EPIDEMIOLOGICAL METHODS FOR MITIGATING HEALTH IMPACTS OF ARSENIC IN SOUTH EAST ASIA REGION OF THE WORLD HEALTH ORGANIZATION

Deoraj Caussy, Ph.D., Environmental Epidemiologist, Department of Sustainable Development and Healthy Environment, Office of the South East Asia Region.

Ground water contamination, in excess of the World Health Organization (WHO) guideline value of 10 µg/L, has been observed in many parts of the world including India, Bangladesh, Thailand, Myanmar, Nepal, China, Taiwan and Vietnam among others. In the South East Asia Region of WHO, it is currently estimated that about 40 million persons may have been exposed to contaminated ground water at various concentrations of arsenic and almost a quarter of a million exposed subjects are already showing overt symptoms of chronic arsenic poisoning. A review of the epidemiological data shows that there is a need for internationally accepted criteria based on evidence in the following areas: Exposure assessment, case-definition and case management. This paper reviews the epidemiological methods that can be used for controlling the health effects of arsenic contamination by providing evidence-based tools and guidelines in the form of standard case definition and management. It also and presents WHO strategic goals to meet these objectives. Data will be presented on the formulation and validation of standard regional protocol for case definition and case management and other areas of risk-management.

CORRESPONDING AUTHOR: Deoraj Caussy, Ph.D., Department of Sustainable Development and Healthy Environment, World Health Organization, Office of the South East Asia, World Health House, Ring Road, New Delhi 110 002, INDIA. Email: caussyd@whosea.org
1 INTRODUCTION

Human exposure to toxic dose of arsenic is widespread in some parts of the world. The most prevalence source is that due to drawing underground water from an aquifer that is naturally contaminated with arsenic or drinking water contaminated with arsenic from mining activities. These exposures can result in numerous health outcomes including dermal manifestations of melanosis and keratosis and eventually cancer (reviewed in WHO 2001 and Caussy 2003). Thus, a number of strategies have been used to limit the exposure and mitigate the adverse health outcomes. Theoretically, the levels of arsenic in water can be reduced by engineering control and this has been done to varying success in Chile, Hungary and India and is being tried in elsewhere. Similarly, the various control options have been used to mitigate the health impact; however, to control health impacts require an understanding and application of the epidemiological principles of public health practice. This article reviews the methods and applications of epidemiological principles that have been used for controlling the health impacts of arsenic in South East Asia and may be applicable elsewhere.

2 SIZE OF ARSENIC CONTAMINATION IN SOUTH ASIA

The epidemiology of arsenic contamination and projected health impacts in five arsenic-affected member states of Bangladesh, India, Nepal, Myanmar and Thailand is shown in Figure 1 below.

In West Bengal, India approximately 5 million persons are consuming groundwater containing arsenic exceeding 50 µg/L that is their national standard. Recent reports point to the presence of arsenic in the states of Bihar and Uttar Pradesh, implying wider contamination of groundwater. Of the 5 million exposed subjects about 1 million is expected to develop some kind of arsenicosis disease. Already 220,000 subjects are showing signs of
arsenicosis.

Figure 1: Epidemiology of Arsenicosis in South East Asia

The arsenic contamination in Thailand originates from tin mining containing arsenite and arsenate. The main affected area is the district of Nakorn Si Thammarat however “hot spots” are being identified in other provinces also. A health survey estimated that approximately 6,120 of potentially 24,566 exposed subjects were showing symptoms of arsenicosis in the affected district.

Arsenic contamination of ground water in Nepal is around the active flood plains of River Koshi in 17 Terai districts namely in Nawalparasi, Rautahat, Bara and Bardia. The arsenic concentration is up to 170 µg/L. It is estimated that 5 million people may be exposed and about 1 million will develop the disease. To date close to 2,000 subjects are showing signs of arsenic diseases in the form of dermal lesions.

In Myanmar, arsenic contamination has been found in the sunken tube wells in Thabaung, Laymyethan and Hethada townships of the delta and coastal areas. The exact number of exposed people is not known but two suspected cases of arsenicosis have been detected.
The arsenic crisis in Bangladesh has been described as one of the worst cases of mass poisoning in world history. Exposure to arsenic in Bangladesh is through consumption of water obtained from some 8-12 million tube wells distributed throughout the country. The map below shows that 59 of the 64 districts of the country have at least 10% of its tube well that contain water in excess of the national standards.

The precise number of affected persons in Bangladesh is not known, but most estimates put the number of people being exposed to arsenic concentration at around 25 million, exceeding the Bangladesh national standard of 50 µg/mg/L. Five million of persons are projected to develop arsenicosis and about 200,000 subjects have already developed signs of arsenicosis. A disease burden of this magnitude is binding on WHO to address the health aspects.

Table 1 below summarizes the case-load for each country of the region.

<table>
<thead>
<tr>
<th>Country</th>
<th>Number of subjects exposed</th>
<th>Number of projected cases</th>
<th>Number of Disease cases reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bangladesh</td>
<td>25-30 million</td>
<td>5 million</td>
<td>200,000</td>
</tr>
<tr>
<td>India</td>
<td>5 million</td>
<td>1 million</td>
<td>200,000</td>
</tr>
<tr>
<td>Nepal</td>
<td>5 million</td>
<td>1 million</td>
<td>186,000</td>
</tr>
<tr>
<td>Thailand</td>
<td>250,000</td>
<td>2,000</td>
<td>186,000</td>
</tr>
</tbody>
</table>
Thus, the highest patient case-load for the whole region is found in Bangladesh.

### 3 EPIDEMIOLOGICAL METHODS FOR THE CONTROL OF ARSENIC

One of the principal aims of environmental epidemiology is to provide a data-base upon which public actions and policy can be made. Various methods have been used for gathering data in field of arsenic contamination and it associated health risk. However, a systematic way of gathering data for action is the application of the health risk paradigm as advocated by the National Research Council (NRC) and the World Health Organization (WHO). The application of the health risk paradigm for characterizing the exposure and outcome to arsenic have been reviewed elsewhere (Caussy 2003 and Caussy 2004). This article will review the implementation and application of the health risk paradigm for arsenic.

#### 3.1 Knowledge gaps of the existing data-bases

Scientists and policy-makers depend on data-bases of local exposure dose, pathways and associated health outcomes to make scientific recommendation and institute management strategies.

A review of the current epidemiological global and regional data show that large data bases on arsenic contamination are lacking. Furthermore, the existing regional arsenic data bases are fraught with many uncertainties on the types of exposure dose, duration of exposure and health outcomes. In particular, the following gaps need to be addressed from the point of view of public health control, 1) lack of validity of arsenic testing; 2) lack of objective criteria for defining a clinical case; 3) lack of information on outcomes of low-dose exposure to arsenic as well as 5) lack of information on the role of cofactors in modifying the onset and prognosis of arsenicosis, and, 6) lack of Environmental Technology Verification (ETV) on arsenic removal.
The following epidemiological knowledge gaps have either been or are being addressed for arsenic mitigation in the South East Asia Region of WHO.

1 **Standardization of laboratory testing for arsenic**

The validity of any prevalence estimate is contingent on accurate laboratory measurement of arsenic in groundwater. Currently, there are many commercial test and locally-developed test kits that are widely used in our Region, but the results do not show a high degree of concordance among various assays in the field (Aggarwal P, IAEC, 2001). Therefore, in an effort to standardize laboratory testing, Regional Office of WHO in South East-Asia has supported formulation of Standard Operating Procedure (SOP) for the testing of arsenic and is in the process of introducing QA/QC in an effort to strengthen the laboratories involved in testing arsenic.

2 **Formulation of integrated exposure assessment**

Arsenic is present in most of the major environmental matrices but in different chemical forms and concentration levels. Of particular importance is the occurrence of arsenic in the food chain in relation to the arsenic intake from drinking water.

In collaboration with the Agency for Toxic Substance and Disease Registry (ATSDR) in Atlanta, GA, WHO has developed an integrated exposure assessment module to quantify the arsenic intake from various sources of food items and water. Preliminary results show that the risk of arsenic intake from food chain is negligible (less than 50 µg/ per day in relation to the massive daily dose from water.

3 **Standardization of ETV for arsenic removal**

The prohibitive cost of arsenic removal technologies on a large scale has prompted the search for alternative sources. These include: confirmation and use of “green” tube wells, use of deeper aquifers in areas where there is a well-developed aquiclude separating the upper and deeper parts of the aquifers, promotion of rain-water, consideration of piped schemes based on central supply of surface water treatment or higher yielding deeper, arsenic-free tube-wells, and using a packet of chemicals for household treatment. Some examples include the so-called “tea bag” treatment developed in the region and
also by the Pan American Center of Sanitary Engineering and Environmental Sciences in Peru, Lima.

These principles have been exploited into commercial device that can be operated on large scales or house-hold devices. However, the performance of these devices for the removal of arsenic is not equal since the removal can be dependent on the presence of other chemicals or impurities. Since the efficacy of these technologies varies, a number of different protocols exist. Therefore, as the need existed to develop protocols for the independent verification of arsenic-safe water technologies, WHO has supported the development of the ETV for arsenic under collaboration with US E.P.A. The next focus is to train national experts in national centers of excellence in the use of the protocols.

4 Formulation and validation of a uniform case-definition

The accurate detection of arsenic cases is the cornerstone for good case management and reporting. Until now, no uniform case definition of arsenicosis has been developed or validated regionally or internationally. Formulation of criteria for classifying cases into the categories of suspected, probable, and confirmed has been developed in the form of a regional algorithm developed by a series of multi-disciplinary expert panel in the field. The illustrated algorithm has been validated under field conditions and allows.
These algorithms have been incorporated in the form of a Field Guide for the detection, Management and surveillance of arsenicosis and a trainers handbook has also been developed to accompany the use of these guides in training of health care workers.

5 Health research for providing data on management of arsenicosis patients

Scientists and policy-makers in the field of arsenic mitigation require evidence-based data to manage the arsenicosis patients and make policy recommendations. In particular data is needed on the type of treatment to be used, the biomarker or predictor of arsenicosis and the health effects of chronic exposure to low-dose of arsenic.

a) There is no universal medical treatment for chronic arsenicosis, although a number of clinical treatments have been advocated. The lack of currently available proven therapy for clinical management of chronic arsenic poisoning has led to a number of unsubstantiated therapeutic measures being used for treating arsenicosis. Some chelating agents which are effective in acute poisoning, are ineffective in most patients with chronic poisoning. Recently, a number of chemical compound like DMPS etc have been tried but are either too expensive to be
used on a large-scale or are not effective. Anti-oxidants have gained popularity in cancer treatment and other inflammatory conditions and have been tried with limited success in the treatment of arsenicosis patients. However, there is no large-scale double-blinded clinical trial on the use of anti-oxidants in arsenicosis to date, therefore WHO is in the process of conducting such a trial in partnership with others.

b) The epidemiologic observation to-date shows that in most populations between 25-35% of exposed subjects develop arsenicosis disease. The etiology of arsenicosis maybe multifactorial (Caussy, 2003), however if one could identify biologic markers or co-factors of progression to disease significant progress will be made in the prevention of the disease. Thus, if one can identify particular dietary habits as cofactors, then appropriate intervention measures could be targeted at those factors for the prevention of arsenicosis onset. These results will have potential public health implications. Towards this end, WHO has collaborated with both the Centers for Disease Control and ICDDR,B in the conduct of case-control studies on the role of nutritional cofactors in the genesis of skin lesions.

c) The long-term risk of exposure to low doses of arsenic in largely unknown. Some data are available from Taiwan but there is a dearth of regional data. It is conceivable that such exposure may not lead to skin manifestations but to increase in internal cancers. This can only be addressed in a cohort study. Therefore, WHO is in the process of conducting a cohort study to characterize the natural history of arsenicosis.

4 USE OF RISK ASSESSMENT DATA

4.1 Scientific Uses

The data gathered during bridging the existing knowledge-gaps can be used for various scientific uses such as prioritizing research- promoting development of new methods and standard setting. However, the greatest contribution has been in the area of training of health care workers in case-detection, surveillance and management using WHO method. For instance the WHO training module and guide have been used to achieve consistency of surveillance and diagnosis as well as training of health care workers and ensure objective means to evaluate intervention measures.
4.2 Management

Similarly policy makers can use the epidemiological information for the development of regulatory option, set priorities, improve decision making, and formulate risk-reduction policies. However, so far the application of WHO protocol has been incorporated in the national arsenic policy in Bangladesh and is being use in other countries as standard procedures the diagnosis of patients and testing of arsenic.

One interesting use of the risk assessment data of arsenic in the food chain. The figure illustrates the application of the precautionary principle in instances where the decision has to be made in the face of limited data. An important consideration for risk assessment is not just the ingested dose of arsenic but also the chemical form of it since inorganic arsenic is relatively more toxic than organic one (WHO 2001). The concentration of arsenic depends on the daily intake dose from various food items. The effective dose of arsenic to cause toxicity depends on the on the bioavailability of the arsenic from the matrices (Caussy 2003).

**Health Risk from Food chains Lack of large data base: Precautionary Principle**

Exposure is affected by

- **Species**: Organic or inorganic
- **Concentration**: In the daily intake dose
- **Bioavailability**: What is the bioavailability in the food chain

**Implications of wrong risk analysis**:

- Raise Fear,
- Waste resources,
- Ignore problem,

However, in the absence of all these parameters one has to make risk management strategies using the precautionary principles (Cornell-Pate). Thus, if one makes the wrong risk analysis there is risk of raising unwarranted fear in the community and of wasting important resources...
by discarding the food items grown in the arsenic contaminated region. On the other hand if arsenic intake from the food item is an important contribution to the daily intake dose of arsenic from food chain and one recommended that this is not an important source, then an important health risk problem would have been overlooked.

5 WHO STRATEGIC GOALS
In order to provide a unifying approach to all the above risk assessment method, WHO-SEARO has developed a strategic plan consisting of three goals as shown in the Figure below. These goals are: 1) application of the health risk paradigm for responding to the needs of the arsenic-affected countries through exposure assessment, risk determination and risk management, 2) strengthening the infrastructure of the country and 3) capacity building in the form of human resource development.
5.1 Application of the health risk paradigm to support the countries
The application of the health risk paradigm has for exposure assessment, risk determination and risk management has been discussed under section 3.1 in depth.

5.2 Strengthening Infrastructure for Arsenic Mitigation

Realizing the role of infrastructure for arsenic mitigation, the Regional Office is strengthening key existing infrastructures in India, Bangladesh, Thailand and Nepal. Two aspects are being addressed: strengthening of reference laboratory and setting up of an arsenic network.

In order to monitor and validate arsenic testing and arsenic removal technologies, centers are being supplied with equipment and reagents as well as training in the use of the protocols.

A regional network has been created by cross-linking available national and international centers of excellence and collaborating centers with international ones. The illustration below shows that there is a national network in Bangladesh, India, Nepal and Thailand and that some of these centers can serve as WHO centers of excellence and collaborating centers.
5.3 Capacity-building through Human Resource
Concerted response to arsenic mitigation can only occur if a critical number of human resources are developed in the field of arsenic diseases. The Regional Office has supported human resource development by developing standard training curriculum and materials. Use of these materials has resulted in a cadre of trained trainers in each country that can impart further training to the local health care personnel.

6 CONCLUSIONS
The methods of environmental epidemiology thus provide insight into where the priority should be directed and also provide key information for the policy makers and scientists alike. However, for a more comprehensive approach to the arsenic mitigation, a multi-disciplinary team encompassing environmentalist, engineers and toxicologists should work in close collaboration.

7 REFERENCES


Caussy D and Than Sein U. Health Risk Assessment Arsenic Contamination in the South East Asia Region: Evidence-based practices in norm setting. CSIRO (in press) 2004


