,000 in the first phase). The community health research workers (CHRWs) will introduce the field team to the community. There will be 10 teams (each consisting of one male FRA and one female FRA). The team will move from village to village until the entire area is covered. Skin manifestations of arsenicosis (melanosis, keratosis, leucomelanosis and hyperkeratosis) will be confirmed following criteria developed in consultation with expertise in this field. They will work for the whole Matlab DSS area encompassing 220,000 population after finishing the intervention area. Individuals with skin lesions will be invited to the Matlab central health facility for confirmation by physician. The diagnosis of skin lesions by the physicians will be validated by the dermatologist in a randomly selected sub sample of cases. Screening of skin changes will precede the screening of arsenic water concentrations in tube wells, but will be closely linked in time to avoid possible biases. Photographs of the skin lesion will be taken by a digital camera under standardised conditions and used for validation of the findings by an expert panel. The validation will be used for retraining of the field staff and for quality control.

## Measurement of blood pressure

The physician will further examine the individuals as well as measure blood pressure. Blood pressure will be taken after rest and relaxation for at least 15 minutes in sitting position according to the protocol recommended by the World Health organization.

Blood pressure will be measured 3 times by mercury column sphygmometer and the lowest value will be taken as the proper value.

### Assessment of arsenic in tube wells

Approximately 9000 tube wells (4500 in each phase) in the Matlab area will be screened by use of Merck field kits, and tube wells with concentrations of arsenic above 50 µg/L will be classified as arsenic contaminated. A field team comprising of a FRA (field research assistant) and SS (Sastha Sabika, BRAC) will analyse tubewell water. This screening of water will take place *after* the screening of arsenicosis in order to avoid biases. On the same occasion water samples will be taken and frozen for analysis by atomic absorption spectrophotometry (AAS) at the ICDDR,B laboratory in Dhaka. The initial semi-quantitative screening test is needed for the interaction with the community members and initial mitigation activities. The AAS analysis is needed for the dose-effect analysis over the whole range of arsenic concentrations in tube wells. A random sub-sample of 600 tube well water samples will be selected for repeated examination by AAS over time in order to study seasonal variation and time trends (quarterly testing). The arsenic screening activities will be closely co-ordinated with the mitigation activities. The initial advice on alternative water sources will immediately be given and discussed with the affected household when the filed test kit result is ready. The strategy for the long-term mitigation activities is summarised below.

### Use of tube well water as drinking water

Information on use of tube wells (initiation of tube well, depth of tube well, GIS coordinates of tube wells, start of use as source of drinking water) is partly available in the current HDSS databases. These data will be checked on the household and individual level in order to generate exposure data for a specific tube well as well as for all individuals. For each individual a retrospective history of sources of drinking water will be taken, based on field experiences from West Bengal. In addition, a 24-recall of water intake will be taken.

### Assessment of nutritional status

Some information on nutritional status of the Matlab population is already available in the Matlab databases (arm circumference on all children, weight of women 13-44 years of age in half of the area). Additional information is needed to assess the modifying effect by nutritional status on arsenic-related health problems. Anthropometric status (weight, height) will be measured on all identified cases of arsenicosis and two randomly selected referents for case-referent analysis.

### Ascertainment of cause of death in the adult population

As part of the routine HDSS activities all deaths in the surveillance area are registered and a structured interview is performed with the relatives in order to register the symptoms preceding death or known diseases leading to the death of the individual. This

information is used in a standardised way to classify the causes of death. The information on cause of death is an integrated part of the HDSS databases.

## Case-referent study of arsenicosis of skin

All identified cases from 5 years of age and above with arsenic-related skin lesions will be identified as cases. Arsenic causes a variety of benign skin lesions including hyperpigmentation, hyperkeratosis, leucomelanosis, and, more rarely, squamous cell carcinomas (14). Referents will be randomly selected from the HDSS databases (from 5 years of age).

Cases and referents will be invited to the Matlab central facility or, when appropriate, to the sub-centres. Photographs will be taken of skin lesions under standardised conditions and used for validation of the findings by an expert panel. Anthropometric measurements will be taken (weight, height). Blood samples will be taken for haemoglobin assessment by HemoCue® and for later analyses of relevant micronutrient status. The cases will be carefully re-examined in order to identify suspected skin cancer. Blood pressure will be measured, urine will be tested for glucose and protein, and evaluation will be done for peripheral vascular disease and peripheral neuropathy. Patients with arsenic-related diseases demanding proper treatment (e.g. skin cancers) will be referred to appropriate level of care for treatment.

## Laboratory analyses

Water samples from tube wells will be collected in the villages and frozen to -20°, thereafter transported to Dhaka and analysed for total arsenic by AAS at the ICDDR,B laboratory.

First-morning urine samples will be collected with assistance from Community Health Research Workers, frozen and stored in -86° C freezers. Samples will be transported on dry ice to Karolinska Institutet, Sweden for analysis of inorganic arsenic and its methylated metabolites. These analyses will be conducted at Division of Metals and Health, Institute of Environmental Medicine, Karolinska Institutet, Sweden (Professor Marie Vahter). From the case-referent study all urine samples will be analysed for total arsenic. In a subsample with elevated values (estimated to 75%) speciation will be performed. In the clinical follow up of cases with skin lesions urine samples will be take on a quarterly basis to evaluate the cessation of exposure to arsenic. We estimate that two such follow up urine collections will be done per patient during a 2-year period.

Blood samples from the case-referent study will be analysed for S-zinc and selenium (atomic absorption spectrophotometry). Parts of the samples will be stored for additional analyses (folic acid, β-carotene).

## Sample size calculations

*Cohort analyses.* In the 220,000-population sample, 190,000 are 5 years of age and above, according to our demographic surveillance, and included in the skin screening. A conservative estimate, based on local data from other arsenic-exposed Bangladeshi communities, indicates that 0.5% of the population may have arsenic-related skin changes, i.e. 950 individuals. If the average exposure periods are 15 years and three quarters of the population are exposed to "toxic" levels, relative risks for skin changes among exposed (using 50μg/L as cut off for exposure) down to the level of 1.2 may be demonstrated, and with a dichotomous stratification (e.g. by gender) down to the level of 1.3. This implies that the sample size will allow for stratification and still maintain enough power to demonstrate the anticipated and even lower relative risks.

If three years of data on pregnancies and reproductive outcomes are included in the analysis, using a case-referent approach in the analysis, relative risks on the level of 1.4 may be detected for the outcomes miscarriage, stillbirth or neonatal death, respectively. Including a longer time period than 3 years provides more pregnancies for the retrospective analysis and increases the power. The disadvantage may be a potentially decreased quality of the exposure information.

A 5-year retrospective cohort analysis of cancer and cardiovascular deaths would allow for a detection of excess risks on the level of OR 1.4 and 1.2, respectively, given the mortality reported in those diagnoses 1996-2000 and a cut-off exposure level of 500 μg/L. If the duration of exposure and the latency periods so allows a longer period for the analysis may be included.

*Case-referent analysis.* Assuming that 75% of non-cases are "exposed" (e.g. to arsenic levels >50μg/L) and that 2 referents are selected per case of skin lesions an OR of 1.2 may be detected. If stratifying into two groups, e.g. by sex, an OR of 1.3 may be detected (given that $\alpha$=0.05 and 1-$\beta$=0.80). The sample size in the case-referent study will suffice to detect any clinically relevant differences between (two) groups in hemoglobin, S-ferritin, S-zinc and S-β-carotene, according to our experience and available information on serum levels and variances from anemia studies in Bangladesh.

A random sub-sample of water from 600 tube wells will be assessed repeatedly on a quarterly basis in order to monitor time trends and evaluate seasonal variation. This sample size will allow a detection of overall seasonal differences of 30 μg/L (based on a mean of 212 μg/L, and a SD of 184 μg/L).

After a short period of mitigation activities, e.g. when 1/10 households have shifted to alternative water sources, a difference of a few percent in the point prevalence of diarrhoeal diseases caused by the intervention may be detected (presuming an overall point prevalence in under-five children of 8%).

*Exposure assessment.* Arsenic exposure level will be categorized on different levels and will account for duration in order assess dose-effect relations.

| Design | Population | Outcome, estimated number of cases | Exposure level | Proportion exposed in population | Lowest detectable RR (figure for phase 1* between brackets) | Sample size |
|---|---|---|---|---|---|---|
| Cohort | 190,000 | Skin lesions (0.5% of the sample = 950) | >50 µg/L | 75% | 1.17; 95% CI 1.01-1.36; (1.3) | Total population surveyed |
| Cohort, case-referent | 19,000 pregnancies (3 years of surveillance) | Miscarriages (n = 662) | >500 µg/L | 10% | 1.37; 95% CI 1.02-1.82; (2.0) | Case referent analysis: 662 cases 1324 referents |
| Cohort, case-referent | 19,000 pregnancies (3 years of surveillance) | Stillbirths (n = 551) | >500 µg/L | 10% | 1.40; 95% CI 1.02-1.91; (2.0) | Case-referent analysis: 551 cases, 1102 referents |
| Cohort, case-referent | 17,300 live births (3 years of surveillance) | Neonatal deaths (n=702) | >500 µg/L | 10% | 1.36; 95% CI 1.03-1.80 (1.8) | Case-referent analysis: 702 cases, 1404 referents |
| Cohort | ICDDR,B surveillance 1996-2000 | Cancer deaths >14 years of age during last 5 years (n=425) | >500 µg/L (assuming sufficiently long exposure) | 10% | 1.37; 95% CI 1.03-1.82; (1.55) | 5 years surveillance, 675,000 person years |
| Cohort | ICDDR,B surveillance 1996-2000 | Cardio-vascular deaths > 14 years of age during last 5 years (n=840) | >500 µg/L | 10% | 1.23; 95% CI 1.00-1.51; (1.46) | 5 years surveillance, 675,000 person years |
| Case-referent | 190,000 | Skin lesions, n = 950 | >50 µg/L | 75% | 1.20; 95% CI 1.00-1.45; (1.3) | 950 cases, 1900 referents. When stratifying for 1 background factor OR ≥ 1.3 detectable |

** Phase 1: study in the 110,000 population with 97,000 individuals >4 years.*

### *Arsenic mitigation intervention by BRAC*

BRAC, one of the largest national non-governmental organizations, has a proven capacity for field-level programme implementation, socio-economic research, a strong institutional network and experience in training community members in testing tube well water for arsenic. BRAC's action research on community based arsenic mitigation includes the following major components.

#### The safe water option implementation plan

This component of the project aims at installing safe water options in arsenic affected areas in Matlab. Priority will be given to villages where the arsenic problem is acute. The safe water options will be installed after testing of tube wells is completed and the

alternative options are evaluated. Monitoring of the water quality and social acceptance of the alternative options will be carried out during the project period.

### Situation analysis and participatory decision making

The BRAC Community Health Workers from each village in the area will be jointly trained by BRAC and ICDDR,B in the health effects of arsenic, arsenic testing, and alternative water sources. This training will also be co-ordinated with the government arsenic project BAMSWP. ICDDRB and BRAC staff will jointly perform the testing of tube wells, described above. Villages meetings will be held with a cross section of villagers as part of the testing process. Once all tube wells have been tested, the results will be presented to the village community in a second meeting. At that meeting, alternative sources of safe drinking water will also be discussed. A limited list of solutions is approved by the project and will be promoted. This list of options may change over time, if indicated and advised by government and other stakeholders. Since villagers have little or no experience with alternative safe water sources, demonstration of different alternative safe water systems will be done, with no cost to the community. However, the community would decide where the system would be located, and commit themselves to maintain the system.

### System implementation

Identified alternative safe water options will be construction of BRAC's Technical Advisor. BRAC engineer will oversee the construction and commissioning of the process.

*Table. Different safe water options initially selected for the project.*

| Option | Water sources | Location | Families served |
|---|---|---|---|
| Pons sand filter (PSF) | Surface water | Community | 40-60 |
| Rain water harvesting (RWH) | Rain water | Family | 1 |
| Two chamber treated unit | Surface water | Community | 6-10 |
| Safi filter | Ground water | Family | 1 |

*Pond and sand filters.* In areas where deep tube wells are not feasible, it is possible to treat surface water from ponds, that are exclusively reserved for drinking purposes and to make it safe for drinking and cooking. DPHE, supported by UNICEF, has designed a community-based slow sand filtration system, called *pond sand filter*, which can remove bacteria from surface water by filtering it through a large tank filled with sand and gravel. It is now being successfully used in arsenic-effected areas. Community members must periodically clean pond sand filters by washing the top layers of sand.

*Deep wells.* Deep wells, deeper that 80 meters, are free from arsenic. Dhaka city water and the water sources of the southern part of Bangladesh (where salt water enters the shallow aquifer) are therefore mostly free from arsenic. Although more expensive than shallow wells, deep wells could be an alternative. If such wells are dug carelessly, there is a possibility of "shunting" the aquifers and allowing water from the higher, arsenic-

contaminated aquifer contaminate the lower aquifer. It is unclear whether, in a longer perspective, pumping would increase the arsenic content in those wells.

*Rainwater harvesting.* Like pond sand filters rainwater-harvesting systems have been used in the coastal districts for years, and are being introduced in arsenic-affected areas. Rainwater harvesting system use a tin rooftop or sometimes a sheet of plastic, to collect rainwater and store it is large cement tanks. Users let the first few minutes of rainfall without collecting the water, to clean roof and gutters. Once in the tank, the rainwater can be safely stored indefinitely without being contaminated by bacteria. With a large enough tank, a family can store enough water for drinking and cooking all through the dry season.

*Monitoring of water quality and use of water.* Water quality of all alternate safe water options will be monitored and tested, especially for diarrhoeal pathogen contamination. BRAC staff will visit each village on a regular basis to monitor the operation and maintenance of alternative water systems and motivate to promote safe water use. After distribution or construction of any option among the villagers it requires continuous monitoring of the use of each and every option at least for few months because people are used to the tube well water and may find the alternative options more complicated.

### Evaluation of impact and possible negative consequences of intervention

The operation and maintenance of the alternative water systems will be monitored by BRAC, see above. The shift to alternative arsenic-free water sources might imply an increased exposure to pathogens that could result in increased rates of diarrhoeal diseases in vulnerable groups, i.e. infants and children. The occurrence of diarrhoeal diseases is monitored as par of the health and demographic surveillance, by monthly home visits and interviews. The occurrence of diarrhoeal diseases in children of households with new water sources will be compared to households without such changes, considering possible confounding, e.g. by age.

## *Potential impact*

This project will generate new knowledge on doses of arsenic exposures and effects on health, i.e. the occurrence of skin lesions and negative reproductive outcomes, such as miscarriages, stillbirths, and neonatal mortality. The toxic effects on skin will be evaluated in relation to age, sex, and nutritional status. Further, the studies will provide answer to the question if the arsenic contamination of the drinking water already is resulting in excess mortality among adults. Such information is much needed in the discussion and forecasting of the arsenic-related health consequences in Bangladesh. The results would further give a solid epidemiological platform for a better understanding of the speed by which arsenic-related diseases and health manifestations develop in the currently arsenic-exposed Bangladeshi population, and the effect of an arsenic mitigation intervention. ICDDR,B and the Matlab surveillance system offer unique possibilities for such studies. Due to the already collected health data of that system the answers to these important questions may be provided within a 2-year project period.

## Facilities Available

Describe the availability of physical facilities at the place where the study will be carried out. For clinical and laboratory-based studies, indicate the provision of hospital and other types of patient's care facilities and adequate laboratory support. Point out the laboratory facilities and major equipment that will be required for the study. For field studies, describe the field area including its size, population, and means of communications. **(TYPE WITHIN THE PROVIDED SPACE).**

The Matlab research and services infrastructure is presented in the text above. These facilities are unique and make this project possible. The health and demographic surveillance system will provide a lot of the necessary information needed. A strong research team has been formed with strong competence in epidemiology, arsenic epidemiology, nutrition, clinical sciences, reproductive epidemiology and biochemistry. Excellent partners have been identified in the area of arsenic mitigation (BRAC) and arsenic biochemistry (professor Marie Vahter, Karolinska Institutet). The ICDDR,B biochemistry laboratory has already an AAS equipment for arsenic analysis (only total arsenic), but the procurement of another AAS equipment would considerably increase the capacity.

## Data Analysis

Describe plans for data analysis. Indicate whether data will be analyzed by the investigators themselves or by other professionals. Specify what statistical softwares packages will be used and if the study is blinded, when the code will be opened. For clinical trials, indicate if interim data analysis will be required to monitor further progress of the study. **(TYPE WITHIN THE PROVIDED SPACE).**

The investigators will review all questionnaires and data forms for accuracy, consistency and completeness. After editing, data will be entered for editing and cleaning. Periodical checks will be performed by running and reviewing frequency distributions and cross-tabulations. The HDSS has a series of data quality controls that will further ensure the completeness and correct identities of the information. Cohort analysis, and multivariable modelling of doses and effect will be done by use of SPSS 10.0 or other appropriate software, as well as case-referent analysis and logistic regression modelling.

The modelling of doses and effects will include some different options in order to demonstrate alternative approaches and how robust the estimates are. It will include calculations of standardized morbidity ratios (SMR), standardized rate ratios (SRR), and Cox regression analyses catering for possible influence by age, sex and other confounding factors.

## Ethical Assurance for Protection of Human Rights

Describe in the space provided the justifications for conducting this research in human subjects. If the study needs observations on sick individuals, provide sufficient reasons for using them. Indicate how subject's rights are protected and if there is any benefit or risk to each subject of the study.

The study will include invitation for testing of tube well water, inspection of skin for arsenic skin lesions, and, in a sub-set of the population, blood sampling for micronutrients, and urine sampling for arsenic analyses. The water testing and the screening for skin lesions will benefit the parsons in the affected households and proper advice will be given to affected households and individuals. The blood sampling is not of immediate benefit to the individual participant, although the assessment of haemoglobin may be useful for anaemic individuals who may benefit from iron therapy. The urine sampling is not of immediate benefit to the participants, although the assessment of total arsenic will be useful for some individuals in getting further advice to change to arsenic-free drinking water. However, due to logistic reasons there will be a delay in the analysis of arsenic in urine. Informed consent will be sought, and participants will be free to refrain totally from participation or from some part of the study. The study is linked to a mitigation activity for which a major national NGO, BRAC, is responsible. To benefit from that activity will not be conditionally linked to the participation in the study. The proposal will be reviewed by the Ethical Review Committee at ICDDR,B, Dhaka, Bangladesh.

## Use of Animals

Describe in the space provided the type and species of animal that will be used in the study. Justify with reasons the use of particular animal species in the experiment and the compliance of the animal ethical guidelines for conducting the proposed procedures.

Not applicable

# Literature Cited

Identify all cited references to published literature in the text by number in parentheses. List all cited references sequentially as they appear in the text. For unpublished references, provide complete information in the text and do not include them in the list of Literature Cited. There is no page limit for this section, however exercise judgment in assessing the "standard" length.


1. Chowdhury UK, Biswas BK, Chowdhury TR, Samanta G, Mandal BK, Basu GC, et al. Groundwater Aresnic Contamination in Bangladesh and West Bengal, India. Environ Health Perspect 2000;108:393-397.
2. Chowdhury TR, Basu GK, Mandal BK, Biswas BK, Samanta G, Chowdhury UK, et al. Arsenic poisoning in the Ganges delta. Nature 1999;401(6753):545-6; discussion 546-7.
3. Tondel M, Rahman M, Magnuson A, Chowdhury IA, Faruquee MH, Ahmad SA. The Relationship of Arsenic Levels in Drinking Water and the Prevalence Rate of Skin Lesions in Bangladesh. Environ Health Perspect 1999;107(9):727-729.
4. British Geological Survey. Arsenic contamination of groundwater in Bangladesh. http://www.bgs.ac.uk/arsenic/bangladesh.html; Access date April 2001.
5. Guha Mazumder DN, Haque R, Ghosh N, De BK, Santra A, Chakraborty D, et al. Arsenic levels in drinking water and the prevalence of skin lesions in West Bengal, India. Int J Epidemiol 1998;27(5):871-7.
6. Vahter M. Methylation of inorganic arsenic in different mammalian species and population groups. Sci Prog 1999;82(( Pt 1)):69-88.
7. Hsueh YM, Wu WL, Huang YL, Chiou HY, Tseng CH, Chen CJ. Low serum carotene level and increased risk of ischemic heart disease related to long-term arsenic exposure. Atherosclerosis 1998;141(2):249-57.
8. Hsueh YM, Chiou HY, Huang YL, Wu WL, Huang CC, Yang MH, et al. Serum beta-carotene level, arsenic methylation capability, and incidence of skin cancer. Cancer Epidemiol Biomarkers Prev 1997;6(8):589-96.
9. Hsueh YM, Cheng GS, Wu MM, Yu HS, Kuo TL, Chen CJ. Multiple risk factors associated with arsenic-induced skin cancer: effects of chronic liver disease and malnutritional status. Br J Cancer 1995;71(1):109-14.
10. Brown KG, Boyle KE, Chen CW, Gibb HJ. A dose-response analysis of skin cancer from inorganic arsenic in drinking water. Risk Anal 1989;9(4):519-28.
11. NRC, editor. Arsenic in Drinking Water. Washington, DC: National Academy Press; 1999.
12. Golub MS, Macintosh MS, Baumrind N. Developmental and reproductive toxicity of inorganic arsenic: animal studies and human concerns. J Toxicol Environ Health B Crit Rev 1998;1(3):199-241.
13. DeSesso JM, Jacobson CF, Scialli AR, Farr CH, Holson JF. An assessment of the developmental toxicity of inorganic arsenic. Reprod Toxicol 1998;12(4):385-433.

14. Shannon RL, Strayer DS. Arsenic-induced skin toxicity. Hum Toxicol 1989;8(2):99-104.

## Dissemination and Use of Findings

Describe explicitly the plans for disseminating the accomplished results. Describe what type of publication is anticipated: working papers, internal (institutional) publication, international publications, international conferences and agencies, workshops etc. Mention if the project is linked to the Government of Bangladesh through a training programme.

The findings will be communicated to other actors and stakeholders in the area of arsenic contamination of ground water and its health effect in Bangladesh. This will be done through reports (more popular as well as scientific reports) and through a workshop with invited participants at the Matlab training Centre during the second year of the project.

The findings will be used for the projections of health effects caused by the arsenic catastrophe in Bangladesh (burden of arsenic-induced diseases, disabilities and death). The findings will also be used in order to recommend appropriate actions in order to protect foetuses and newborns, in order to plan some aspects of the health services to arsenic-exposed communities, and in order to evaluate appropriate alternative water sources.

A narrative and a financial report will be submitted to the funding partners every 6 months. After completion of the project (at 24 months) a final report will be submitted to donors within another 2 months.

## Collaborative Arrangements

Describe briefly if this study involves any scientific, administrative, fiscal, or programmatic arrangements with other national or international organizations or individuals. Indicate the nature and extent of collaboration and include a letter of agreement between the applicant or his/her organization and the collaborating organization. **(DO NOT EXCEED ONE PAGE)**

The mitigation program will be collaborated with Research and Evaluation Division, BRAC, Bangladesh (Director research, Dr Mushtaque Chowdhury). BRAC, a non-governmental organisation, has initiated an arsenic mitigation program. The organisation has gained considerable experience of field-testing of tube wells by field kits used by trained village health workers (VHW). BRAC has been running projects with UNICEF/DPHE (with participation by Grameen Bank and Dhaka Community Hospital) to involve communities in finding safe sources of drinking water once unacceptable arsenic levels in tube well water have been detected.

The arsenic biochemistry is collaborated with professor Marie Vather, Institute of Environmental Medicine, Division of Metals and Health, Karolinska Institutet, Stockholm. Professor Marie Vather is a leading expert on health effects of arsenic exposure and arsenic biochemistry. She has been involved in the planning of the project,

and will be responsible for overseeing the arsenic biochemistry activity. Her laboratory will be running the analysis of the urine samples.

# Biography of the Investigators

May 2001

## CURRICULUM VITAE

| NAME | CURRENT POSITIONS | ADDRESS |
|---|---|---|
| Lars Åke Persson<br>Born 1947-07-23 (Id 470723-1439) | Professor, International Public Health, Umeå University, Sweden (leave of absence since March 1, 1999)<br>Director, Public Health Sciences Division, ICDDR,B: Centre for Health and Population Research, Dhaka, Bangladesh | Public Health Sciences Di<br>ICDDR,B<br>GPO Box 128, Mohakhali CA.<br>Dhaka 1000, Bangladesh<br>Phone +880 2 9885155<br>Fax +880 2 8826050<br>e-mail persson@icddrb.org |

EDUCATION/TRAINING

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | YEAR(s) | FIELD OF STUDY |
|---|---|---|---|
| Uppsala University, Sweden | MD | 1973 | Medicine |
| Sandöskolan, Sweden | Certificate | 1972-73 | Aid and disaster relief training |
| Swedish Board of Health and Welfare | Certificate | 1973 | Tropical/international medicine |
| Gävle Hospital and Västernorrlands landsting, Sweden | Internship | 1973-74 | Medicine, Surgery, General pra |
| Dept Paediatr, Örnsköldsviks sjukhus, Sweden | Residency | 1974-76 | Paediatrics |
| Dept Paediatrics, Umeå University, Sweden | Residency | 1978-79 | Paediatrics |
| Dept Child Psychiatry, Umeå University, Sweden | Residency | 1979 | Paediatrics/child psychiatry |
| Dept Infectious Diseases, Umeå University, Sweden | Residency | 1979 | Paediatrics/inf dis |
| Swedish Board of Health and Welfare | Specialist | 1980 | Paediatrics |
| Umeå University, Sweden | PhD | 1984 | Paediatrics/Paediatric Nutrition |
| Dept Paediatrics, Umeå University, Sweden | Docent | 1990 | Paediatrics |
| Umeå University, Sweden | Professor | 1998 | International Public Health |

PROFESSIONAL EXPERIENCE

| | |
|---|---|
| 1976-1978 | Medical Officer, Ndolage Hospital, Tanzania |
| 1980-1983 | Fellow, Social Medicine, Umeå University, Sweden |
| 1983-1984 | Fellow, Dept Paediatrics, Umeå University, Sweden |
| 1984-1985 | Medical Advisor, Institute for Protection of Children's Health, Hanoi, Vietnam |
| 1985-1986 | Fellow, Dept Paediatrics, Umeå University, Sweden |
| 1986-1990 | Senior lecturer/researcher in Paediatrics/Epidemiology, Umeå University, Sweden |
| 1990-1997 | Associate professor, Dept Epidemiology and Public Health, Umeå University, Sweden |
| 1998- | Professor in International Public Health, Umeå University, Sweden |
| 1999- | Director, Public Health Sciences Division, ICDDR,B, Dhaka, Bangladesh |

LANGUAGES

Swedish - mother-tongue; English – fluent; Kiswahili – fluent; Spanish – fair; German – fair; French – fair

RESEARCH ADVISOR

*Completed theses*

| Title | Degree | Student | Year |
|---|---|---|---|
| Infant mortality in transitional Nicaragua | PhD | Rodolfo Peña | 1999 |
| Adolescent pregnancies in Nicaragua. The importance of education. | PhD | Elmer Zelaya Bladon | 1999 |
| Child health in Somalia. An epidemiological assessment in rural communities during a pre-war period. | PhD | Mariam M Ibrahim | 1998 |

| | | | |
|---|---|---|---|
| Utilisation of reproductive health services in Vietnam | Licentiate | Ngo Van Toan | 1996 |
| Teenage sexuality and reproduction in Nicaragua. Gender and social differences | Licentiate | Elmer Zelaya Bladon | 1996 |
| Social patterning of child health in Vietnam | Licentiate | Dinh Phuong Hoa | 1996 |
| Family planning and reproductive patter in rural Vietnam | Licentiate | Hoang Thi Hoa | 1996 |
| Risk factors for future cardio-vascular diseases. A longitudinal study from adolescence to adulthood | PhD | Erik Bergström | 1995 |
| Studies for health planning in rural Somalia. Community perceptions and epidemiological data. | Licentiate | Abdulaziz S Aden | 1994 |
| The causation of konzo. Studies on a paralytic disease in Africa. | PhD | Thorkild Tylleskär | 1994 |
| Community involvement in epidemiology and preventive work - the case of a Swedish community | PhD | Inger Brännström | 1993 |

*Current research students*

| Title of project/planned thesis | Intended degree | Student | Planned year of defence |
|---|---|---|---|
| The multifactorial aetiology of coeliac disease. Studies of the Swedish epidemic. | PhD | Anneli Ivarsson | 2001 |
| Effectiveness of iron supplementation programmes in pregnancy. The impact of dose frequency on compliance, side effects and haematological outcome | PhD | Zia Hyder | 2001 |
| Micronutrient status and functional outcomes in infancy. Intervention studies in Indonesia and Sweden. | PhD | Torbjörn Lind | 2002 |
| Trauma exposure, resilience factors and mental health of refugee children in Sweden. | PhD | Stephen Goldin | 2002 |
| Equity in child health in Vietnam | PhD | Dinh P Hoa | 2002 |

RESEARCH PROJECTS

| Project | Role in project | Funding agency | Year(s) |
|---|---|---|---|
| Arsenic in tube well water and healt consequences | Principal investigator | Sida, WHO | 2001- |
| Socioeconomic determinants of child survival during warfare and rapid social transition. Infant mortality in Bavi district, Vietnam, 1965-98 (Collaborative project with Department of Social Paediatrics, Institute for Protection of Children's Health, Hanoi | Principal investigator | SAREC | 1999- |
| Pilot studies of arsenic exposure through drinking water and health consequneces in Matlab, Bangladesh | Principal investigator | USAID | 2000- |
| Combined interventions to promote maternal and infant health (Collaborative project between ICDDR,B, UNICEF, and Cornell University, USA) | Principal investigator | UNICEF, National Institute of Health (NIH) and Fogarty | 2000- |
| Studies of the public health consequences of violence against women in Bangladesh (Collaboration ICDDR,B, Naripokkho, Bangladesh and WHO) | Co-investigator | Asian Development Bank (ADB) | 2000- |
| Development of a questionnaire instrument for evaluation of causes of adult female deaths and maternal mortality, and the evaluation of causes of death in a nation-wide survey in Bangladesh (Collaboration with Johns Hopkins University) | Principal investigator | USAID through Johns Hopkins | 2000- |
| Iron and zinc deficiency during infancy - causes, | Principal | SAREC, MFR | 1995- |

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|---|---|---|---|
| functional outcomes and the effect of an intervention. A cohort study in central Java. (Collaboration with Gadjah Mada University and Dept Nutrition UC Davis) | investigator | | |
| Determinants of compliance with iron and zinc supplementation in infancy. A cohort study in Central Java | Principal investigator | SAREC | 1997- |
| Vitamin A supplementation and immunisation in practice in Bangladesh. A cohort study of the equity and effectiveness in preventing under five mortality (Collaboration with Research and Evaluation Division, BRAC, Bangladesh) | Principal investigator | SAREC | 1997- |
| Effectiveness of iron supplementation programmes in pregnancy. The impact of dose frequency on compliance, side effects and haematological outcome (Collaborative project with BRAC, Bangladesh and Dept Nutrition, UC Davis) | Co-investigator | SAREC | 1996- |
| Exposure to trauma, resilience factors, and mental health of refugee children in Sweden (Collaboration with Dept Child Psychiatry, Umeå university) | Principal investigator | Swedish Council for Planning and Co-ordination of Research (FRN), and from Swedish Council for Social Research (SFR) | 1994- |
| Swedish Multicentre study of the incidence and aetiology of coeliac disease | Co-investigator, member of the steering committee | Swedish council for forestry and agricultural research (SJFR), The Swedish Foundation for Health Care Sciences and Allergy Research (Vårdal), and "Front-line research funds" of the Västerbotten county council. | 1991- |
| Swedish participation in the multi centre study "Euro Growth Study" regarding feeding, growth and micronutrient health of infants 0-3 years of age | Principal investigator | Umeå university research funds (Central component financed by European union) | 1991-1998 |
| Health systems research in Vietnam (Collaborative project with Ministry of Health, Vietnam, Medical Faculty, Hanoi, IHCAR, KI, Nordic School of Public Health, Göteborg, and Epidemiology, Umeå University, Sweden. | Co-principal investigator | SAREC | 1991-1999 |
| Reproductive and child health in Nicaragua (Collaborative project with the Municipality Health Services, the Autonomous Nicaraguan University, and the Movimiento Comunal, León, Nicaragua) | Principal investigator | SAREC | 1990-1999 |
| Risk indicators in adolescence for future cardio-vascular diseases, the Umeå Youth Study | Co-principal investigator | Swedish council for social research (SFR) | 1988-1995 |
| The epidemiology of Epidemic Spastic Paraparesis (Konzo) in Zaire (Collaborative project between Nutrition Institute in Kinshasa (CEPLANUT), ICH, Uppsala University, and Epidemilogy, Umeå University, Sweden) | Co-investigator | SAREC | 1988-1994 |
| Swedish Childhood Diabetes Study | Co-investigator | MFR | 1986-1991 |
| Epidemiology in the planning of Primary Health Care (Collaboration with Community health department, Medical Faculty, Somali National University, Mogadishu, Somalia) | Co-investigator, later principal investigator | SAREC | 1982-1992 |

| | | | |
|---|---|---|---|
| Swedish multicentre study on food habits and nutrient intake in childhood in relation to health and socio-economic conditions (Collaborative study with Sedish Food Administration and Uppsala University) | Co-investigator | Swedish Food Administration | 1979-1986 |

TEACHING

- Course organiser and teacher at international course in Health and Demographic Surveillance and Advanced Analysis of Longitudinal Data, in Matlab, Bangladesh (2001)
- Course organiser and teacher at International Training Course in Epidemiology for Public Health in Matlab and Dhaka, Bangladesh (2000)
- Teacher in Epidemiology at courses in Epidemiology and research methodology at ICDDR,B, Dhaka (1999-)
- Course co-organiser and teacher at 5 credit course in nutritional epidemiology at Umeå University (1997- 1998).
- Production of the text book "Epidemiology for Public Health" (by Lars Åke Persson and Stig Wall) based on the teaching experiences and international courses during the 1980s and 1990s. See publication list number 100.
- Course organiser and teacher in 5 credit course in public health, epidemiology and biostatistics as part of the introductory semester for biomedicine students at the medical faculty, Umeå University (1996-1998).
- Director of studies at the Department of Epidemiology and Public Health, Umeå University and development of the curriculum and core course content of the Masters' of Public Health program at Umeå University (1994-95).
- Course organiser and teacher at courses in Epidemiology, 10 credits, which is part of the post graduate program in Public Health at Umeå University (1991-present). This course as well as the entire Public Health program is given in English with course participants from many countries. Also organiser and teacher in Advanced Epidemiology (10 credits) from 1994 to 1998.
- Invited teacher in nutritional epidemiology at the ESPGAN summer school in Austria, 1995.
- Teacher in international health, nutrition and epidemiology at 10 credit courses in International Health at Umeå University. (1991-present).
- Teacher in international health and nutrition at courses at the Swedish Agricultural University. (1986-1996).
- Organiser and teacher in international health (2 credits) within a multidisciplinary course (10 credits) on "Conditions in low income countries" at Umeå University. (1989)
- Co-ordinator and teacher at yearly research training courses (summer school) in "Epidemiology and Field Research Methods" with participants from Africa, Asia and Latin America as well as European countries in Umeå. (1988-present). These courses are intensive courses of 2-3 weeks duration, including a lot of "hands-on" experience of epidemiology.
- Invited speaker at the SAREC supported research seminar "Infections of the gastrointestinal and respiratory tract" at the National Institute of Hygiene and Epidemiology, Hanoi, Vietnam. (1988).
- Co-ordinator and teacher in courses in "Epidemiology and Field Research Methodology" at the Olof Palme Institute in Hanoi, Vietnam (1986), at King Edward's Medical College in Lahore, Pakistan (1986), at the Medical Faculty in Mogadishu, Somalia (1987), in Luanda, Angola (1987), in Harare, Zimbabwe (1988) and in Matagalpa, Nicaragua (1988). Intensive courses of 1-2 weeks duration. The teaching methods developed have been evaluated and reported in the Bulletin of the World Health Organization (see publication list number 25). Course material developed in English and Spanish (see publication list number 82 and 88).
- Teacher and course organiser for the courses in paediatrics at Medical Faculty, Umeå University. (1985-1987). Responsible for three courses of three months duration each.
- Teacher/organiser of seminars, courses and weekly post-graduate training of paediatricians and nurses at the Olof Palme Institute for Protection of Children's Health, Hanoi, Vietnam and at various regional hospitals in Vietnam. (1984-85). Several hours of teaching each week. Development of course material, which was replicated in training activities on lower levels in the health care system.
- Teacher and co-organiser of a research training course supported by SAREC "Epidemiology in Primary Health Care" in Mogadishu, Somalia. (1984). Intensive course of one week's duration.

- Teacher in Social Medicine and Epidemiology for medical students at the Department of Social Medicine Medical Faculty, Umeå University. (1980-83). Course organiser, a few weeks of teaching per semester.
- Teacher in International Health and International Paediatrics for medical students at the Medical Faculty, Umeå University. (1978-1995).
- Teacher in Paediatrics and Child Health Care at Ndolage Nurses' Training School, Ndolage Hospital, Tanzania. (1976-78)..

ADVISORY COMMITTEES, EXPERT MISSIONS ETC.

- Member, Research Evaluation Committee, ICDDR,B (1999-)
- Executive board member, International Society for Research on Human Milk and Lactation (1998-)
- Member of the quality assurance group at the Medical Faculty, Umeå University (1997-1999).
- Faculty opponent at the defence of the PhD thesis of Bo Burström, Karolinska Institutet, "Risk factors for measles mortality. Studies from Kenya and 19th century Stockholm" (1996).
- Representative of the Medical Faculty in the Equal Opportunity Committee of Umeå University (1996-1999).
- Member of the research training committee (Forskarutbildningskomittén) at the Medical Faculty, Umeå University (1996-1999)
- Member of the advisory board for research grant applications to Swedish Medical Society (Svenska Läkaresällskapet) (1996- 1999)
- Chairman of the advisory group for research grants from the Joint Committee of the Northern County Councils at Umeå University. (1995)
- Co-ordinator of the program support by the Swedish Public Health Institute to Umeå University for research on Child and Adolescent Health. (1993-1999)
- Advisor to SIDA in its support to Tanzania Food and Nutrition Centre, Dar es Salaam. (1993-1999)
- Member of the research ethics committee at the Medical Faculty, Umeå University. (1993-1999)
- Member of the SAREC advisory board for research in health and nutrition. (1990-1997)
- Member of the board of the Working group of paediatric epidemiology of the Swedish Paediatric Association. (1990-1994)
- Faculty opponent at the defence of the PhD thesis of Redda Tekle-Haimanots "Epidemiology of neurological disorders in Ethiopia" at Umeå University. (1990).
- Secretary and member of an evaluation team for the SAREC supported Pakistani-Swedish research project "Breast feeding in a developing country" at King Edward Medical College, Lahore, Pakistan. (1989)
- Member of a working group of the Swedish Board of Health Welfare regarding the "Biological Development of Swedish Children". (1988-1990)
- Temporary WHO Adviser (Epidemiology) regarding "Research and action for the promotion of oral health within primary health care" (1987-1988)
- Member of the Swedish Research Council's (Forskningsrådsnämndens) advisory group on methodology in dietary studies. (1980-85)
- Member of the project group "Processing of epidemiological data in a developing country - development of a micro-computer system."(1982-84)
- Referee for a number of scientific journals, e.g. Acta Paediatrica, International Journal of Epidemiology, American Journal of Clinical Nutrition, Scandinavian Journal of Social Medicine, Scandinavian Journal of Public Health, Journal of Health, Population and Nutrition (member of the editorial committee of the last mentioned journal).

ORIGINAL PUBLICATIONS

1. Persson LÅ, Samuelson G, Johansson E, Osland-Johansson T. Vad äter svenska spädbarn? Se till hela familjens matvanor. [What do Swedish infants eat. Look at the food habits of the whole family].Läkartidningen 1982;79:3813-3816.
2. Samuelson G, Osland-Johansson T, Persson LÅ. Kvinnans kostvanor och näringsintag under graviditet. Näringsforskning 1983;27:22-25.
3. Brändström A, Broström G, Persson LÅ. The Impact of Feeding Patterns on Infant Mortality in a Nineteenth Century Swedish Parish. Journal of Tropical Pediatrics 1984;30:154-159.
4. Persson LÅ. Nutrition and health in infancy and childhood. An epidemiological approach to the assessment of dietary habits, their determinants and implications. Thesis. Umeå University Medical Dissertations New Series No 119. Umeå University, Umeå 1984.
5. Bruce Å, Hagman U, Persson LÅ, Samuelson G, Sjölin S. Näringsintag hos svenska barn. Resultat från en multicenterstudie 1980-1981. [Dietary intake among Swedish children. Results from a multi-centre study]. Vår Föda 1984;36:Suppl 2.
6. Persson LÅ, Johansson E, Samuelson G. From Breastmilk to Family Food. Infant Feeding in Three Swedish Communities. Acta Paediatr Scand 1984;73:685-692.
7. Persson LÅ, Johansson E, Samuelson G. Dietary intake of weaned infants in a Swedish community. Human Nutrition:Applied Nutrition 1984;38A:247-254.
8. Persson LÅ, Stecksén-Blicks C, Holm AK. Nutrition and health in childhood: causal and quantitative interpretations of dental caries. Community Dent Oral Epidemiol 1984;12:390-7.
9. Persson LÅ. Dietary habits and health risks in Swedish children. Human Nutrition:Clinical Nutrition 1984;38C:287-297.
10. Persson LÅ, Carlgren G. Measuring Children's Diets: Evaluation of Dietary Assessment Techniques in Infancy and Childhood. International Journal of Epidemiology 1984;13:506-517.
11. Persson LÅ. Multivariate approaches to the analysis of breast-feeding habits. Bulletin of the World Health Organization 1985;63:1129-1136.
12. Persson LÅ. Infant feeding and growth - a longitudinal study in three Swedish communities. Annals of Human Biology 1985;12:41-52.
13. Persson LÅ, Holm AK, Arvidsson S, Samuelson G. Infant feeding and dental caries - a longitudinal study of Swedish children. Swed Dent J 1985;9:201-6.
14. Hagman U, Bruce Å, Persson LÅ, Samuelson G, Sjölin S. Food Habits and Nutrient Intake in Childhood in Relation to Health and Socio-economic Conditions. A Swedish Multicentre Study 1980-81. Acta Paediatr Scand 1986; Suppl 328.
15. Thu NX, Cung HB, Liem NT, Cuóng PT, Persson LÅ. Surgical treatment of congenital cystic dilation of the biliary tract. Acta Chir Scand 1986;152:669-674.
16. Persson LÅ, Samuelson G. Vikt, längd och könsmognad bör sättas i relation till barns blodtryck. Läkartidningen 1987;84:109-110.
17. Blom L, Lundmark K, Dahlquist G, Persson LÅ. Estimating Children's Eating Habits. Validity of a Questionnaire Measuring Food Frequency Compared to a 7-Day Record. Acta Paediatr Scand 1989;78:858-64.
18. Persson LÅ, Samuelson G, Sjölin S. Nutrition and health in Swedish children 1930-1980. Three nutrition surveys in a northern Swedish county. Acta Paediatr Scand 1989;78:865-72.
19. Owour Omondi L, Persson LÅ, Staugård F. Determinants for breast-feeding and bottle-feeding in Botswana. J Tropical Pediatrics 1990;36:28-33.

20. Aden AS, Brännström I, Mohamud KA, Persson LÅ, Wall S. The growth chart - a road to health chart? Maternal comprehension of the growth chart in two Somali villages. Paediatric and Preinatal Epidemiology 1990;4:340-350.

21. Dahlquist GG, Blom LG, Persson LÅ, Sandström AIM, Wall SGI. Dietary factors and the risk of developing insulin dependent diabetes in childhood. BMJ 1990;300:1302-1306.

22. Tylleskär T, Banea M, Bikangi N, Fresco L, Persson LÅ, Rosling H. Epidemiological evidence from Zaire for a dietary etiology of konzo, an upper motor neuron disease. Bull World Health Org 1991;69:581-589.

23. Ibrahim MM, Persson LÅ, Omar MM, Wall S. Breast-feeding and dietary habits of children in rural Somalia. Acta Paediatrica 1992;81:480-483.

24. Blom LG, Persson LÅ, Dahlquist GG. A high linear growth is associated with an increased risk for childhood diabetes. Diabetologia, 1992;35:528-533.

25. Persson LÅ, Wall S. Epidemiology teaching and the community perspective. World Health Forum 1992;14:37-41.

26. Bergström E, Hernell O, Persson LÅ. Dietary changes in Swedish adolescents. Acta Paediatrica 1993;82:472-480.

27. Persson LÅ, Aden AS, Ibrahim MM, Omar MH, WallS. Famine in Somalia. The Lancet 1993;341:1478.

28. Brännström I, Weinehall L, Persson LÅ, Wester PO, Wall S. Changing social patterns of risk factors for cardiovascular disease in a Swedish community intervention programme. Int J Epidemiol 1993;22:1026-1037.

29. Brännström I, Persson LÅ, Wall S. Towards a Framework for Outcome Assessment of Health Intervention: Conceptual and Methodological Considerations. European Journal of Public Health 1994;4:125-130.

30. Ibrahim MM, Aden AS, Omar MH, Wall S, Persson LÅ. Diarrhoea among children in rural Somalia. Maternal perceptions, management and mortality.Annals of Tropical Paediatrics. 1994;14:215-222.

31. Brännström I, Persson LÅ, Wall S. Gender and social patterning of health - The Norsjö cardiovascular preventive program in northern Sweden 1985-1990. Scand J Prim Health Care 1994;12:155-61.

32. Blomquist H K:son, Jonsbo F, Serenius F, Persson LÅ. Supplementary feeding in the maternity ward shortens the duration of breast feeding. Acta Paediatrics 1994;83:1122-6.

33. Bergström E, Hernell O, Lönnerdal B, Persson LÅ. Sex differences in iron stores of adolescents. What is normal? J Pediatr Gastroenterol Nutr 1995;20:215-24.

34. Dewey KG, Peerson JM, Brown KH, Krebs NF, Michaelsen KF, Persson LA, Salmenpera L, Whitehead RG, Yeung DL. Growth of breastfed infants deviates from current reference data: A pooled analysis of U.S., Canadian and European datasets. Pediatrics 1995;96:495-503.

35. Tylleskär T, Banea M, Bikangi N, Nahimana G, Persson LÅ, Rosling H. Dietary determinants of a non-progressive spastic paraparesis (Konzo): a case-referent study in a high incidence area of Zaire. Int J Epidemiol 1995;24:949-56.

36. Bergström E, Hernell O, Persson LÅ, Vessby B. Serum lipids in adolescents are related to family history, infant feeding and physical growth. Atherosclerosis 1995;117:1-13.

37. Hoa DP, Thanh HT, Höjer B, Persson LÅ. Young child feeding in a rural area in the Red River delta, Vietnam. Acta Paediatrica 1995;84:1045-9.

38. Bergström E, Hernell O, Persson LÅ. Insulin resistance syndrome in adolescents. Metabolism 1996;45:908-914.

39. Toan NV, Hoa HT, Trong PV, Höjer B, Persson LÅ, Sundström K. Utilisation of reproductive health services in rural Vietnam - equal chances to plan and protect pregnancies? J Epidemiol Comm Health 1996;50:451-455.

40. Hoa HT, Toan VN, Johansson A, Höjer B, Hoa VT, Persson LÅ. Child spacing and two-child policy in practice in rural Vietnam. BMJ 1996;313:1113-6.

41. Hoa DP, Thanh HT, Hoa VT, Höjer B, Persson LÅ. Maternal factors influencing the occurrence of low birth weight in northern Vietnam. Ann Trop Pediatr 1996;16:327-33.

42. Ibrahim MM, Omar HM, Persson LÅ, Wall S. Child mortality in a collapsing African society. Bull World Health Organ 1996;74:547-552.

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ORIGINAL PUBLICATIONS, MANUSCRIPTS

69. Åsling Monemi K, Peña R, Ellsberg MC, Persson LÅ. Violence against women increases the risk of infant and child mortality. A case-referent study in Nicaragua. Submitted.

70. Ivarsson A, Hernell O, Nystrom L, Persson LA. Increased coeliac disease risk in children born in the summer reflects causal environmental exposure(s) with a seasonal pattern. Submitted.

71. Ivarsson A, Persson LA, Nystrom L, Hernell O. The Swedish celiac epidemic with a prevailing two-fold higher risk in girls compared to boys reflects gender specific genetic risk factors. Submitted.

72. Valladares E, Ellsberg M, Pena R, Högberg U, Persson LA. Physical partner abuse during pregnancy is a risk factor for low birth weight; a case-referent study in Nicaragua. Submitted.

73. Andersson T, Persson LÅ, Bergström S, Högberg U. Grand multipara with surviving infants have no increased risk of maternal deaths; a cohort study from 19th century Sweden. Manuscript.

74. Ruhiye DM, Persson LÅ, Ekström E-C. Social epidemiology of stunting and wasting among children in rural Tanzania. Manuscript.

75. Persson LÅ, Dahlkvist G, Cedermark G, Jansson A, Nilsson U, Westin V. Diet, growth and the risk of insulin-dependent diabetes mellitus in childhood. A matched case-referent study. Manuscript.

76. Ibrahim MM, Stenlund H, Wall S, Persson LÅ. Morbidity and dietary determinants of linear growth in early childhood: a cohort study in rural Somalia. Manuscript.

77. Peña R, Liljestrand J, Persson LÅ. Spacing and infant mortality determinants in Nicaragua. Submitted.

78. Jeppsson A, Persson LÅ. Harmful traditional health practices in Ethiopia; Health care providers' perceptions. Submitted.

79. Zelaya E, Ellsberg M, Herrera A, Berglund S, Liljestrand J, Persson LÅ. Education prevents adolescent pregnancy. A population based case-referent study in León, Nicaragua. Submitted.

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81. Goldin S, Levin L, Persson LA, Hägglöf B. Child war trauma: a comparison of clinician, parent and child assessments. Submitted.

REVIEWS, DISCUSSION PAPERS, BOOKS, CHAPTERS ETC.

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97. Bergström E, Blomqvist HK, Holm AK, Hägglöf B, Persson LÅ (red). Folkhälsorapport Norrland. Barns och ungdomars hälsa. [Public Health Report of Northern Sweden. Health of children and adolescents]. Mimeograph. Umeå universitet, Umeå 1992.

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101. Persson LÅ. Kostfaktorer och risk för typ 1 diabetes hos barn och ungdomar. [Dietary factors and risk for type 1 diabetes among children and adolescents]. In: Anonymous. Tema Barn. Symposier vid Svenska Läkaresällskapets riksstämma 1995. Stockholm;Spris förlag, 1995

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106. Persson LÅ. Searching for cost-effective solutions to major nutrition problems in the world. Experiences from Bangladesh. Scand J Nutr 1999;43:158-59.

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109. Rahman M, Streatfield K, Persson LA. Combating the Bangladesh tube well water arsenic calamity: the role of the health services. Report to the World Bank, March 2001. Mimeograph. Dhaka ICDDR,B, 2001.

**BIOGRAPHICAL SKETCH**

May 2001

## CURRICULUM VITAE

| NAME | CURRENT POSITIONS | ADDRESS |
|---|---|---|
| Mahfuzar Rahman<br>Born 1966-06-01 | Epidemiologist, Public Health Sciences Division, ICDDR,B: Centre for Health and Population Research, Dhaka, Bangladesh | Public Health Sciences Di<br>ICDDR,B<br>GPO Box 128, Mohakhali CA.<br>Dhaka 1000, Bangladesh<br>Phone +880 2 9885155<br>Fax +880 2 8826050<br>e-mail mahfuzar@icddrb.org |

EDUCATION/TRAINING

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | YEAR(s) | FIELD OF STUDY |
|---|---|---|---|
| Rajshahi Medical college, Rajshahi, Bangladesh | MBBS | 1992 | Medicine |
| Faculty of Health Sciences, Linköping University, Sweden | PhD. | 1994-99 | Epidemiology |
| Johns Hopkins University, School of Hygiene and Public Health, Baltimore, MD | Post-graduate Training | 1998 | Summer Graduate Epidemiology Program (Epidemiology and Biostatistic) |

RESEARCH AND PROFESSIONAL EXPERIENCE:

*1992-1993* - *Internship training,* Rangpur Medical College Hospital, Rangpur

*1993-1994* - *Public Health Physician*- Bangladesh Red Crescent Society.

*1994-1999* - *Research Coordinator*- SIDA

2000 (Jan-May) - *International Fellow,* Public Health Sciences Division, ICDDR'B

2000 (June- till)- *Arsenic and Environmental Epidemiologist*, Public Health Sciences Division, ICDDR, B: Centre for Health and Population Research.

RESEARCH PROJECTS

| Project | Role in project | Funding agency | Year(s) |
|---|---|---|---|
| Arsenic in tube well water and healt consequences | Principal Co-investigator | Sida, WHO | 2001- |
| Pilot studies of arsenic exposure through drinking water and health consequneces in Matlab, Bangladesh | Principal Co-investigator | USAID | 2000- |
| Arsenic expsoure, hypertension and skin lesion in Bangladesh | Principal investigator | Linköping Universititet Grant | 1998- |
| Arsenic in drinking water and diabetes mellitus | Principal investigator | Planning grant SAREC/SIDA | 1996- |

ADVISORY COMMITTEES, EXPERT MISSIONS ETC.

- Referee for a number of scientific journals, e.g. Health Policy and Planning.

**Original publication**


1. Rahman M, Axelson O. Arsenic exposure and diabetes mellitus- a second look at case-control data from Swedish copper smelter. *Occupational Environmental Medicine 1995; 52:773-774.*

2. Rahman M, Wingren G and Axelson O. Diabetes mellitus among Swedish art glass workers- an effect of arsenic exposure? *Scandinavian J Work Environmental Health 1996;22:152-5.*

3. Rahman M, Tondel M, Ahmad AS, Axelson O. Diabetes mellitus associated with arsenic exposure in Bangladesh. *American Journal Epidemiology 1998; 148:198-203.*

4. Rahman M, Tondel M, et al. Hypertension and arsenic exposure in Bangladesh. *Hypertension 1999;33:74-8.*

5. Rahman M, Tondel M, et al. Relations between arsenic exposure, skin lesions, and glucosuria. *Occupational Environmental Medicine* 1999:56:277-281.

6. Tondel M, Rahman M, et al. The relationship between arsenic levels in drinking water and the prevalence of skin lesions in Bangladesh. *Environmental Health Perspectives 1999; 107:727-729.*

7. Hasnat AH and Rahman M. Environmental pollution and chronic arsenicosis in Bangladesh. *J Occupational Health 1999; 41:207-208.*

8. Axelson O, Rahman M, Tondel M. A comment on some epidemiological observations on non-malignant chronic effects of arsenic exposure. *Europian J Oncology 2000; suppl. (5): 63-68.*

9. Smith AH, Lingas EO, Rahman M. Contamination of drinking-water by arsenic in Bangladesh: a public health emergency. *Bulletin World Health Organization 2000; 78: 1093-1103.*

10. Milton AH, Rahman M. Respiratory effects and arsenic contaminated well water. In Press, *Asia-Pacific Journal Public Health.*

11. Rahman M. Nonmalignant Health Effects of Arsenic Exposure. Doctoral Thesis. *Linköping University Medical Dissertation. No 612, Linköping, 1999, Sweden.*

12. Rahman M, Axelson O. Arsenic ingestion and health effects: Some epidemiological observation. In: W Chappell, CO Abernathy and RL Calderon (eds.): *Arsenic exposure and health effects*: proceedings of the Forth International Conference on Arsenic Exposure and Health Effects, June, 2000, San Diego, California. Oxford: Elsevier Science, Ltd., In Press.

13. Milton AH, Hasan Z, Rahman A, Rahman M. Chronic Arsenic Poisoning and Respiratory Effects in Bangladesh. *Journal Occupational Health 2001;43: 136-140.*

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14. Rahman M, Chowdhury IA. Arsenic in drinking water. How much is too much? *In Touch* 1998; Feb: 1-2

15. Chowdhury IA, Rahman M. Counseling in family planning perspectives. *In Touch* 1998; May:1-3

16 Tondel M, Rahman M. Arsenic poisoning in Bangladesh- the largest disaster in our time? Folkhälsovetenskapligt Centrum Nyhetsblad; 1998:8. *(Swedish).*

17. Rahman M, Streatfield K, Persson LA. Combating the Bangladesh tube well water arsenic calamity: the role of the health services. Report to the World Bank, March 2001. Mimeograph. Dhaka ICDDR,B, 2001.

18 Smith AH, Rahman M. Arsenic in drinking water: A public health concern. *Medicine Digest 2001;Jan-March.*

19 Rahman M. Epidemiological assessment of arsenic contamination in SEARO countries and elsewhere. Report to the SEARO, WHO, New Delhi, 2001. Mimeograph. Dhaka ICDDR,B, 2001, *in progress.*

## Budget Justifications

Please provide one page statement justifying the budgeted amount for each major item. Justify use of man power, major equipment, and laboratory services.

Commitment is expressed in person-time. Project period 24 months.

*Staff.* ICDDR, B has got an excellent group of field staff, public health specialists, epidemiologists, bio-statisticians, social scientists, laboratory scientists and clinicians for the study. This personnel is financed by individual research projects in relation to the time they allocate to the project. Lars Åke Persson is principal investigator for the project and has had the principal role in the planning. He will have the primary responsibility for all parts of the project and will provide scientific expertise on the development and analysis of the results of various outcomes. He is allocating 4 months of his time to the project.

Mahfuzar Rahman is arsenic epidemiologist and will have the day-to-day responsibility for the field work and be involved in all steps of the project. Dr. Mahfuzar Rahman will also ensure co-ordination and will provide scientific expertise within whole project, serves as an expert physician in the field and on the development and analysis of the results of the various outcomes; 24 months.

Drs. Abbas Uddin Bhuyia, will serve as Co-Investigator and will provide scientific expertise in his respective area, responsible for ethnographic study within the project; will be responsible for the qualitative components of the study; involvement 3 months.

Shams El Arifeen is child health epidemiologist and will be involved in the epidemiological analysis of reproductive outcome. His involvement is 1 month.

SM Akramuzzaman is clinical scientist and involved in the planning for skin screening, clinical follow-up and analysis of reversibility of skin lesions; 2 months.

Eva-Charlotte Ekström is nutrition epidemiologist and consultant to the Centre. She has been involved in the design of the nutrition aspects and will lead the analysis of those parts; 3 months.

Md. Khalequzzaman is public health physician and epidemiologist and will be involved in the planning and analysis for skin screening, and patient follow-up, 2 months.

Peter Kim Streatfield is demographer and epidemiologist and will be responsible for the entire arsenic-related HDSS system, the GIS application, and will be involved in the analysis of arsenic effects on reproductive outcomes and mortality outcomes; 3 months.

Our GIS expert recently left, he is being replaced; 4 salary months.

Nigar Shahid will be involved in the analysis of reproductive outcomes; 2 months.

MA Wahed will be in charge of the arsenic analyses at ICDDR,B lab, and will provide scientific and technical expertise on the assessment of arsenic and biochemical outcomes; 3 months.

Md. Yunus is senior public health physician and has the overall responsibility for the Matlab health research program, including the clinical activities and the field activities; 3.5 months.

J Chakraborty is Senior Manager in Matlab, will guide and facilitate the implementation of the project activities in Matlab facilitate the implementation of the project activities in Matlab. 5 months committed.
HR Chowdhury is Senior Medical Officer and will supervise the clinical management of patients with arsenicosis, 5 months.
Four medical officers (2 male and 2 female) will be responsible for the examination of patients with skin changes and other arsenic-related health problems; 48 salary months.

*Dr Mushtaque Chowdhury*, Director of the Research and Evaluation Division at BRAC, and Co-Investigator, will be co-ordinating the activities with the ICDDR, B team, coordinating the field activities for the arsenic mitigation. *Professor Marie Vather*, Institute of Environmental Medicine, Division of Metals and Health, Karolinska Institutet, Stockholm, will serve as Co-Investigator and will be responsible for the analysis of the urine samples.

A field laboratory manager is in charge of the handling of the samples of urine, water and blood, 12 months. The field manager is having the responsibility of coordinating and overseeing the activities of the field staff, 24 months. A field research officer (ethnography) is conducting the ethnographic interviews (12 months), supervised by the social scientist. A clerk is managing the project office (12 salary-months). Senior Health Research Assistants perform parts of clinical examination and take blood samples (24 salary-months), Field Research Assistants are performing the skin screening in the field; totally 240 salary months. One Data Managing Assistant manages data entry (24 months), supervised by a data manager (8 months). The role of the ICDDR,B community health research workers in the area is to inform about the project in each household, and to give assistance in the field for the field team (78 salary months).

Analyses will be performed of total arsenic in urine in individuals with arsenicosis and controls, and in clinical follow up of the arsenicosis patients (total 2850 samples) and AAS analysis of arsenic in tube well water (9000 tube wells plus seasonal follow up, 1800 samples). Analysis of Hb will be done immediately in Matlab and of micronutrients later at a biochemistry laboratory.

Funds are allocated for local travel Dhaka-Matlab and within Matlab and for some international travel, mainly for the contact with partners at Karolinska Institute.

We propose the procurement of -86°C freezers. The very large number of samples (water, urine, serum) makes it necessary to totally procure 3 freezers. The WHO budget also includes funds for procurement of a AAS with auto sampler H-generator (Hshimabzu, Japan). Configuration: Atomic Absorption Spectrophotometer, Furnace kit, Auto sampler, High temperature burner head, Hydride vapour generator. Some renovation is needed in the laboratory space in Dhaka and preparation of facilities for the clinical follow-up in Matlab.

The institutional overhead includes managing costs for the project in finance and personnel department, costs of managing the field site in Matlab and the clinical services

linked to the project. (The lower rate in the Sida budget is motivated by the Sida/SAREC core contribution to the Centre).

The arsenic mitigation activity that is performed by BRAC is calculated based on their previous experiences and adjusted for the population size and the estimated arsenic contamination in the area. See separate budget sheet and description in the text above.

## Other Support

Describe sources, amount, duration, and grant number of all other research funding currently granted to PI or under consideration. (DO NOT EXCEED ONE PAGE FOR EACH INVESTIGATOR)

| | |
|---|---|
| UNICEF | 640,000 3 years |
| USAID | 20,000 |
| JHU | 20,000 |

# Check List

After completing the protocol, please check that the following selected items have been included.

1. Face Sheet Included ☐
2. Approval of the Division Director on Face Sheet ☐
3. Certification and Signature of PI on Face Sheet, #9 and #10 ☐
4. Table on Contents ☐
5. Project Summary ☐
6. Literature Cited ☐
7. Biography of Investigators ☐
8. Ethical Assurance ☐
9. Consent Forms ☐

Detailed Budget ☐

*ARSENIC AND HEALTH*. Budget ICDDR,B, and BRAC (mitigation component)

*Matlab, 220,000 population* Project period 24 months

Sida contribution approximate, depending upon exchange rate (calculated for 1 US$=10 SEK). Salary increase after 1 year 2.5% included.

*Salaries incl. benefits and taxes

Revised May 8, 2001.

| Professional staff | Name | Rate/m $ | Person-months/units Sida | WHO | ICDDRB/ other | Cost Sida | WHO | ICDDRB/ other | Total cost |
|---|---|---|---|---|---|---|---|---|---|
| Epidemiologist, PI, D1* | LÅ Persson | 13125 | - | - | 4.0 | - | - | 53,156 | 53,156 |
| Child health epidemiologist | Shams El Arifeen | 6930 | - | - | 1.0 | - | - | 7,017 | 7,017 |
| Clinical scientist NOC* | SM Akramuzzaman | 1218 | 1.0 | - | 1.0 | 1,233 | - | 1,233 | 2,466 |
| Social scientist P5* | Abbas Bhuiya | 9091 | 1.0 | - | 2.0 | 9,205 | - | 18,409 | 27,614 |
| Nutrition epid. consultant P4 | Eva-Charlotte Ekström | 4667 | 2.0 | - | 1.0 | 9,451 | - | 4,725 | 14,176 |
| Clinical scientist NOC* | Md Khalequzzaman | 1471 | 2.0 | - | - | 2,979 | - | - | 2,979 |
| Arsenic epidemiologist, NOC* | Mahfuzar Rahman | 1016 | 15.0 | 6.0 | 3.0 | 15,431 | 6,172 | 3,086 | 24,689 |
| Demographer, P5* | Peter Kim Streatfield | 11877 | 1.0 | - | 2.0 | 12,025 | - | 24,051 | 36,076 |
| GIS expert, NOC* | To be named | 1016 | 2.0 | - | 2.0 | 2,057 | - | 2,057 | 4,115 |
| Senior scientist NOD | Nigar Shahid | 1858 | 1.0 | - | 1.0 | 1,881 | - | 1,881 | 3,762 |
| Head, arsenic lab NOC* | Mr Wahed | 1505 | 1.5 | - | 1.5 | 2,286 | - | 2,286 | 4,571 |
| Head, Matlab | Md Yunus | 2475 | 1.0 | - | 2.5 | 2,506 | - | 6,265 | 8,771 |
| Senior manager, NOC* | J Chakraborti | 1467 | 1.5 | 1.5 | 2.0 | 2,226 | 2,228 | 2,971 | 7,427 |
| Senior physician, NOC* | Hafizur R Chowdhury | 1125 | 1.0 | 2.0 | 2.0 | 1,139 | 2,278 | 2,278 | 5,695 |
| Consultant, Dermatologist | To be named | 500 | 2.0 | 1.0 | 1.0 | 1,013 | 1,000 | 1,000 | 3,013 |
| Medical officers (male & female | To be named | 659 | 24.0 | 6.0 | 18.0 | 16,014 | 4,003 | 12,010 | 32,027 |
| *Subtotal professional staff* | | | | | | *79,447* | *15,682* | *142,426* | *237,555* |
| Field staff | | | | | | | | | |
| Field laboratory management,GS5 | | 351 | 9.0 | - | 3.0 | 3,198 | - | 1,066 | 4,265 |
| Field manager, NOA | | 659 | 24.0 | - | - | 16,014 | - | - | 16,014 |
| Field research officer, ethnography GS6 | | 456 | 2.0 | 4 | 6.0 | 923 | 1,847 | 2,770 | 5,540 |
| Clerk/Admin Assistant, CSA Matlab, GS4 | | 269 | 4.0 | 8 | - | 1,089 | 2,179 | - | 3,268 |
| Senior Health Research Assistant, GS4 | | 269 | 12.0 | 6 | 6.0 | 3,268 | 1,634 | 1,634 | 6,537 |
| Field Research Assistants, water collection,GS3 | | 225 | 12.0 | 12 | - | 2,734 | 2,734 | - | 5,468 |
| Field Research Assisstant, skin screening, GS3 | | 225 | 150.0 | 45 | 45.0 | 34,172 | 10,252 | 10,252 | 54,675 |
| Data Management, GS6 | | 456 | 4.0 | 2 | 2.0 | 1,847 | 923 | 923 | 3,694 |
| Data Management Assistant, GS 3 | | 225 | 18.0 | 6 | - | 4,101 | 1,367 | - | 5,468 |
| Community health workers, GS2 | | 189 | 36.0 | 18 | 24.0 | 6,889 | 3,445 | 4,593 | 14,926 |
| *Subtotal field staff* | | | | | | *74,235* | *24,380* | *21,238* | *119,854* |
| Operating expenses | | Rate $ | | | | | | | - |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Lab supplies water collection | | | | | | 2000 | - | | 2,000 |
| Lab As species urine Karolinska | 15 | 900 | 0 | 0 | 13,500 | - | | | 13,500 |
| Lab As total in urine Karolinska | 5 | 2125 | 725 | 0 | 10,625 | 3,625 | - | | 14,250 |
| As field test screening | 0.35 | 9000 | 0 | 0 | 3,150 | - | - | | 3,150 |
| As in water. AAS (ICDDRB) | 3 | 6400 | 2600 | 1800 | 19,200 | 7,800 | 5,400 | | 32,400 |
| Analyses Hb. zinc | 6 | 1275 | 0 | 0 | 7,650 | - | - | | 7,650 |
| Analyses selenium. folic acid beta carotene | 10 | 0 | 0 | 1275 | - | - | 12,750 | | 12,750 |
| *Subtotal operating expenses* | | | | | *56,125* | *11,425* | *18,150* | | *85,700* |
| | | | | | | | | | |
| Travel | | | | | | | | | |
| Local travel. in/between Dnaka Matlab | | | | | 1,000 | 500 | 1,000 | | 2,500 |
| International travel | 1400 | 2 | 0 | 2 | 2,800 | - | 2,800 | | 5,600 |
| *Subtotal travel* | | | | | *3,800* | *500* | *3,800* | | *8,100* |
| | | | | | | | | | |
| Capital expenditure | | | | | | | | | |
| Digital camera for documenting skin lesions | 900 | 1 | 0 | 0 | 900 | - | - | | 900 |
| GIS additional equipment and software | 1500 | 1 | 0 | 1 | 1,500 | - | 1,500 | | 3,000 |
| Freezer for samples -86 degree C | 10000 | 1 | 1 | 1 | 10,000 | 10,000 | 10,000 | | 30,000 |
| AAS | | | | | | 45,000 | | | 45,000 |
| Renovation of lab for AAS | | | | | | 2,000 | | | 2,000 |
| Preparation clinical follow up room Matlab | | | | | | | 5,000 | | 5,000 |
| *Subtotal capital expenditure* | | | | | *12,400* | *57,000* | *16,500* | | *85,900* |
| | | | | | | | | | |
| Other expenditures | | | | | | | | | |
| Printing. photocopies | | | | | 1,000 | 250 | - | | 1,250 |
| Training and dissemination | | | | | 2,000 | 500 | | | 2,500 |
| Communication (e mail fax phone) | | | | | 1,000 | 750 | | | 1,750 |
| Unforeseen expenditures | | | | | 1,000 | 500 | | | 1,500 |
| *Subtotal other expenditure* | | | | | *5,000* | *2,000* | - | | *7,000* |
| | | | | | | | | | |
| Direct cost | | | | | 231,007 | 110,987 | 202,114 | | 544,108 |
| Level of institutional overhead | | | | | 15% | 25% | 25% | | |
| Institutional overhead cost | | | | | 34,651 | 27,747 | 50,529 | | 112,926 |
| BRAC mitigation component (see separate sheet) | | | | | 72,510 | 60,110 | - | | 132,620 |
| Total | | | | | 338,168 | 198,843 | 252,643 | | |
| Grand total | | | | | | | | | 789,655 |

Investigator: Last, first, middle Persson Åke Lars

**International Centre for Diarrhoeal Disease Research, Bangladesh**
**Voluntary Consent Form**
(Cross-sectional survey)

**Title of the Research Project:** Arsenic in tube well water and health consequences

**Principal Investigator:** Prof. Lars Åke Persson

In Bangladesh, water of majority of the tube wells is contaminated with arsenic the levels of which exceed the WHO recommended safe limits of 50 µg/L. The arsenic content of water of some tube wells from all areas of the Matlab Surveillance System of ICDDR,B was tested in 1997 and 2001. It was found that water of over 3/4$^{th}$ of the tested tube wells contained arsenic in quantities that exceeds the WHO-recommended safe limit. High level of arsenic in drinking water may cause many health problems including various types of skin lesions, reproductive and cardiovascular diseases, and even cancers. These problems are more common in relatively younger males and in those suffering from protein energy malnutrition.

We are conducting a research study, and the main purpose of our study are to measure the levels of arsenic in the tube well water and to examine if people have arsenic-related health problems such as skin lesions. We would also investigate if some factors such as general health and nutritional status of people influence arsenic toxicity. Results of this study would help determine arsenic-related health problems and to determine preventive measures against them.

After determining the arsenic content in the tube well water, we would meet people in your community to discuss about its preventive measures including discussion on the ways to get arsenic-free water. This part of the study would be done in collaboration with BRAC.

We request for your permission to enrol you and your family members older than five years into our study. We will examine you and your family members for arsenic-related skin lesions, which would take about 30 minutes. We may refer you and/or your family members to Matlab Health Centre for further examination by a physician, and if we do so, we would bear the travel costs.

We assure you that all information obtained from you and your family members including findings of physical examination would be kept strictly confidential, and none other than the investigations of this study will have an access to the information.

There is no risk involved in the examination of the skin. You may decide not to participate in the study or parts of the study, and may also withdraw from the study at any time without affecting any service provided to you and to your family members by the Centre. You may or may not get any direct benefit by participating in this study; however, the information obtained is likely to help protect the society from arsenic toxicity.

If you are willing your and your family members' participation in the study please indicate that by putting your signature or left thumb impression in the specified space below.

Thank you for your cooperation.

| **Signature of Interviewer** | **Signature /thumb impression of the participant or guardian of the participant** | **Signature of Witness** |
|---|---|---|
| **Date:** | **Date:** | **Date:** |

# আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র, বাংলাদেশ
## স্বেচ্ছা-সম্মতি পত্র (পরিসংখ্যান)

**গবেষণার নামঃ** নলকূপের পানিতে আর্সেনিক ও স্বাস্থ্যের উপর তার প্রভাব

**প্রধান গবেষকঃ** প্রফেসর লার্স অকে পার্সন

বাংলাদেশের অধিকাংশ নলকূপের পানি আর্সেনিক দ্বারা দূষিত এবং এর মাত্রা বিশ্ব স্বাস্থ্য সংস্থা নির্ধারিত নিরাপদ মাত্রা, প্রতি লিটারে ৫০ মাইক্রোগ্রাম'এর চেয়েও বেশী। ১৯৯৭ ও ২০০১ সালে আই,সি,ডি,ডি,আর,বি'র মতলব সার্ভেইলেন্স সিস্টেমের অন্তর্গত সকল এলাকার কিছুকিছু নলকূপের পানি পরীক্ষা করে দুই তৃতীয়াংশেরও অধিক নলকূপের পানিতে বিশ্ব স্বাস্থ্য সংস্থা নির্ধারিত নিরাপদ মাত্রার বেশী পরিমানে আর্সেনিক পাওয়া গেছে। পানীয় জলে অতিরিক্ত পরিমান আর্সেনিক থাকলে তা বিভিন্ন ধরনের স্বাস্থ্য সমস্যা যেমন ত্বকের অসুখ, প্রজনন ও হৃৎপিন্ডের সমস্যা, এমনকি ক্যান্সারও ঘটাতে পারে। অপেক্ষাকৃত কমবয়সী পুরুষ ও অপুষ্ট লোকজনের এধরনের সমস্যা হবার সম্ভাবনা বেশী।

আমরা এক গবেষণা করছি যার মূল উদ্দেশ্য নলকূপের পানিতে আর্সেনিকের পরিমান নির্ধারন করা ও লোকজনের মধ্যে আর্সেনিকের কারনে সৃষ্ট স্বাস্থ্য সমস্যা যেমন ত্বকের অসুখ আছে কিনা তা পরীক্ষা করা। এ গবেষণায় আমরা আরোও দেখতে চাই যে মানুষের সাধারন স্বাস্থ্য ও পুষ্টি আর্সেনিকের কারনে সৃষ্ট স্বাস্থ্য সমস্যাগুলোকে প্রভাবিত করে কিনা। আমাদের এই গবেষণা আর্সেনিকের কারনে সৃষ্ট স্বাস্থ্য সমস্যার বিষয়ে জানতে ও তাদের প্রতিরোধমূলক ব্যবস্থা নির্ণয়ে সহায়তা করবে।

নলকূপের পানিতে আর্সেনিকের পরিমান নির্ণয়ের পর আমরা আপনার এলাকার লোকজনের সাথে এর প্রতিরোধমূলক ব্যবস্থা সম্মন্ধে আলোচনা করবো এবং আর্সেনিক-মুক্ত পানি পাবার উপায় সহ এর প্রতিরোধমূলক অন্যান্ন বিষয়ে কথাবার্ত্তা বলবো। গবেষণার এই ভাগে ব্র্যাক আমাদের সহযোগী হিসাবে কাজ করবে।

আমরা আমাদের এই গবেষণায় আপনার এবং আপনার পরিবারের ৫ বছরের বেশী বয়সের সকল সদস্যের অন্তর্ভূক্তির জন্যে আপনার অনুমতি চাচ্ছি। আমরা আপনার এবং গবেষণায় অন্তর্ভূক্ত আপনার পরিবারের সকল সদস্যের আর্সেনিক জনিত ত্বকের কোন সমস্যা আছে কিনা তা পরীক্ষা করবো, এবং এজন্যে ৩০ মিনিট সময় লাগবে। আমরা আপনাকে এবং/অথবা আপনার পরিবারের অন্য সদস্যকে একজন চিকিৎসক দ্বারা আরোও পরীক্ষার জন্যে মতলব স্বাস্থ্য কেন্দ্রে পাঠাতে পারি; সেক্ষেত্রে আমরা যাতায়াতের সমস্ত খরচ বহন করবো।

আমরা আপনাকে নিশ্চয়তা দিচ্ছি যে আপনার এবং আপনার পরিবারের সকল সদস্যের শারীরীক পরীক্ষার ফলাফল সহ সমস্ত তথ্য গোপনীয় রাখবো এবং শুধুমাত্র এ গবেষণার গবেষক ছাড়া অন্য কেউই তা জানতে পারবেনা।

এই গবেষণায় ত্বকের পরীক্ষার ফলে আপনার এবং আপনার পরিবারের সদস্যের কোন রকম বিপদের সম্ভাবনা নেই। আপনি এই গবেষণায় অথবা গবেষণার যে কোন অংশে যোগদান নাও করতে পারেন, এমনকি যোগদানের পরেও যে কোন সময় আপনি আপনার সম্মতি প্রত্যাহার করতে পারবেন। এর ফলে আপনি বা আপনার পরিবারের সদস্যের কেউই এ কেন্দ্রের প্রচলিত স্বাস্থ্য সেবা থেকে বঞ্চিত হবেন না। এই গবেষণায় অংশ গ্রহনের ফলে আপনার কোন প্রত্যাক্ষ লাভ নাও হতে পারে, তবে এই গবেষণায় ফলাফল সমাজকে আর্সেনিক-জনিত স্বাস্থ্য সমস্যা থেকে বাঁচাতে সাহায্য করতে পারে।

আপনি এই গবেষণায় আপনার এবং আপনার পরিবারের সদস্যের অন্তর্ভূক্তির আমাদের প্রস্তাবে রাজী থাকলে দয়া করে নীচের নির্দ্দিষ্ট স্থানে আপনার স্বাক্ষর অথবা টিপসই দিন।

আপনার সহযোগীতার জন্যে ধন্যবাদ।

| | | |
|---|---|---|
| সাক্ষাতকার গ্রাহকের স্বাক্ষর | অংশগ্রহনকারী/ অভিভাবকের স্বাক্ষর/টিপসই | সাক্ষীর স্বাক্ষর |
| তারিখঃ | তারিখঃ | তারিখঃ |

Investigator: Last, first, middle Persson Åke Lars

**International Centre for Diarrhoeal Disease Research, Bangladesh**
**Voluntary Consent Form** (Referent for further examination)

**Title of the Research Project:** Arsenic in tube well water and health consequences

**Principal Investigator:** Prof. Lars Åke Persson

Thank you for participating in the study and coming today to the clinic. Let us remind you about the purpose of the study in case you do not remember.

The purpose of our research study is to understand if and to what extent, arsenic-contaminated drinking water has resulted in adverse health effects, especially skin lesions in the population. We will also study if other factors such as general health and nutritional status help protect people against the arsenic toxicity. Such information will be useful for prevention of arsenic-related health problems in Bangladesh.

We request you/your family member to help us by participating in the study. We have not found any arsenic-related skin lesions during your physical examination, but we would like to examine your general health and nutritional status for the purpose of our study. We will similarly examine general health and nutritional status of other people who have suspected arsenic-related skin lesions.

A medical doctor at the Matlab Health Centre will examine your general health, measure your blood pressures, and examine your skin. A trained senior research assistant will collect 4.0 ml blood (less than one teaspoonful) from a vein of your forearm under aseptic precautions. There is minimal risk associated with this procedure, and you will feel momentary mild pain during the needle prick. The blood will be examined for haemoglobin concentration, and levels of some vitamins and minerals. We will also request you to provide us with small amount of your urine (about 5.0 ml i.e. one teaspoonful) for determining presence of arsenic. If you have arsenic-related disease(s) that require proper treatment, we will refer you to appropriate health care facilities.

We assure you that we shall strictly maintain confidentiality of the information we collect from you/your family members, and none other than the investigators of this study would have an access to the information.

Your participation in our study is voluntary. You may decide not to participate in the study or parts of the study, and also to withdraw from the study at any time without affecting any of the services offered to you and your family members by the Centre.

You may ask any question about this study, and I shall be happy to provide answer to them. If you have any problem or further question you may also contact your healthy care worker or Dr. Hafizur Rahman Chowdhury at the Matlab Hospital of ICDDR, B or Prof. Lars Ake Persson in Dhaka at the following phone number 9885155.

If you/ your family member is willing to participate in the study, please sign your name or give left thumb impression below.

| **Signature of Interviewer** | **Signature /thumb impression of the participant or guardian of the participant** | **Signature of Witness** |
|---|---|---|
| **Date:** | **Date:** | **Date:** |

## আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র, বাংলাদেশ
## স্বেচ্ছা-সম্মতি পত্র (অতিরিক্ত পরীক্ষার জন্য)

**গবেষণার নামঃ** নলকূপের পানিতে আর্সেনিক ও স্বাস্থ্যের উপর তার প্রভাব

**প্রধান গবেষকঃ** প্রফেসর লার্স অকে পার্সন

গবেষণায় অংশগ্রহনের জন্যে আপনাকে ধন্যবাদ। আপনার হয়তোবা মনে নাও থাকতে পারে, সেজন্যে আমরা এ গবেষণার উদ্দেশ্য আপনাকে মনে করিয়ে দিতে চাই।

আমাদের এ গবেষণার উদ্দেশ্য হচ্ছে আর্সেনিক-দূষিত পানীয় জল লোকজনের স্বাস্থ্যের উপর কোন ক্ষতিকর প্রভাব ফেলছে কিনা বা তার পরিমান কত তা নির্নয় করা, বিশেষতঃ ত্বকের সমস্যা। আমরা আরোও দেখতে চাই যে, আর্সেনিকের কারনে সৃষ্ট স্বাস্থ্য সমস্যায় লোকজনের সাধারন স্বাস্থ্য ও পুষ্টির কোন প্রভাব আছে কিনা। এসব তথ্য বংলাদেশে আর্সেনিকের কারনে সৃষ্ট স্বাস্থ্য সমস্যা প্রতিরোধে সহায়তা করবে।

আমরা এই গবেষণায় আপনার এবং আপনার পরিবারের সদস্যের অন্তর্ভূক্তির মাধ্যমে আমাদেরকে সহায়তা করার জন্যে আপনাকে অনুরোধ করছি। আমরা আপনাকে এর আগে পরীক্ষার সময় আপনার ত্বকে আর্সেনিক-সম্পর্কিত কোন সমস্যা দেখতে পাইনি। কিন্তু আমরা আপনার সাধারন স্বাস্থ্য ও পুষ্টির অবস্থা নির্নয়ের জন্যে আপনাক আরোও পরীক্ষা করতে চাই। একই ভাবে, আমরা যাদের মাঝে আর্সেনিক-জনিত ত্বকের সমস্যা দেখতে পেয়েছি তাদেরকেও আমরা পরীক্ষা করবো।

মতলব স্বাস্থ্য কেন্দ্রে একজন চিকিৎসক আপনার সাধারন স্বাস্থ্য, রক্তচাপ ও ত্বকের পরীক্ষা করবেন। একজন প্রশিক্ষন-প্রাপ্ত স্বাস্থ্য-সহকারী সব ধরনের সতর্কতার সাথে, জীবাণু-মুক্ত অবস্থায়, আপনার/আপনার পরিবারের সদস্যের বাহুর শিরা থেকে ৪ মিঃলিঃ (১ চা-চামচেরও কম) রক্ত সংগ্রহ করবেন। রক্ত সংগ্রহের সময় সূঁচের আঘাত জনিত সাময়িক, মৃদু ব্যথা ছাড়া এ-পরিমান রক্ত সংগ্রহের কারনে আর কোন ক্ষতির সম্ভাবনা খুবই কম। এই রক্ত হিমোগ্লোবিন, ভিটামিন, ও খনিজ লবনের পরিমান নির্নয়ের জন্যে ব্যবহৃত হবে। আমরা মূত্রে শর্করার পরিমান নির্নয়ের জন্যে সামান্য পরিমানে মূত্রের নমুনাও সংগ্রহ করবো। আপনি/আপনার পরিবারের কোন সদস্য আর্সেনিক-সম্পর্কিত কোন সমস্যায় আক্রান্ত হলে আমরা তার যথাযথ চিকিৎসার জন্যে উপযুক্ত স্বাস্থ্য কেন্দ্রে পাঠাবো।

আমরা আপনাকে সম্পূর্ন নিশ্চয়তা দিচ্ছি যে আপনার এবং আপনার পরিবারের সকল সদস্যের শারীরীক পরীক্ষার ফলাফল সহ সমস্ত তথ্য গোপনীয় রাখবো এবং শুধুমাত্র এ গবেষণার গবেষক ছাড়া অন্য কেউই তা জানতে পারবেনা।

গবেষণায় আপনার/আপনার পরিবারের সদস্যদের অংশগ্রহন সম্পূর্নভাবে আপনার ইচ্ছাধীন। আপনি ইচ্ছে করলে সম্পূর্ন বা আংশিকভাবে এই গবেষণায় অংশগ্রহন থেকে বিরত থাকতে পারেন, এমনকি অংশগ্রহনের পরেও, যে কোন সময় আপনার সম্মতি প্রত্যাহার করতে পারবেন। এসবের ফলে আপনি বা আপনার পরিবারের সদস্যদের কেউই এ প্রতিষ্ঠানের প্রচলিত সেবা কিংবা সহযোগীতা থেকে বঞ্চিত হবেন না।

আপনি আমাকে গবেষণা সম্মন্ধে যে কোন প্রশ্ন করতে পারেন, এবং আমি খুশী মনে তার উত্তর দেবো। আপনার কোন সমস্যা হলে বা অন্য কোন প্রশ্ন থাকলে আপনি আমাদের স্বাস্থ্য-কর্মী অথবা ডাঃ হাফিজুর রহমান চৌধুরীর সাথে মতলব হাসপাতালে, অথবা প্রফেসর লার্স অকে পার্সনের সাথে ঢাকায় ৯৮৮৫১৫৫ নম্বর টেলিফোনে যোগাযোগ করতে পারবেন।

আপনি এই গবেষণায় আপনার এবং আপনার পরিবারের সদস্যের অন্তর্ভূক্তির আমাদের প্রস্তাবে রাজী থাকলে দয়া করে নীচের নির্দ্দিষ্ট স্থানে আপনার স্বাক্ষর অথবা টিপসই দিন।

আপনার সহযোগীতার জন্যে ধন্যবাদ।

| | | |
|---|---|---|
| সাক্ষাতকার গ্রাহকের স্বাক্ষর | অংশগ্রহনকারী/ অভিভাবকের স্বাক্ষর/টিপসই | সাক্ষীর স্বাক্ষর |
| তারিখঃ | তারিখঃ | তারিখঃ |

Investigator: Last, first, middle Persson Åke Lars

**International Centre for Diarrhoeal Disease Research, Bangladesh**
**Voluntary Consent Form** (Cases for further examination)

**Title of the Research Project:** Arsenic in tube well water and health consequences

**Principal Investigator**: Prof. Lars Åke Persson

Thank you for participating in the study and coming today to the clinic. Let us remind you about the purpose of the study in case you do not remember.

The purpose of our research study is to understand if and to what extent, arsenic-contaminated drinking water has resulted in adverse health effects, especially skin lesions in the population. We will also study if other factors such as general health and nutritional status help protect people against the arsenic toxicity. Such information will be useful for prevention of arsenic-related health problems in Bangladesh.

Our recent investigation showed that the tube well water in your area contains high amount of arsenic. In the recent examination at your home we found skin lesions in you/ your family member(s) that could be due arsenic. If you agree your/ your family members' participation in the study, a medical doctor will examine your general health, measure your blood pressures, and further examine your/ your family members' skin lesions. We will take pictures of your skin lesions using a camera for final diagnosis by an external expert. A trained senior research assistant will collect 4.0 ml blood (less than one teaspoonful) from a vein of your forearm under aseptic precautions. There is minimal risk associated with this procedure, and you will feel momentary mild pain during the needle prick. The blood will be examined for haemoglobin concentration, and levels of some vitamins and minerals. We will also request you to provide us with small amount of your urine (about 5.0 ml i.e. one teaspoonful) for determining presence of arsenic. If you have arsenic-related disease(s) that require proper treatment, we will refer you to appropriate health care facilities.

We assure you that we shall strictly maintain confidentiality of the information we collect from you. All records from this study at the Matlab Hospital or the Dhaka Offices of ICDDR,B will be kept under lock and key and only the researchers responsible for this study will have access to the information. The study records will not have your personal identification, and we would use a code number instead.

Your participation in our study is voluntary. You may decide not to participate in the study, and also to withdraw from the study at any time without affecting any of the services offered to you and your family members by the Centre. You may ask any question about this study and I shall be happy to provide answer to them. If you have any problem or further question you may also contact your healthy care worker or Dr. Hafizur Rahman Chowdhury, at the Matlab Hospital of ICDDR, B or Prof. Lars Ake Persson in Dhaka at the following phone number 9885155.

If you/ your family member is willing to participate in the study, please sign your name or give left thumb impression below.

| **Signature of Interviewer** | **Signature /thumb impression of the participant or guardian of the participant** | **Signature of Witness** |
|---|---|---|
| **Date:** | **Date:** | **Date:** |

## আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র, বাংলাদেশ
## স্বেচ্ছা-সম্মতি পত্র (বিশেষ পরীক্ষার জন্য)

**গবেষণার নামঃ** নলকূপের পানিতে আর্সেনিক ও স্বাস্থ্যের উপর তার প্রভাব

**প্রধান গবেষকঃ** প্রফেসর লার্স অকে পার্সন

গবেষণায় অংশগ্রহনের জন্যে আপনাকে ধন্যবাদ। আপনার হয়তোবা মনে নাও থাকতে পারে, সেজন্যে আমরা এ গবেষণার উদ্দেশ্য আপনাক মনে করিয়ে দিতে চাই।

আমাদের এ গবেষণার উদ্দেশ্য হচ্ছে আর্সেনিক-দূষিত পানীয় জল লোকজনের স্বাস্থ্যের উপর কোন ক্ষতিকর প্রভাব ফেলছে কিনা বা তার পরিমান কত তা নির্নয় করা, বিশেষতঃ ত্বকের সমস্যা। আমরা আরোও দেখতে চাই যে, আর্সেনিকের কারনে সৃষ্ট স্বাস্থ্য সমস্যায় লোকজনের সাধারন স্বাস্থ্য ও পুষ্টির কোন প্রভাব আছে কিনা। এসব তথ্য বংলাদেশে আর্সেনিকের কারনে সৃষ্ট স্বাস্থ্য সমস্যা প্রতিরোধে সহায়তা করবে।

সম্প্রতি একটি পরীক্ষাতে আপনি যে এলাকায় বসবাস করেন সে এলাকার নলকূপের পানিতে অধিকমাত্রায় আর্সেনিক পাওয়া গেছে। সেই সাথে আপনার/আপনার পরিবারের সদস্যের শারীরীক পরীক্ষার সময় কিছু ত্বকের সমস্যা নির্ণীত হয়েছে যা আর্সেনিকের কারনে হতে পারে। আপনি গবেষণায় আপনার/ আপনার পরিবারের সদস্যের অংশগ্রহনে সম্মত থাকলে মতলব স্বাস্থ্য কেন্দ্রে একজন চিকিৎসক আপনার সাধারন স্বাস্থ্য, রক্তচাপ ও ত্বকের পরীক্ষা করবেন। এরপর ক্যামেরা দিয়ে আপনার/ আপনার পরিবারের সদস্যের আর্সেনিক জনিত ত্বকের দাগের ছবি তুলবো যা পরবর্ত্তীতে বাইরের একজন ত্বক-বিশেষজ্ঞ পরীক্ষা করে তা আর্সেনিক জনিত কি না তা নিশ্চিত করবেন। একজন প্রশিক্ষিত স্বাস্থ্য-সহকারী সব ধরনের সতর্কতার সাথে, জীবাণু-মুক্ত অবস্থায়, আপনার/আপনার পরিবারের সদস্যের বাহুর শিরা থেকে ৪ মিঃলিঃ (১ চা-চামচেরও কম) রক্ত সংগ্রহ করবেন। রক্ত সংগ্রহের সময় সূঁচের আঘাত জনিত সাময়িক, মৃদু ব্যথা ছাড়া এ-পরিমান রক্ত সংগ্রহের কারনে আর কোন ক্ষতির সম্ভাবনা খুবই কম। এই রক্ত হিমোগ্লোবিন, ভিটামিন, ও খনিজ লবনের পরিমান নির্নয়ের জন্যে ব্যবহৃত হবে। আমরা মূত্রে শর্করার পরিমান নির্নয়ের জন্যে সামান্য পরিমানে মূত্রের নমূনাও সংগ্রহ করবো। আপনি/আপনার পরিবারের কোন সদস্য আর্সেনিক-সম্পর্কিত কোন সমস্যায় আক্রান্ত হলে আমরা তার যথাযথ চিকিৎসার জন্যে উপযুক্ত স্বাস্থ্য কেন্দ্রে পাঠাবো।

আমরা আপনাকে সম্পূর্ন নিশ্চয়তা দিচ্ছি যে আপনার এবং আপনার পরিবারের সকল সদস্যের শারীরীক পরীক্ষার ফলাফল সহ সমস্ত তথ্য গোপনীয় রাখবো এবং শুধুমাত্র এ গবেষণার গবেষক ছাড়া অন্য কেউই তা জানতে পারবেনা।

গবেষণায় আপনার/আপনার পরিবারের সদস্যদের অংশগ্রহন সম্পূর্নভাবে আপনার ইচ্ছাধীন। আপনি ইচ্ছে করলে সম্পূর্ন বা আংশিকভাবে এই গবেষণায় অংশগ্রহন থেকে বিরত থাকতে পারেন, এমনকি অংশগ্রহনের পরেও, যে কোন সময় আপনার সম্মতি প্রত্যাহার করতে পারবেন। এসবের ফলে আপনি বা আপনার পরিবারের সদস্যদের কেউই এ প্রতিষ্ঠানের প্রচলিত সেবা কিংবা সহযোগীতা থেকে বঞ্চিত হবেন না।

আপনি আমাকে গবেষণা সম্মন্ধে যে কোন প্রশ্ন করতে পারেন, এবং আমি খুশী মনে তার উত্তর দেবো। আপনষর কোন সমস্যা হলে বা অন্য কোন প্রশ্ন থাকলে আপনি আমাদের স্বাস্থ্য-কর্মী অথবা ডাঃ হাফিজুর রহমান চৌধুরীর সাথে মতলব হাসপাতালে, অথবা প্রফেসর লার্স অকে পার্সনের সাথে ঢাকায় ৯৮৮৫১৫৫ নম্বর টেলিফোনে যোগাযোগ করতে পারবেন।

আপনি এই গবেষণায় আপনার এবং/অথবা আপনার পরিবারের সদস্যের অন্তর্ভূক্তির আমাদের প্রস্তাবে রাজী থাকলে দয়া করে নীচের নির্দ্দিষ্ট স্থানে আপনার স্বাক্ষর অথবা টিপসই দিন।

আপনার সহযোগীতার জন্যে ধন্যবাদ।

| | | |
|---|---|---|
| সাক্ষাতকার গ্রাহকের স্বাক্ষর | অংশগ্রহনকারী/ অভিভাবকের স্বাক্ষর/টিপসই | সাক্ষীর স্বাক্ষর |
| তারিখঃ | তারিখঃ | তারিখঃ |

**Draft questionnaire for pilot testing**
**26/08/01**

DRAFT OUTLINE FOR QUESTIONNAIRE

# Arsenic in tubewell water and health cconsequences

এই সমীক্ষায় অংশগ্রহণ করার জন্য আপনাকে ধন্যবাদ। আপনার উত্তর এবং আপনার পরিচয় গোপন রাখা হবে।

আপনার নাম কি? (পূর্ন নাম ও পদবী) : .....

**Interviewer: Please record the following**

1. Village : .....

2. Union : .....

3. Date of interview: .....

4. Interviewer name

5. Time of commencement of the interview: .....

6. Time of ending of thinterview: .....

**Notes if any:** .....

.....

.....

(Note to interviewer: The next pages refer to houses lived in and water sources during the years in each house. The purpose is to identify each house a participant lived in, the major water sources used in the house, and significant changes in the water sources such as a new tube-well.)

**Draft questionnaire for pilot testing**
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## PART 1
## QUESTIONNAIRE FOR SKIN LESION

**Subject Code:** /__/__/__/__/__/__/__/

1a. Does the participant show signs of hyperpigmentation, hypopigmentation of skin, or both? (Yes=1, No=2) /__/

1b. If participant has pigmentation changes, write down the extent of it in this area (where was it most prominant?) (Body=1, Trunk=2, Palm=3, Sole=4) /__/

1c. If participant has pigmentation changes, write down the extent of it in this area (where was it most prominant?) /__/
No pigmentation=0, Melanosis (early stage)=2, Hyperpigmentation=3, Hypopigmentation=4, Both occurring side-by-side=5)

2. If participant has pigmentation changes: (Yes=1, No=2) /__/
2a. আপনার শরীরে প্রথম কবে থেকে এই ছিটছিটে দাগ দেখা গিয়েছিল (বছর)? /__/__/
2b. শরীরে কোন জায়গায় প্রথম এরকম দাগ দেখা দিয়েছিল (বর্ণনা দিন)? /__/__/

2c. তখন আপনার বয়স কত ছিল? /__/__/

3. গত দুই বছরে আপনি কি দাগের কোন রকম পরিবর্তন দেখেছেন? /__/

(Improved=1, Worsened=2, Not changed=3)
4. Does the participant shows the signs of kerotoses on the palms or soels or both, and or other areas (s). (*please enter responses here, Ys=1, No=2*) /__/
4a. If the participant has kerotoses, write down the extent of it in this area (where was it most prominent or marked) /__/
(Palms=1, Soles=2, Both=3)
5. If participant shows signs of kerotoses: Is it nodular, elevated or flat? /__/
(Nodular=1, Elevated=2, Flat=3)
6a. কত বছর আগে আপনি আপনার ত্বকের শক্ত হওয়া প্রথম লক্ষ্য করেন? /__/__/

6b. শরীরে কোন জায়গায় প্রথম ত্বক শক্ত হয়েছিল (বর্ণনা দিন)? .....
6c. তখন আপনার বয়স কত ছিল? /__/__/

Subject Code:/__/_/__/__/__/__/

## PART 2. QUESTIONNAIRE for First Clinic Visit (performed by physician)

☐ Participant has no skin lesions → Go to Physical Exam

| Physicial Examination for Skin Lesions | | | | |
|---|---|---|---|---|
| Melanosis | | Palm | Sole | Trunk |
| | Spotted | | | |
| | Diffuse | | | |
| Keratosis | | | | |
| | Spotted | | | |
| | Diffuse | | | |
| Leucomelanosis | | | | |
| | Spotted | | | |
| | Diffuse | | | |
| Hyperkeratosis | | | | |
| | Spotted | | | |
| | Diffuse | | | |

| Physical Examination Protocol | | | |
|---|---|---|---|
| Clubbing | | | |
| | Present/Absent | | |
| Vyanosis | | | |
| | Present/Absent | | |
| Basal | | | |
| | Present/Absent | | |
| | | | |
| **Vascular System** | | | |
| | Right Extremity | | Left Extremity |
| Blood Pressure | | | |
| | Systolic | Diastolic | Systolic Diastolic |
| Edema | | | |
| | Grade as millimeters of depression at distal shin just above ankle | | Grade as millimeters of depression at distal shin just above ankle |
| Pulse | | | |
| | Rate/minute | | Rate/minute |

| Hepatic System | |
|---|---|
| Hepatomegally | |
| | Grade as Cm below costal margin at mid-clavicular line in expiration) |
| Asoites | Absent |
| | Present |
| Spider Telangectasias | Absent |
| | Present |
| Jaundice | Absent |
| | Present |
| | |

| Neurologic System | | |
|---|---|---|
| | Right Lower Extremity | Left Lower Extremity |
| Pinprick sensation | Yes/No | Yes/No |
| | Normal/Hypoethesia/Hyperesthesia/ Dysthesia | Normal/Hypoethesia/Hyperesthesia/ Dysthesia |
| Distribution | | |
| | dermatomal/stocking-glove | dermatomal/stocking-glove |
| Kinaesthesia | | |
| | Normal/Abnormal | Normal/Abnormal |

Standing height (m) /___/. /___/___/___/
Weight (kg) /___/___/. /___/___/
Ambient temperature (deg. C) /___/___/. /___/

## Respiratory System

Preamble

এখন আপনার বুকের রোগ সম্বন্ধীয় কিছু প্রশ্ন জিজ্ঞাসা করবো। সেগুলি হ্যাঁ অথবা "না" তে উত্তর দিন।

Cough

1. আপনার কাশির কোন সমস্যা আছে কি? Yes No

2. কত মাস/বছর ধরে আপনার কাশির অসুখ আছে? Month _____ Year _____

3. বছরে শীতের তিন মাসের বেশীর ভাগ দিনেই কি আপনার কাশী হয়? Yes No

Phlegm

4. বছরের মধ্যে অন্ততঃ তিন মাস ধরে প্রতিদিনই কি কাশিতে ভোগেন? Yes No

Periods of cough and phlegm

5. গত তিন বছরের অন্ততঃ তিন সপ্তাহ ধরে বা তার বেশী সময়ের জন্য আপনি কাশিতে ভুগেছেন কি? Yes No

If Yes
4b. কাশির এধরনের সমস্যা কি আপনার একাধিকবার হয়েছে? Yes No

Breathlessness

5a. আপনি তাড়াতাড়ি হাঁটতে গেলে বা একটু উচুঁতে উঠতে গেলে কি হাঁপিয়ে যান? Yes No

If Yes
5b. আপনি কি আপনার সমবয়সী ব্যক্তিদের সংগে একই তালে হাটতে গেলে হাঁপিয়ে যান? Yes No

If Yes
5c. আপনি কি স্বাভাবিকভাবে সমান জমিতে হাঁটার সময় শ্বাস-কষ্টের কারনে দাড়িয়ে বিশ্রাম নেন? Yes No

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Wheezing

6. গত এক বছরের মধ্যে কখনো নিঃশ্বাস নেবার সময় বুকের মধ্যে সাঁই সাঁই শব্দ হয়েছে কি? Yes No

7a. যখন এরকম শব্দ করে নিঃশ্বাস নেন তখন কি শ্বাসকষ্ট বোধ করেন?
Yes Not appreciable

If Yes
7b. শ্বাসকষ্ট যখন থাকেনা তখন কি আপনার শ্বাস-প্রশ্বাস স্বাভাবিক থাকে কি? Yes No

7. গত এক বছরের মধ্যে শ্বাসের এই কষ্টের জন্যে কখনো মাঝরাতে আপনার ঘুম ভেঙে যেত কি? Yes No

Chest illnesses
8. গত তিন বছরে আপনার কি এমন কোন বুকের রোগ হয়েছিল যার ফলে
আপনি এক সপ্তাহ কোন কাজ করতে পারেননি? Yes No

If Yes
8a. সেই সময় কি আপনার কফ বের হতো? Yes No

If Yes
8c. গত তিন বছরে আপনার কি একবারের বেশী এরকম অসুখে ভুগেছেন? Yes No

Past illnesses
নিচের এই বিষয়গুলি সম্বন্ধে আপনাকে আগে কোন ডাক্তার প্রশ্ন করেছিলেন কি?
9a. বুকে কোন আঘাত লাগা বা অপারেশন করা Yes No
.....
9b. হার্টের অসুখ (Cardiac disease) Yes No
.....
9c. তিন বছর ধরে বছরে এক নাগাড়ে তিন মাস খুব কফ উঠে কিনা Yes No
(Bronchitis)
.....
9d. নিউমোনিয়া (pneumonia) Yes No
.....
9e. শ্বাস নেয়ার সময় বুকে সুঁচ ফোটার মত ব্যথা ও জ্বর বা বুকে জমা Yes No
(Pleurisy)
.....
9f. ফুসফুসের যক্ষা TB Yes No
.....
9g. হাঁপানি (Asthma) Yes No
.....
9h. অন্যান্য বুকের রোগ (Other respiratory disease) Yes No
.....
9i. এলার্জি, হাঁচি ও চোখ লাল (Allergy & Corneal congestion) Yes No
.....
Tobacco smoking
10a. আপনি কি এখন ধূমপান করেন? Yes No

If No
10b. এই বছরে প্রতিদিন আপনি কটা সিগারেট / বিড়ি পান করেছেন? ..... exsmoker
..... never smoked

If participant never smoked, omit question on smoking → Go to Spirometry
If participant is a smoker or is an ex-smoker, complete the table below:

| 14c. আপনি এখন বা আগে সাধারণত ঃ কি ধরনের ধূমপান করেন / করতেন | 14d. ছুটির দিন ছাড়া আপনি এখন দিনে ক'বার ধূমপান করেন | 14e. আপনি ছুটির দিনগুলোয় এখন কবার করে ধূমপান করেন |
|---|---|---|
| ---------- biri | ---------- /day | ---------- /day |
| ---------- marketer cigarettes | ---------- /day | ---------- /day |
| ---------- hand rolled cigarettes | ---------- /day | ---------- /day |
| ---------- hukkah | ---------- /day | ---------- /day |

## BIOLOGICAL SAMPLE

**URINE**

1. Was a urine sample taken from this participant? Yes ____ No ____
2. Result of urinary protein test _____
3. Result of urinary glucose _____
4. If no urine sample could be obtained give an explanation. If participant has blood in urine ask about menstruation if female or about urinary tract infections or other possible causes if male.
5. If positive for glucose ask participant following questions
6. Do you have diabetes? Yes ___ No ___ Don't Know ____
7. Do you have blood sister or brother who has diabetes? Sister ___ Brother ___ Don't know ___
8. Do you have a mother or father who has diabetes? Mother ___ Father ___ Don't know ___
9. At what age did you develop diabetes? Yrs. _____

**BLOOD**

1. Was a blood sample taken from this participant? Yes ____ No ____
2. If not, explain why blood sample could not be collected

PHOTOGRAPHS OF SUBJECTS WITH SKIN LESIONS

1. Were photographs taken of this participant? Yes ____ No ____
2. If no, explain why photograph could not be taken

Subject Code:/__/__/__/__/__/__/

## PART 3. Questionnaire on Tubewell Water History

পরবর্তী প্রশ্নগুলি আপনার বর্তমান বাসস্থান সম্পর্কে।

1. আপনার বর্তমান ঠিকানা কি?

Para /Village.....

Union .....

2. আপনি এবং অন্যান্য সকলে কি একই কল, নাকি একের বেশী কল, নাকি অন্য কল / উৎস থেকে জল পান করেন?

- Just one
  কোথাকার জল পান করছেন?
  (Probe: What is it? For example, which tubewell, pond? What is the location?)
  কল, পাত কুয়ো, পুকুর, না টাইম কল?

  Sample collected? Y N

- More than one
  কতগুলো জায়গা থেকে জল পান করছেন? .....

3. পরবর্তি প্রশ্নের উত্তর 'হ্যা' কিংবা 'না' তে দিন।
   আপনি যখন এই বাড়িতে প্রথম আসেন তখন থেকে কি আপনার জলের উৎস একই আছে যা আপনি বর্তমানে ব্যবহার করছেন?

## CURRENT HOUSE (first change in water source)

[Note: This page is for the current house. To know if there was a change in the water source while the participant was resident in it. If there was more than one change then add separate pag for each changes].

1a. এই বাড়িতে থাকাকালিন আপনি কতবার জলের জায়গা বদল করেছেন? .....

1b. কত বৎসর আগে আপনি বর্তমান জলের জায়গা বদল করেছেন? .....

Tubewell Identification number (ID) /__/__/__/__/__/__/__/

Duration (years) /__/__/

## SECOND TO LAST HOUSE (or house before last)

আমাদের পরের প্রশ্নগুলো হচ্ছে আপনি আগে যেখানে থাকতেন তার সম্বন্ধে ?

1. বর্তমান বাড়ির আগে আপনি কোথায় থাকতেন?
2. আপনার আগের বাড়িতে আপনি / আপনার বাড়ির সকলে কি একটা, না একের বেশী কল, না অন্য কোন জায়গা থেকে জল খেতেন?

Sample collect?

-Just one
একই জলের জায়গা ? Y N
(probe: What is it? For example, which tubewell, pond? What is the location?)
.....→ (Go to Q3)

- More than one
কতগুলো জায়গা থেকে জল খেতেন? .....

3a. আপনি ঐ বাড়িতে কত বৎসর বাস করেছেন? .....

Tubewell Identification number (ID) /___/___/___/___/___/___/
Duration (years) /___/___/

## THIRD TO LAST OR PRESENT HOUSE

পরের প্রশ্ন গুলি আপনার আগের এবং তারও আগের বাড়ির সম্পর্কে।

1. বর্তমান বাড়ির আগের বাড়ির আগে আপনি কোথায় থাকতেন?
Village .....
Union .....
2. ..... সেই বাড়িতে আপনি এবং আপনার বাড়ির সকলে কি এক, নাকি একের বেশী জলের উৎস থেকে জল খেয়েছিলেন?

Sample collected? Y N

- Just one
জলের জায়গা কি ছিল?
(probe: What is it? For example, which tubewell, pond? What is the location?)
.....→ (Go to Q3)
- More than one
কতগুলো উৎস থেকে জল পান করতেন? .....

3. ..... বাড়িতে আপনি এবং আপনার বাড়ির সকলে কি এক না একের বেশী জলের জায়গা থেকে জল খেয়েছিলেন?

Sample collected? Y N

- Just one
জলের উৎস কি?
(probe: What is it? For example, which tubewell, pond? What is the location?)

- More than one
কতগুলো উৎস থেকে জল পান করতেন? .....

Tubewell Identification number (ID) /___/___/___/___/___/___/
Duration (years) /___/___/

## WATER SAMPLES

THIS SECTION IS TO BE COMPLETED BY FIELD ASSISTANTS
WATER

1. Total water samples collected for this participant: _____

2. [fill in with the code for the residence or work; e.g., current house, current water source would be

| Residence | Tubewell ID | Duration of use |
|---|---|---|
| residence (current )<br>option 1 [explain]<br>option 2 [explain] | | |
| Residence (previous 1)<br>option 1<br>option 2 | | |
| Residence (previous 2)<br>option 1<br>option 2 | | |
| Residence (previous 3)<br>option 1<br>option 2 | | |

## VOLUMES OF WATER CONSUMED

আপনি আজ কতটা পানীয় ব্যবহার করেছেন সে সম্পর্কে আমি আপনাকে কিছু প্রশ্ন করবো।

In the next questions ask about the volumes of fluids currently consumed. Ask about what the participants first drink after getting up from sleep this morning. Then ask about the rest of the morning. When you get to the time of interview, switch to asking about previous days up to the last drink of last night. For the size of container, a small cup is of 100 cc, a small glass is of 250 cc, medium 500 cc, and large mug 750 cc.

| | কি ধরনের পানীয় ছিল | পাত্রটা কি ধরনের ছিল (e.g. Glass, Cup or Bowl) | পত্রটি কত বড় ছিল (in c.c.) |
|---|---|---|---|
| সকালে ঘুম থেকে উঠার **Breakfast** পর আপনার | | | |
| প্রথম পানীয় কি? | ---------- | ---------- | ---------- |
| দ্বিতীয় পানীয় কি? | ---------- | ---------- | ---------- |
| তৃতীয় পানীয় কি? | ---------- | ---------- | ---------- |
| দুপুরে খাওয়ার **Lunch** পর আপনার | | | |
| প্রথম পানীয় কি? | ---------- | ---------- | ---------- |
| দ্বিতীয় পানীয় কি? | ---------- | ---------- | ---------- |
| তৃতীয় পানীয় কি? | ---------- | ---------- | ---------- |
| চতুর্থ পানীয় কি? | ---------- | ---------- | ---------- |
| বিকালে এবং তারপরে | | | |
| প্রথম পানীয় কি? | ---------- | ---------- | ---------- |
| দ্বিতীয় পানীয় কি? | ---------- | ---------- | ---------- |
| তৃতীয় পানীয় কি? | ---------- | ---------- | ---------- |
| চতুর্থ পানীয় কি? | ---------- | ---------- | ---------- |
| রাতের খাবারের সময়ে **Dinner** এবং তার পরে | | | |
| প্রথম পানীয় কি? | ---------- | ---------- | ---------- |
| দ্বিতীয় পানীয় কি? | ---------- | ---------- | ---------- |
| তৃতীয় পানীয় কি? | ---------- | ---------- | ---------- |
| চতুর্থ পানীয় কি? | ---------- | ---------- | ---------- |
| | | Total _____ | _____ |

## PAST VOLUMES CONSUMPTION

পরবর্তী প্রশ্নগুলি গত পাঁচ বছরে আপনি যে পরিমান পানীয় গ্রহন করেছেন সেই সম্বন্ধে

1. তুলনামূলকভাবে আপনি এখন যতটা জল পান করেন পাঁচ বছর আগেও কি সেই পরিমান পান করতেন নাকি তার থেকে বেশী বা কম খেতেন? More _____
   Less _____
   Same _____
   যদি কম /বেশী খেয়ে থাকেন তাহলে তার পরিমানটা বলুন

   ☐ No change

| বেশী/কম পান করেছেন? | কি পরিমান এবং কি ধরনের পাত্রে? (e.g. glass) | কত বড় পাত্রে? (in ccs) |
|---|---|---|
| [Example : more | 1 medium glass | 500 cc] |
| ---------- | ---------- | ---------- |

2. এবার অন্যান্য জলীয় খাবারের ব্যপারে একই প্রশ্ন করবো (যেমন: এখনকার থেকে তুলণামূলক ভাবে পাঁচ বছর আগে আপনি চা, সরবত বা মাদক পানীয় কতটা বেশী/কম খেতেন?)

☐ No change

| কী ধরনের পানীয় গ্রহন করেন? | কতটা বেশী/কম খেতেন? | কি পরিমান এবং কি ধরনের পাত্রে? | কত বড় পাত্রে? |
|---|---|---|---|
| | বেশী/কম পান করেছেন? | কি পরিমান এবং কি ধরনের পাত্রে? (e.g. glass) | কত বড় পাত্রে? (in ccs) |
| | [Example : more | 1 medium glass | 500 cc] |
| | ---------- | ---------- | ---------- |

# Arsenic in tube well water and health consequences

## Abstract Summary for Ethical Review Committee

The discovery of arsenic in groundwater in Bangladesh has aroused widespread concern. Major proportions of tube wells for drinking water in the country are contaminated with arsenic. Experiences from other countries indicate that the consequences of this exposure will be extensive and include excess incidence and mortality in cancers and cardio-vascular diseases. However, the knowledge base is weak on the weight of this new burden of diseases and on the speed by which it develops. Little is known about the reproductive health consequences, and about the possible aggravating role of the widespread malnutrition in Bangladesh on arsenic-induced health effects.

The overall objective of this project is to establish a strong epidemiologic platform of research on levels of arsenic exposure through drinking water, occurrence of arsenic skin lesions, consequences for reproductive outcome, effect on adult mortality, modifications of effects by the nutritional status, and effects of an intervention with alternative water sources.

We propose screening for skin lesions in the 220,000 population, and assessment of arsenic content by atomic abortion spectometry (AAS) of the 9000 tube wells of the Matlab surveillance area. Information from testing of all 9000 tube wells, individual information on water used for drinking, and results of screening for arsenic-related skin lesions in the entire 220,000 population (excluding infants) will be entered into the data bases of Matlab HDSS. This information will enable analysis of doses of arsenic in relation to presence of arsenic skin lesions. Efforts will be made to assess the calendar time at start of the identified skin lesion, enabling a *retrospective cohort analysis* of current exposure (as a proxy for exposure levels over time); duration of exposure to the arsenic contaminated water, and onset of skin changes. *A second retrospective cohort analysis* will be performed on current exposure, duration of exposure, and reproductive events, such as spontaneous abortions, still birth, and early neonatal deaths during the last three years (this information is also available in HDSS system). This will enable us to evaluate the effects of arsenic exposure as a reproductive toxin in humans. *A third cohort analysis* will relate the arsenic exposure to overall adult mortality (mortality information including cause of death from the HDSS system) and specifically to mortality in cardio-vascular diseases and cancers during the last five years. A *case-referent* study of the modification by current nutritional status on arsenic-induced skin lesions will be nested into the first cohort analysis. Individuals with arsenic skin lesions (above 5 years of age) will be selected as cases, and two referents will be randomly selected from the HDSS databases. Nutritional status of cases and referents will be assessed by anthropometry and blood samples will be taken for nutritional biochemistry. Urine samples will be taken from cases and referents as soon as the cases are identified for analysis of arsenic methylation patterns as well as current exposure levels. BRAC, a Bangladesh NGO, will be responsible for the *arsenic mitigation* component. Initial advice of temporary alternative drinking water sources will be given (arsenic-free tube wells in the

neighbourhood) followed by promotion of alternative sources of safe drinking water (rainwater harvesting, treated surface water, and treated arsenic contaminated ground water). *A follow-up* will be performed of individuals with skin changes as to levels of arsenic species in urine (change in exposure), as well as to assessment of reversibility of skin lesions, assessed by clinical examination. The consequences of a shift to other water sources will also be evaluated, including monitoring of diarrhoeal diseases through the surveillance system in Matlab.

**Strategies to address ethical issues**

1. The latency (i.e. the time from first exposure to manifestation of disease) for arsenic-caused skin lesions, in particular keratosis, is typically of the order of 10 years. However, latency much shorter as well as longer than 10 years may occur. In order to assess the burden of arsenic-induced health problems age- and gender-specific information on the occurrence of such effects is needed, as well as an improved understanding of the exposure to arsenic over time. The ingested arsenic is methylated and excreted in urine. Children have reportedly a lower degree of methylation of arsenic than adults. Children are found to have arsenic skin lesions long before expected latency periods. Some studies indicate a lower degree of arsenic methylation in men than in women, especially as compared to pregnant women. Poor nutritional status might increase the health effects of arsenic through variations in the arsenic methylation capability. Vitamin A status in the population may be related to susceptibility to arsenic related diseases. The risk of skin cancer in arsenic-exposed individuals has been associated to beta-carotene levels. The general nutritional status (as expressed by anthropometry), the antioxidant status and other micronutrients such as zinc status may play an important role in modifying the body's response to arsenic exposure. Due to the vast number of pregnant women exposed to the arsenic contaminated water, even a relatively small risk of abortions, stillbirths and early neonatal deaths related to arsenic in drinking water would have a major public health impact in Bangladesh, The appropriate treatment for arsenic-induced skin changes is a shift to arsenic-free drinking water. However, there is insufficient knowledge to what extent these skin changes disappear when the individual is no longer drinking the contaminated water. There is anecdotal information available that less advanced skin changes are reversible, but unknown if this also is the case for more advanced lesions. Measurements of urine arsenic levels are needed to judge if the exposure has seized. A better understanding of the potential reversibility is needed from a clinical as well as a public health point of view. A shift to alternative arsenic-free water sources may potentially imply a shift to pathogen-contaminated water. This is especially the case when surface water will be used as the new water source, but may also be the case when harvesting rainwater. In most mitigation projects so far some control of pathogens has taken place, e.g. by cultivating samples from the new drinking water source. This is an important intermediate step, but a monitoring of diarrhoeal diseases in vulnerable groups, i.e. infants and children, is also needed. The Matlab surveillance system has included a monitoring of diarrhoeal diseases in all

children below 5 years of age. This information can be used in order to evaluate if the shift to alternative water sources increases the risk for diarrhoea.

2. There may be minimal risks involved in this study. Medical doctors will examine all subjects participate in Matlab health centre for general health, measure blood pressure and examine skin. A trained senior research assistant will collect 4 ml blood (less than one teaspoonful) from veins of forearm with all aseptic precautions. There is minimal risk associated with this procedure. There is no risk involving skin examination.
3. Standardised procedure of collection of blood, and urine samples will be used.

4. Identification of all study participants will remain confidential. Study staff will use records only. Every effort will be made to keep the records confidential as possible. All data forms will be kept in a locked file cabinet. Data will be analysed and published without reference to any name or identity.

5. The participants will be signing a consent form informing them of the nature of the study, its rationale, and its risks and benefits. The informed consent document will embody the elements of the consent as described in the Declaration of Helsinki, and the ICH Harmonized Tripartite Guidelines for Good Clinical Practices. The investigator or designate will describe the protocol to the participant or the legal guardians of potential subjects face to face. The subject information and consent form may be read to the participants of all participants, but in any event, the investigator will give the parent's ample opportunity to inquire about the details of the study and ask questions before signing the consent form. We will insure that health research workers and physicians are trained to recognise symptoms and clinical signs of arsenicosis.
6. The suspected individuals of arsenicosos will be interviewed in the Matlab health centre as well as to their houses. The interview will not take more than 15 minutes.

7. This study will assist in understanding to what extent arsenic-contaminated drinking water have resulted in adverse health effects, especially skin lesions. We will also study if other factors, i.e. general health and nutritional status help protect the individual against the arsenic toxicity. Such information will be useful for prevention of arsenic-related health problems in Bangladesh.

8. We will use the records from ICDDR, B health and demographic surveillance system at Matlab.