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MEDICAL GEOLOGY NEWSLETTER

Cogeoenvironment Working Group on Medical Geology
Newsletter No. 5

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- ARSENIC
- LEAD
- AIR QUALITY
- MEDICAL GEOLOGY IN THE SLOVAK REPUBLIC
- MEDICAL GEOLOGY:EARTH SYSTEMS CONFERENCE

Ribeira Valley, State of Sao Paolo, Brazil

Inside this issue:

MESSAGE FROM THE CHAIRMAN, Olle Selinus

Since the previous newsletter many things have happened. After my long illness we have started many activities and I have the impression that the snowball has just started rolling, getting bigger and bigger. One of the main activities this year has so far been short courses on Medical Geology.

Short courses

A series of short seminars on metals, health, and the environment are now carried out around the world. The leaders are Jose Centeno, Bob Finkelman, and Olle Selinus. In addition to these, local scientists are also invited to demonstrate Medical Geology work going on in their respective regions.

Metal ions occur naturally in rocks, soils, gases, and waters in both harmless and harmful forms and concentrations. Natural concentrations can be extraordinarily high and have caused serious health problems. Metals are important in environmental health and in the study of human diseases (pathology) because of their potential toxic effects on one or more organs. Exposure to toxic metal ions may occur via three principal routes: percutaneous absorption, ingestion, or inhalation. Dermal toxicity results from local tissue responses through direct contact of the metal with skin, or alternatively, may represent a manifestation of systemic toxicity following ingestion or inhalation. Allergic contact dermatitis induced by nickel is an example of a local tissue response. The adverse cutaneous reactions resulting from chronic ingestion or inhalation of arsenical compounds exemplify systemic toxicity. A variety of toxic pathology responses in human tissues and organs (i.e., skin, liver, heart, kidney) associated with both acute and chronic exposures to metals are described. The aim of the Seminar is to provide examples where both deficiencies of trace elements as well as toxic exposures of metals may be involved in physiologic changes and the development of human diseases. We discuss the impacts of metal ions and trace elements on human health as illustrated with examples of arsenic poisoning from contaminated water in the Bengal Delta (India and Bangladesh) and Taiwan, as well from coal combustion in southwest China. Studies associated with lung cancer risk in an occupational cohort of chromate production workers are described. An overview of clinical aspects of toxic metal exposures including discussions of essentiality and clinical manifestations are presented.

The Seminars are intended for geologists, ecologists, chemists, biologists, occupational and environmental scientists, medical professionals, toxicologists, epidemiologists, pathologists and any other health, environmental and geo-sciences professional with interest on the effect of toxic metal ion species on environmental and human health. An important aim of the Seminars is to provide the opportunity for forming contacts and networks between professionals working in different areas of the field.

Short Course Leaders are Dr. José A. Centeno, Chief, Biophysical Toxicology Division, United States Armed Forces Institute of Pathology , Washington DC and Dr. Robert B. Finkelman, Coal Quality Coordinator, Research Scientist, United States Geological Survey, Reston, VA, USA and Dr. Olle Selinus, Geological Survey of Sweden, Chairman of our working group.

Please keep yourself informed on the website for new and planned courses. If you have any suggestions for new venues, please mail me.

This year we have had two short courses in Chile (March) and St Petersburg, Russia (May). More courses are planned in Japan (November), probably China (November), Lithuania (May 2003), Edinburgh, UK (September 2003) and probably some other places also. If you are interested please contact me. We have possibility for limited sponsoring.

Publications

Information and news on the working group has been published in different journals. One highlight has been an article (for the first time!) in the well known journal, Scientific American. Bob Finkelman, USGS, wrote an article on coal and health effects (February 2002).

Website

The website is continuously updated, at least twice a month, often even more often. The site has about 800 visitors a month which I consider to be good and I have got several new members and contacts through this site. The site is planned to be expanded soon. Therefore I have to move it to another, larger web server. This will be done in August but I will link the new site to the old one so there will be no problems for you when it is moved.

Special status for the working group

To address issues in geoscience which are emerging as important, and which have not received due consideration to date, the Commission COGEOENVIRONMENT establishes specialist International Working Groups to investigate and promote the issues to the international community. Working Groups are established for a defined lifetime (in the order of 1 or 2 four-year terms). Each Working Group is overseen by an elected Officer of COGEOENVIRONMENT who has freedom to approach experts worldwide for their input to the objectives of the Working Group. A primary aim of each Working Group has been the production and publication of monographs or textbooks on their subject of investigation. To assist with information dissemination, Working Groups aim to develop websites, and to present specific workshops/ training courses on their specific topic in different countries of the world.

As a result of the significant achievement our working group has been given Special Project status by the IUGS. In March 2002 the IUGS announced that the International Working Group on Medical Geology would be assigned Special Project status and will now operate directly under the IUGS. The Commission is proud of the very significant achievements of this Working Group and will continue to assist the IUGS with the Special Project activities as required

Medical Geology Registry

The Armed Forces Institute of Pathology, Washington DC, USA has received approval from the American Registry of Pathology to establish a registry on Medical Geology. The Registry on Medical Geology serves as the liaison between the medical/pathology community and the earth sciences, environmental and public health professionals. The aims of the Registry on Medical Geology are:

1. To facilitate the interactions between the Medical/Public Health community and the Earth Sciences, Toxicologists, and other related areas;
2. To provide a centralized facility for the sharing of information, materials and research projects on Medical Geology;
3. To provide opportunities for training (i.e., postdoctoral, postmedical, visiting scientist/professor, etc.) on medical research with particular emphasis on Medical Geology, Environmental and Environmental Epidemiology research; and
4. To develop educational materials, publications and activities (courses, workshops, symposia, conference) on medical geology research topics.

Sponsorship comes from the International Union of Geosciences (IUGS) through COGEOENVIRONMENT and the International Working Group on Medical Geology.

ICSU

After the success of the short course in Zambia 2001, we have applied for money from ICSU (International Council of Scientific Unions) for more courses in different countries in 2002. I am glad to say that one of the very few approved applications was ours on short courses on Medical Geology.

Other meetings

The working group and IGCP project is involved in several meetings around the world, with special sessions or symposias on medical geology. For a complete list please see the web site. I will just mention some of them:

Healthy Ecosystems - Healthy people, Linkages between biodiversity, ecosystem health and human health, June 2002, Washington DC USA.

7th ICOBTE, The International Society of Trace Element Biogeochemistry, Uppsala, Sweden, June 2003

Sixth International Symposium on Environmental Geochemistry, September 2003, Edinburgh, Scotland There are also more conferences in Japan, Turkey and other countries which will be announced.

Newsletter

The newsletter is published biannually. However we rely on material from YOU for the newsletter, so please send shorter papers, information etc., to the newsletter editor (**delliott@cadvision.com**). There are funds for printing the next four issues of the newsletter.

Other information material

We are now producing a CD with all material for the short courses. We will also produce posters, new leaflets and other information material.

Book

The work with the book on Medical Geology is proceeding and the manuscripts are now being mailed to me. This summer, reviewing will be undertaken and we are keeping our schedule. In November 2002 the final manuscript will be sent to Academic Press and the book will be published hopefully before summer 2003.

Finally I hope that all of you regularly have a look at the website (**http://home.swipnet.se/medicalgeology**), send material to the newsletter, and also mail me if you have any questions. The more contacts the better!!

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THE EMERGING DISCIPLINE OF MEDICAL GEOLOGY

Peter Bobrowsky

On November 5, 2001 a Pardee Keynote Symposium was held at the Hynes Auditorium in Boston, Massachusetts as part of the Geological Society of America Annual meeting. Peter Bobrowsky (IUGS) Victoria, British Columbia and H. Catherine W. Skinner (Yale) New Haven, CT were the conveners on behalf of the IUGS and IGCP Project 454 Working Group on Medical Geology.

Ross MacPhee, Dept. of Vertebrate Zoology, American Museum of Natural History, NY., spoke on extinctions of species over the past 50,000 years and proposed that infectious disease introduced to immunologically naïve animal populations by humans as an alternative consideration to the hypotheses of climate change or over-hunting.

H.C.W. Skinner discussed the role of the mineral material in skeletons. She identified the apatite phase as the site and source of a range of elements, with the composition being the result of the nutrition of the species. As a virtual biogeochemical indicator, skeletal samples can now be analyzed with modern analytical systems and tracers to obtain chemical information that can be directly related to the environment in which skeletal materials develop and grow.

Robert Finkelman, U S Geological Survey, Reston, VA described the health impacts of coal burning in Guizhou Province, China, an area where the populace is exposed to toxic levels of As and F resulting in disease and death. He also discussed a disease endemic to an area in the Balkans whose cause may be related to polycyclic aromatic hydrocarbons leached from strata of lignite into domestic waters.

Mickey Gunter, University of Idaho, Moscow, ID reviewed the current state-of-affairs in Libby, Montana where the mining of vermiculite exposed the community to winchite, a fibrous amphibole that accompanies certain economically important mineral species. The health effects have led to a new chapter in the discussions of asbestos issues.

Howard Mielke, Xavier University, New Orleans, LA, showed that Pb exposure in urban environments, predominantly released from leaded gasoline, has had a marked effect on the learning capabilities of some children. This malady is an expression of modern society's activities contributing to human ills while utilizing some of our natural resources.

Chris Metcalf, Environmental and Resource Studies, Trent University, Peterborough, ON, Canada, presented another instance of human interference with the environment. Measurements of the type and amount of estrogens discharged from sewage treatment plants appear to be sufficiently high to alter gonadal development in local fish populations. Monitoring the health of wild life could act as an early warning system for potentially hazardous chemicals, both natural and industrial.

Session participants, and others at the conference, were alerted to the November 2001 issue of *Geotimes* that featured articles on "Geological Sciences and Health". To obtain a copy go to **www.geotimes.org**.

REPORT ON THE MEDICAL GEOLOGY: EARTH SYSTEMS, RESOURCE USE AND HUMAN HEALTH WORKING GROUP AT THE "HEALTHY ECOSYSTEMS / HEALTHY PEOPLE" CONFERENCE SPONSORED BY THE INTERNATIONAL SOCIETY FOR ECOSYSTEM HEALTH, JUNE 6 - 11, 2002, WASHINGTON, D.C.

Joseph Bunnell, USGS and Olle Selinus

By all accounts, the Working Group successfully completed its assignment. On the first day, we had excellent Case Study presentations with lively and interesting question and answer sessions. The second day consisted of a Roundtable Discussion, and everyone participated with insightful, constructive, comments.

The Working Group agreed to continue using the term "Medical Geology," recognizing the need to emphasize the broad definition in the foreseeable future. While it is less than perfect to accurately describe the work we do, we agreed that the term is simple to remember, and is accessible to policy-makers and the public -- two groups identified as critical in our outreach and promotion activities. It was noted that within the USGS, the term Epidemio-Ecology will continue to be used internally due to sensitivities of the non-Geologic Disciplines; *viz*. Biological Resources, Water Resources, and National Mapping. Although it is rumored that the Director's Office will require another name, as the word "ecology" has evidently acquired some negative baggage, at least with the current Administration.

The next item on the Agenda was to discuss ways to promote the growth and expand the credibility of Medical Geology. The International Union of Geological Sciences (IUGS) has recently created a Medical Geology Initiative directly under its Executive Committee. The ties this Union has to the International Council of Scientific Unions (ICSU), and the United Nations Educational, Scientific and Cultural Organization (UNESCO) may also be helpful for information dissemination. In Washington, D.C., the National Museum of Health and Medicine has an exhibit that will run indefinitely highlighting how Medical Geology is used by its parent organization, the Armed Forces Institute of Pathology (AFIP) to study health problems associated with arsenic. The exhibit, "Research Matters: Environmental and Toxicological Effects of Arsenic," explains how geoscience tools are complementing the skills of biomedical and environmental professionals to understand exposure to and effects of toxic metals such as arsenic. Also affiliated with the AFIP is the newly established Medical Geology Registry. This clearinghouse of information and resources should greatly facilitate training and education of future Medical Geologists. It should be beneficial to create a Repository for archived samples under the oversight of the Registry. The Medical Geology community has been represented in symposia at regional and national meetings of the Geological Society of America (GSA). Scientific American magazine used the term "Medical Geology" for the first time in the February 2002 issue. Olle Selinus is editor-in-chief of a textbook on <u>Medical Geology</u> currently in preparation.

We recognized the need to promote the field using popular science and general interest media outlets. To this end, it was agreed that we will produce a 30 - 40 page colorful, glossy, professional-looking pamphlet with assistance from the American Geophysical Institute. Production of an educational video would be helpful, and David Suzuki agreed to consider doing a special television program in his series devoted to Medical Geology issues.

The Working Group decided to create a Medical Geology Publications Advisory Board. This body will help steer authors to appropriate journals. Presently, Medical Geology papers are being published in a wide variety of journals. The Group felt that the Board could help the development of the field by channeling submissions to a smaller number of journals, while avoiding the presently undesirable launching of yet another new technical journal. Specifically, the Journal of Toxicological Pathology and the Journal of Environmental Geochemistry and Health have expressed interest in adding an Editorial Section and featuring a series of special editions, respectively, devoted to Medical Geology. The American Mineralogist is also entertaining the idea of showcasing work in this field.

A number of topics were raised as priorities for the field of Medical Geology. Two main themes seemed to emerge as overriding priorities: study of trace elements, especially the bioavailability thereof, and a need to establish baseline, or background, levels of contaminants/xenobiotics/potentially harmful but naturally-occurring materials in water, soil, air, food, and animal tissue. And the need for research in the specific areas of radioactivity, earth materials, and infectious diseases was pointed out repeatedly. In the short term, the Group felt that we should determine the geographic distribution of diseases, and make maps of them available to the public. We should study the relationship of trace metals to specific diseases. We could simply take all of the information on Medical Geology case studies and put them in one place, such as the Medical Geology website.

It should be a priority of ours to solve a high profile issue, such as Balkan Endemic Nephropathy. We would do well to create a system for establishing and reporting standards for consumer products. For instance, are there Medical Geology issues related to construction materials? As relates to pathogens carried by dust, we could make strides in addressing their taxonomy and pathology. Effects of deficiencies and excesses of trace elements and nutrients in diets need to be better understood. There are likely to be exposure pathways yet to be discovered or fully appreciated. Global change as it affects ecosystem health and development of predictive models fall under the rubric of Priorities in this field. We must not stop at reporting observations of GIS-based correlations between apparent human health problems and environmental factors, but go on to using spatio-temporal statistical analysis and biophysical, pathological, or toxicological mechanistic techniques to demonstrate biological plausibility. Baseline/background determination came up as key to interpreting information relative to weapons of mass destruction. How else would we necessarily know when an anomaly occurs? We need to determine what sampling needs to be routinely done. Processes and mechanistic links need to be further explored. For example, how do metal solubilities, isotopes, modes of occurrence, etc. affect bioavailability? Our creativity is challenged to develop novel applications of existing tools. We need to establish a centralized repository, archive, or reference collection to enable the identification, collection, and validation of materials (*e.g.*, tissues) that indicate origins of disease. Another priority of ours ought to be the continued analysis of research gaps.

AIR QUALITY DOWNWIND OF SOUR GAS FLARING AND PROCESSING OPERATIONS WEST OF CALGARY, ALBERTA, CANADA

A. L. Norman and The University of Calgary ENSC 502 Class of 2000-2001
Environmental Science Program, University of Calgary, Calgary, Alberta T2N 1N4

Flaring, venting and the health effects of emissions from oil and gas processing have been the subject of intense media scrutiny in Alberta, Canada after a series of conflicts between rural residents who feel they are affected by emissions and local government and oil and gas developers. Health impacts due to exposure to flaring and processing emissions have been largely anecdotal, except for a few cases studying the effects on workers in the industry. Until recently, flaring and processing emissions were thought to be relatively harmless, and combustion efficiencies greater than 98% were assumed. Efficient combustion renders toxic compounds such as hydrogen sulphide and benzene into relatively harmless sulphur dioxide and carbon dioxide. Little scientific information on the composition of emissions was available in public documents, and when a recent study showed that flare combustion efficiencies may often drop below 75% under ambient conditions, health concerns escalated (Strosher, 1996).

An undergraduate study designed to address issues important to the community undertook a program to investigate the composition of ambient aerosols downwind of sour gas (natural gas rich in H_2S) flaring and processing and to examine this data in context with respect to community issues. This work was performed as part of a 4th year research-intensive course in the Environmental Science Program (ENSC) program at the University of Calgary. Fifty students examined air quality, legal issues, the role of the media, and perceived health impacts in two communities downwind of sour gas exploration and processing facilities west of the city of Calgary. A six month measurement program contrasted aerosol characteristics and SO_2 concentrations during known flaring and non-flaring periods to that found in Calgary, and in a remote mountain location. Metal, sulphate, PAH, total carbonaceous matter, particulate phase n-alkane, and sulphur dioxide concentrations were determined for known flaring and non-flaring periods. Precipitation, and sulphur contents and stress on spruce trees were also examined as a proxy for longer-term impacts. Health effects related to airborne pollutants are a function of aerosol diameter, so intermittent sampling to collect aerosols less than 4 μm in diameter at both indoor and outdoor sites provided context for community members to assess data on air quality. The role of media in informing community members on oil and gas emissions related issues were studied and members of Priddis (10 km south of Calgary) and Bearspaw (NW Calgary) were canvassed about their perceptions on health impacts. The regulatory framework and mechanisms for resolving disputes and ensuring the health of communities and individuals living downwind of flaring and processing emissions were also examined. Here, a few pertinent results from the air quality portion of the study are presented.

Two known flaring events occurred during the sampling period from July to December, 2000, at the Priddis site. The first consisted of flaring of a 2.7% H_2S well while the second event was in association with a 5% H_2S well. Both flares were approximately 10 km south of the sampling site.

The aerosol characteristics for flaring and non-flaring events were distinct. Polycyclic aromatic hydrocarbon (PAH) concentrations peaked during the two known flaring events and, on average, were 17 times greater than during non-flaring events. Benzo(a) pyrene made up the majority of the total PAHs and was three times higher than the maximum predicted values in the immediate vicinity downwind of the plume (Strosher, 1996). Elevated PAH concentrations corresponded to an increase in sulphur dioxide. Natural sulphur abundance isotope analysis showed that the isotope composition of SO_2 was similar to that expected for sour gas emissions, implicating flaring activities as the source of these compounds.

Total carbonaceous particulate matter from intermittent, low volume sampling at four sites within the city, contained high concentrations of aerosols less than 4 μm diameter and exceeded personal exposure levels for PM_{10} (particulate matter less than 10 μm in diameter) in Alberta. Of particular concern is the fact that metals tend to be found in finer particles. Analysis of outdoor aerosol samples to the west of Calgary showed slightly elevated concentrations for five metals Cd, Cr, Cu, Ni, and Sb, relative to those from the city. In contrast with sulphur dioxide and PAHs, the metal and fine carbonaceous components were not linked to flaring events.

Exposure to sour gas processing and flaring emissions can be inferred from variations in plant characteristics. Conifers become stressed as a result of the excess sulphur and exhibit reduced growth, discoloration of needles, and increased sap production. These effects were observed in trees at both sites. Histochemical analysis showed needles on the sides of trees facing nearby sour gas processing plants were significantly stressed, and isotopes were used to determine that at least half the sulphur in the plants was derived from atmospheric deposition of pollutants from the sour gas processing industry.

In summary, the scientific results from this study revealed where future efforts should be focused in examining the link between possible health effects and sour gas processing and flaring emissions. Of greatest importance, is the presence of PAHs, and especially of benzo(a)pyrene at high concentrations approximately 10 km downwind of two known flaring events. The fact that elevated concentrations were found in conjunction with high sulphur dioxide concentrations and an isotope composition reflecting a sour gas source, suggests this may be an area for further study with respect to health concerns. Total organic carbon in particulate matter and especially in the smaller diameter particles near Calgary is also a health concern, and should be investigated with respect to metals such as Sb, Cr, Cd, Cu, and Ni. Unlike PAHs, these components cannot be attributed to flaring activities but may be related to upstream oil and gas activities or other emissions that are not intermittent. Vegetation was a useful indicator of sulphur stress and can potentially be used as a proxy for investigations on the cumulative effects from sour gas processing and/or flaring.

In addition to the scientific merits of this study, the students, and the community benefited from the educational experience in producing and participating in the project. A more detailed overview of the study, and an upcoming final report can be found on the website **www.ucalgary.ca/~alnorman/airq/airquality.html.**

M. Strosher (1996), Investigations of flare gas emissions in Alberta. *Final Report to Environment Canada, Conservation and Protection, the Alberta Energy and Utilities Board, and the Canadian Association of Petroleum Producers. 117pgs.*

ENVIRONMENTAL PATHOLOGY AND HEALTH EFFECTS OF ARSENIC POISONING: AN INTRODUCTION AND OVERVIEW

Jose A. Centeno[1], Florabel G. Mullick[1], Leonor Martinez[1], Herman Gibb[2], David Longfellow[3] and Claudia Thompson[4]

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I. ***Abstract:***

Arsenic is a ubiquitous element in the earth's crust. It is transported mainly by water, although other natural and anthropogenic sources of exposure to arsenic including burning of arsenic-rich coal, mining, and smelter activities are of increasing concern. A wealth of epidemiologic studies have confirmed the carcinogenicity of inhaled and ingested arsenic, but the pathological characteristics of arsenic-induced cancers have never been examined extensively. Moreover, recent studies appear also to suggest that the health effects of arsenic are systemic and may involve multiple organs.[1-3] In nearly all cases where internal cancers are attributed to arsenic exposure, there has been cutaneous evidence of arsenic adverse effects in the form of arsenical keratosis, hyperpigmentation, and multiple cutaneous malignancies.[4] The aim of this short communication is to provide an overview of arsenic health effects, and to discuss with examples, our recent studies on the environmental pathology of arsenic poisoning including a histopathological description of arsenic-induced lesions. The data were derived from the ***International Tissue and Tumor Repository on Chronic Arsenosis***.[5,*]

II. Arsenic Poisoning: Adverse Health Effects

Skin. Epidemiological and clinical studies reported in the medical literature have confirmed the role of arsenic in the induction of cancers of the skin. Arsenic-induced skin lesions may include keratosis, squamous cell carcinoma and basal cell carcinoma. *Arsenical keratosis* in its fully developed form is a well established clinical syndrome, characterized by several specific pathological features, including hyperkeratosis, parakeratosis, arsenical pigmentation, and squamous cell carcinoma *in situ* (indistinguishable from Bowen's disease). Within the spectrum of keratotic lesion, arsenical keratosis may be differentiated from the more commonly diagnosed actinic keratosis by the absence of epidermal atrophy and basophilic degeneration of the upper dermis. All arsenical skin changes, including keratoses, tend to occur in non-exposed sites with an absence of dermal solar elastosis noted histologically. The lesions are normally most pronounced on the feet and hands, although they can occur on the trunk and other areas of the extremities.

Squamous cell carcinoma *in situ* is the most common form of skin cancer induced by arsenic, which may develop from two to 20 years after exposure. Bowen's Disease is an intraepidermal squamous cell carcinoma, referred to as squamous cell carcinoma *in situ*. It is considered a precancerous dermatosis, in the same group as leukoplakia, senile keratosis, and xeroderma pigmentosum. Histologically, Bowen's Disease presents as intraepithelial atypism, with marked variation in cell and nuclear size and shape. Multinucleated giant cells, and numerous mitotic figures are observed throughout all levels of the epidermis.

Arsenic-induced skin lesions assume protean forms. Besides keratotic lesions and skin cancers, pigmentation disorders represent another characteristic manifestation of arsenic exposure. The pigmentation may be present as hyper- or hypopigmentation. Hyperpigmentation is reported to be one of the most common skin changes seen in people chronically exposed to arsenic. It most often occurs in the trunk, but may be more accentuated in areas that are more heavily pigmented such as the groin and areola. Histologic examination reveals increased melanin pigment in melanocytes in the basal cell of the epidermis extending up to the granular cell layer. Signs of arsenic pigmentation may herald the later development of skin cancer. In one study of patients showing signs of arsenical pigmentation, nearly 90% developed skin cancer. Hypopigmentation occurs as well and may show a characteristic "rain drop" pattern.

Internal Lesions. In addition to skin lesions, including skin cancer, epidemiological studies have provided suggestive evidence linking arsenic exposure to various internal cancers, including angiosarcoma of the liver (see Figure 1), lung cancer, and bladder cancer. In the majority of cases in which the internal cancer is ascribed to arsenic exposure, some dermatological hallmark of arsenic poisoning is identified.[1] Gastrointestinal manifestations have also been reported due to chronic arsenic exposure and includes noncirrhotic portal hypertension (NCPH),[6] hepatic or splenic enlargement, hepatocellular carcinoma (see Figure 2),[5] and liver angiosarcoma.[7] NCPH is a rare, but relatively specific effect that may occur after years of arsenic ingestion at concentrations of 0.01 mg/kg/d. Recent case reports indicate a possible relationship between arsenic exposure and the occurrence of hepatocellular carcinoma; however, epidemiologic studies have not as yet confirmed this association. The increased incidence of hepatocellular carcinoma in arsenic-exposed endemic areas of Taiwan may have an arsenic etiology in addition to a viral causation. The association between arsenic exposure and angiosarcomas of the liver has also been reported. However, most of the published literature has consisted of case reports rather than population-based epidemiological studies.

Figures 1 and 2 present microscopic views of an angiosarcoma and hepatocellular carcinoma, respectively (Reference 5. Centeno JA, et al. *Arsenic-Induced Lesions, 2000*).

Non-Cancer Effects of Chronic Arsenic Poisoning. In addition to internal cancers, recent published studies have suggested an association between arsenic exposure and an increased risk for a variety of non-cancer effects. These include peripheral vascular disease, cardiovascular disease, diabetes, neurological effects, chronic lung diseases (shortness of breath and chest signs), diminished hearing, and cerebrovascular disease.[1-3, 8-10] It is quite apparent that the hazardous effects of arsenic are multi-organ related with extensive system pathology.

Reproductive effects of arsenic in humans has not been extensively investigated. Evidence from both animal and human studies suggests reproductive toxicity from arsenic, but data in humans is still sparse, and the results from laboratory experiments in animals are not conclusive. The evidence from a few human studies suggests that arsenic exposure may increase the incidence of pre-clampsia in pregnant women, decrease birth weight of newborn infants and increase in the risk of malformations and stillbirths, as well as that of spontaneous abortions.[11,12] Although recent laboratory studies suggest an increase

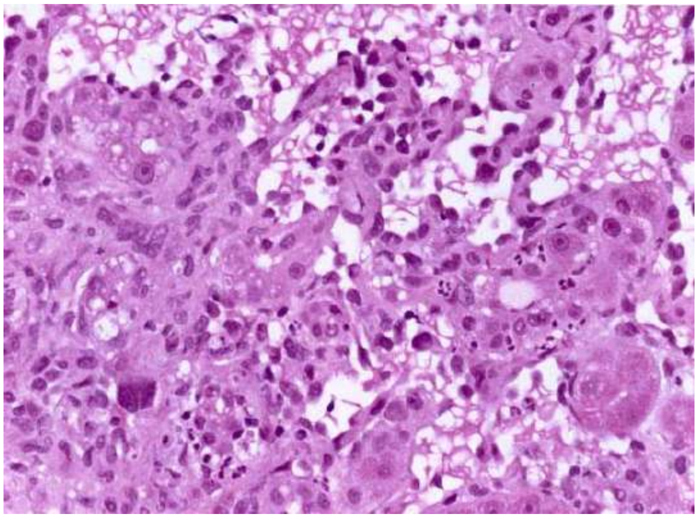

Figure 1. Angiosarcoma of the liver in 15-year-old arsenic exposed patient. The sinusoidal spaces are lined by malignant endothelial cells[5].

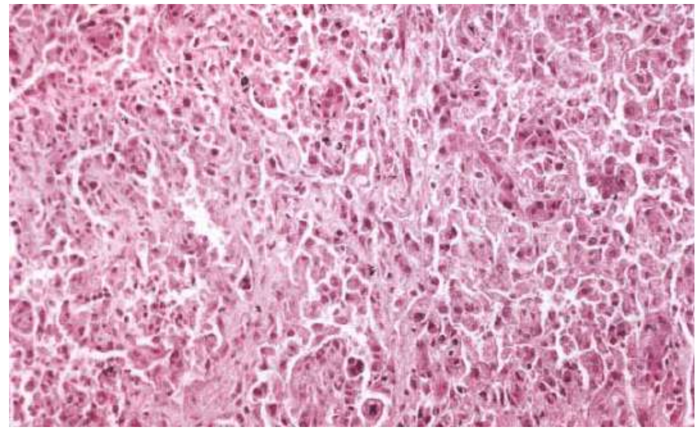

Figure 2. Hepatocellular carcinoma. The nuclei are irregular, hyperchromatic, and occasionally multinucleated[5].

in malformations and stillbirths in animals,[13,14] the effects of arsenic from drinking water in human reproduction have not been adequately studied. In order to assess the potential effects of arsenic in human reproduction, a properly designed epidemiological study in a large enough population is necessary.

In conclusion, the evidence for a casual relationship between cancers of the skin and arsenic exposure is strong and indisputable. Arsenic-induced skin cancers are predictable from exposure biomarkers of the skin, including hyperkeratosis, and hyper- or hypopigmentation. Cancers of the internal organs do not have such distinct exposure biomarkers and thus their association with a particular etiologic agent cannot be established with the same degree of confidence. Nevertheless, chronic arsenic exposure represents a significant risk factor for future development of liver cancer.

*Part of this work has been published in *"Arsenic-Induced Lesions" (April 2000), Armed Forces Institute of Pathology, ISBN:1-881041-68-9.*

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ITTRCA: THE INTERNATIONAL TISSUE AND TUMOR REPOSITORY FOR CHRONIC ARSENIASIS AT THE ARMED FORCES INSTITUTE OF PATHOLOGY

The public health concern for environmental exposure to arsenic has been widely recognized for decades. However, recent human activities have resulted in even greater arsenic exposures and the potential increase for chronic arsenic poisoning on a worldwide basis. This is especially the case in China, Taiwan, Thailand, Mexico, Chile, India, and Bangladesh. The sources of arsenic exposure vary from burning arsenic rich coal (China)[1] and mining activities (Malaysia, Japan) to the ingestion of arsenic contaminated drinking water (Taiwan, Inner Mongolia, China)[2]. The groundwater arsenic contamination in Bangladesh and the West Bengal Delta of India has received the greatest international attention due to the large number of people exposed and the high prevalence of arsenic-induced diseases[3]. Recent estimates suggest that in West Bengal as many as 20-30 million people are at risk from drinking arsenic-contaminated water obtained from thousands of tube wells that appear to be contaminated with naturally occurring arsenic.

Although the health effects associated with chronic arsenic exposure have been reasonably well characterized in those areas around the world with high arsenic levels in their drinking water, the association of adverse health effects with arsenic exposure in the United States is less clear. This is primarily due to the lower exposure levels in the great majority of U.S. drinking water supplies and the lack of research studies that look for health effects in arsenic exposed persons.

Cancer is a well-established arsenic related disease, although the cancer risk at low level exposure is unclear. Equally unclear is whether low-level arsenic exposures may play a role in the incidence in non-cancer health problems in the United States such as immune suppression and cardiovascular disease. This uncertainty in dose effects at low levels has resulted in hotly debated differences in opinion as to the need for stricter government regulation of arsenic in drinking water. Recently, the National Research Council studied the issue and determined that the current drinking water standard for arsenic is too high and recommended that it be lowered[4]. The U.S. Environmental Protection Agency (U.S. EPA), in fact, has proposed lowering the allowable drinking water standard from 50 mg/L to 10 mg/L. The drinking water industry, however, opposes changing the standard on the basis that more information is needed as to how arsenic causes cancer and other health effects, and whether these mechanisms operating at high dose levels also operate at low levels as well.

It is true that the mechanisms by which arsenic may induce adverse health effects are largely unknown. There are two major reasons for this. One is that the sophisticated molecular probes needed to study cellular and biochemical mechanisms have only recently become available, whereas most of the toxicity studies with arsenic were conducted many years before their availability. A second, equally important reason is that properly fixed human tissues from arsenic exposed persons are not available for such sophisticated research studies. The dilemma we face is that now we have the research tools (with even more sophisticated methods on the horizon), but we do not have the human tissues to study.

The Armed Forces Institute of Pathology (AFIP) is participating in an international research effort aimed at the development of an International Tissue and Tumor Repository for Chronic Arseniasis in Humans (ITTRCA). This effort is supported by four other federal agencies, including the U.S. EPA, the National Cancer Institute, the National Institute of Environmental Health Sciences, and the U.S. Geological Survey. The main objective of the ITTRCA is to obtain and archive tissues from persons known to or suspected of having been exposed to arsenic (environmental or occupational) and exhibiting adverse health effects. A component of this repository is to provide a mechanism by which the underlying pathology and morphology of arsenic-induced lesions can be described[5]. The major thrust of the ITTRCA is to facilitate the formulation of a standardized system of nomenclature for the study of skin lesions and other arsenic-induced changes in tissues, to foster the use of archival materials for the development of international collaborative projects on arsenic health effects, to facilitate the use and accessibility of archival materials associated with arsenic exposure, and to develop interlaboratory trials for the analysis and speciation of arsenic in biological tissues. Another unique component of the ITTRCA is the link to a repository of sources (coal, ores, soil, water) for arsenic exposures organized and maintained by the U.S. Geological Survey.

We request that pathologists, clinicians, epidemiologists, toxicologists and public health professionals in the United States and throughout the world participate in this exciting international project. Please contact us for further information about the ITTRCA and the methods for collection and shipment of tissues.

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MEDICAL GEOLOGY RESEARCH IN THE SLOVAK REPUBLIC

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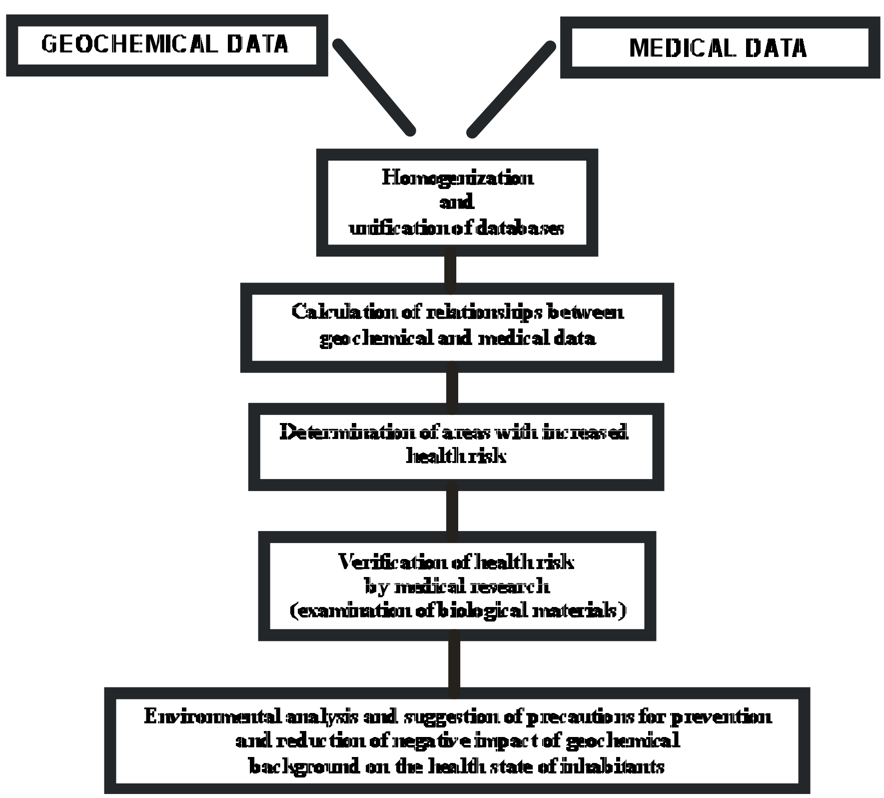
Recently to a greater extent, in Slovakia as well as in many other countries, issues of Medical Geology have being solved in the scope of geological works financed from the state budget. A pilot project of these geological works, which has been solved since 1999, is the project of the Geological Survey of the Slovak Republic – *The evaluation of potential influence of geochemical environment on the health state of population in the region of the Spišsko-Gemerské Rudohorie Mts.* The essential aim of the project is to elaborate and to verify methodical principles of evaluation of the influence of either excess or deficiency of chemical elements within geological environment on the health state of the population in one of the most contaminated regions (covering 1 400 km^2) of the Slovak Republic. Methodological ways of interconnections of geochemical and medical data and their further mutual assessment have being developed, aiming at the final analysis of environmental and medical risks of the area studied. The scheme of work is depicted in Figure 1.

Geochemical data represent national geochemical databases, acquired in the frame of *Geochemical Atlases Programme,* which have been completed with new samples and analyses. The health state of inhabitants of the Slovak Republic is monitored and assessed within 2 873 health-territorial units (HTU), from which 72 represent towns (≥10 000 inhabitants) and 2 801 countryside municipalities (further subdi-

Fig. 1 Scheme of interconnection and evaluation of geochemical and medical data



Element	Health Indicator	R	α	Significance
2 801 HTU – countryside population				
As	*PYLL*	0.049	0.008	++
	$CHLBW_{2500}$	0.063	0.000	+++
	MR_{MT}	0.040	0.031	+
	MR_{MI}	0.063	0.000	+++
Cr	*PYLL*	-0.023	0.205	
	$CHLBW_{2500}$	0.008	0.653	
	MR_{MT}	0.037	0.049	+
	MR_{MI}	-0.046	0.013	+
82 HTU – of the Spišsko-Gemerské Rudohorie Mts.				
As	*PPDP*	0.472	0.000	+++
	$\mathrm{MR_{MTL}}$	0.335	0.002	++
	PYLL	0.284	0.009	++
	$\mathrm{CHLBW_{2500}}$	0.090	0.419	
Bi	*PPDP*	0.454	0.000	+++
	MR_{MTL}	0.148	0.182	
	PYLL	0.198	0.074	
	$\mathrm{CHLBW_{2500}}$	-0.020	0.799	

Table. 1 Relationship between chemical elements contents in stream sediments and the indicators of the health state of population

Note: R – Spearman`s order correlation coefficient; α - confidence level, $\alpha \leq 0.001$– very high dependence **+++**, $\alpha \leq 0.01$– high dependence ++, $\alpha \leq 0.05$– verified dependence **+;** PYLL – directly standardised number of potential years of lost life; $\mathrm{CHLBW_{2500}}$ – percentage of children with low birth weight under 2 500 g of all new-borns; $\mathrm{MR_{MT}}$ – mortality rate due all type of malignant tumours for 100 000 inhabitants ; $\mathrm{MR_{MI}}$ – mortality rate due myocardial infarction for 100 000 inhabitants; PPDP – percentage of previous deaths of population below 65 years.; $\mathrm{MR_{MTL}}$ – mortality rate due to malignant tumours of lungs for 100 000 inhabitants

vided according their number of inhabitants into categories with: ≤500; 501–2 000; 2001–9 999 of inhabitants). As health indicators we use demographic and medical data, (for instance a mean age, reproduction health, total mortality, mortality rate due to malignant tumours, etc.). All medical and demographic data used in the given research represent average values of 5-years period, 1993–1997.

In the evaluation of the potential influence of the geochemical environment on the health state of inhabitants we start from the assumption that increased contents of contaminants in the environment negatively impact on the health state of inhabitants – they manifest themselves by elevation of values of negative indicators or by change of their interactions. We used Spearman`s correlation coefficient to analyse a statistical dependence between an element content within geochemical environment and indicator of the health state. At homogenisation and integration of databases geochemical data are put into the form of health indicators data. Health indicators represent one standardised indication (calculated for 100 000 inhabitants and averaged to a 5-years period) for each administrative district or HTU under evaluation. Geochemical data (as well as one standardised indication representing an average chemical element content in soils, waters, etc. within each administrative district evaluated) have been acquired using two-stage correction (inverse distance and moving median) of primary data. From the viewpoint of various phenomena and causes impacting the health state of population (besides geochemical environment it is influenced mainly by life style, genetic factors, level of health services), correlation coefficients between health state indicators and chemical elements contents in geochemical environment, are relatively low. Their values range around 0.1 (Table 1) in calculations from countrywide data (2 801 HTU for countryside population). In the pilot territory of the Spišsko-Gemerské Rudohorie Mts. (82 HTU), where we can expect an increased influence of the geochemical environment on the health state of population due to a relatively higher degree of contamination of the geological compound of the environment, correlation coefficients values range between 0.3–0.5. Preliminary results depicted in Table 1 show that significant correlation relations between distribution of some chemical elements and occurrence of individual indicators of health state have been statistically approved. In some cases the high level of significance of correlation relations together with published data on the effect of individual chemical elements on human health suggest, that the mentioned stochastic relations would be possibly considered in some cases as causal, e.g., distribution of As versus $CHLBW_{2500}$, PYLL, Cu versus PYLL, Sb versus $CHLBW_{2500}$ and others (for explanations see Table 1). It is being shown definitely that for the solution of this topic it is optimal to use parameters of the countryside inhabitants. It is also probable that chemical elements regarding their relation to individual health indicators might be divided as follows:

Causal elements – with confirmed and approved relation between health indicator and abundance or deficit of chemical elements in the geochemical environment.

Indicative elements – with high stochastic dependence based on the geochemical affinity to the causal elements.

A causality of a negative impact of increased chemical elements contents in the geochemical environment upon the health state of the population of the pilot territory of the Spišsko-Gemerské Rudohorie Mts. is being verified by mutual geochemical and medical research in one of the most contaminated municipalities of the region – the Zlatá Idka Village. The village is characteristic by increased geogenous Sb and As contents in all compounds of the geological environment. Recently, detailed geochemical works are focusing on monitoring of mobility and bioavailability of metals (5-step sequential extraction) of waters, soils and sediments toxicity (tests of acute and chronical toxicity) and at some elements, their valence is also being observed (Sb^{3-5}, As^{3-5}, Cr^{-6}). Parallelly, the State Health Institute of the Slovak Republic has monitored As and Sb contents in biological materials of people (blood, urine, hair and fingernails), as well as contents of the above elements in locally grown vegetables and fruits. In several cases, in biological materials of people and locally grown vegetables and fruits, biological limits for contents of toxic metals have been exceeded.

Recently, the solutions of the issues of the impact of contaminated geological environment on the state of health of the population have reached the stage of preliminary results. The designed methodological principles of joining geochemical data with medical and demographic indicators of the health state of inhabitants will be in-process in all geochemical environments (soils, sediments, ground-, surface waters) and in much wider range of chemical elements and indicators of the health state of inhabitants.

NEWSLETTER CONTRIBUTIONS

Please send contributions to Dr. David Elliott at delliott@cadvision.com.
Short articles, brief news items, conference notices, book reviews, welcome.

HUMAN EXPOSURE TO LEAD FROM A MINING AREA OF BRAZIL

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Introduction

The Ribeira river valley is located in the far south of the state of São Paulo and east side of the state of Paraná, Brazil (Figure 1). The region has been known, since the XVII century, for its deposits of gold, silver, and lead, and other valuable minerals. During the past 50 years the Ribeira river valley had been under the influence of a huge lead refinery and mine working by the side of the river. The plant and the mines stopped all activities at the end of 1995, after which the economic activity of the region is limited to agriculture. Figure 2 shows the hydrographic basin of the Ribeira river.

Environmental evaluations of heavy metals have been performed, aiming specifically at the assessment of the Ribeira river and its tributaries. However, no data on human exposure was produced so far.

It is well known that due to their chemical stability in soil, lead and other heavy metals can persist on the ground for many years, even after the closure of the main source of contamination (Small *et al.,* 1995; Chatterjee and Banerjee, 1999), becoming a permanent source of environmental lead exposure for humans living around.

The objective of this study was to assess the exposure of children and adults in an old mining area, with regard to lead, in the total blood, and the possible association with some chosen variables.

Materials and Methods

The studied population was 334 school children (aged between 7 and 14*)*, and 350 adults (aged between 15 and 70), from three Municipalities of Ribeira Valley (Brazil): Adrianopolis, Ribeira and Iporanga. The localities were chosen due to their proximity to the former lead mines. The refinery was located in a rural area of Adrianopolis. The control group was obtained from a municipality (Cerro Azul) that belongs to Ribeira valley, but was far from the lead refinery and mines.

From June 1999 to September 2000, blood samples were collect from the studied population in schools. Meetings were held at schools with parents and guardians, who agreed to let their children participate in the study and voluntarily signed a proper informed consent form authorizing the blood sample procedures. The same methodology was performed among the adults. The blood lead concentrations were determined by graphite furnace atomic absorption spectrophotometry with Zeeman background correction (model SIMAA 6000, Perkin Elmer).

In a range of 2 km from the refinery, 21 soil samples were collected 5-10cm deep at superficial ground for Pb analysis. Inductively Coupled Plasma/Atomic Emission Spectrometry (ICP/AES) was the method used for lead in soil.

Close to the refinery, a single sample of drinking water was collected from 10 randomly chosen residences. The samples were taken from tap water from public treated water systems, some from wells, and some directly from the river. Graphite furnace atomic absorption spectrophotometry, with Zeeman background correction, was used for lead determinations.

Results and Discussion

The Centers for Disease Control and Prevention from Altlanta, USA (CDC, 1991), associated adverse effects in children at blood lead levels as low as 10 µg/

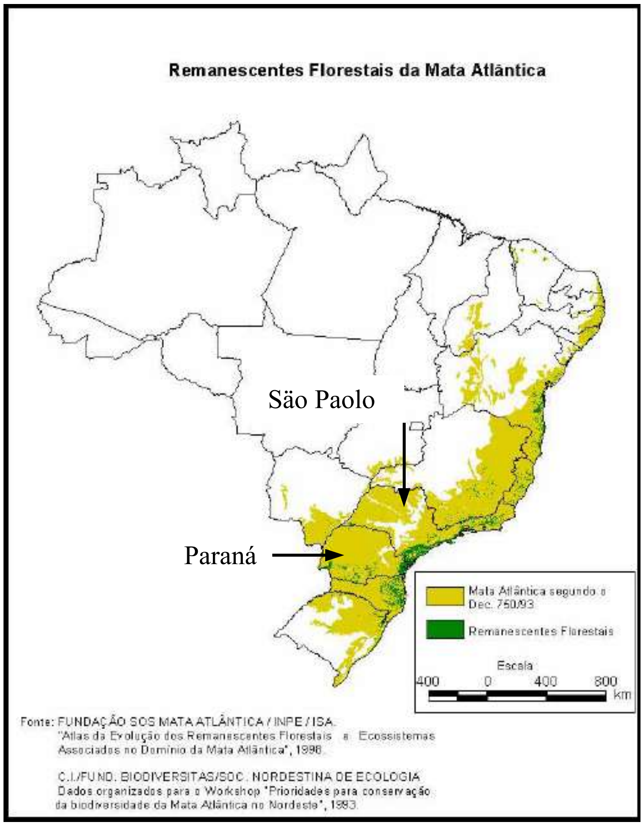

Figure 1. Brazil, showing the Atlantic Forest remains. Paraná is the third state from the south, Säo Paolo is the fourth. The study area is around the border of the two states.

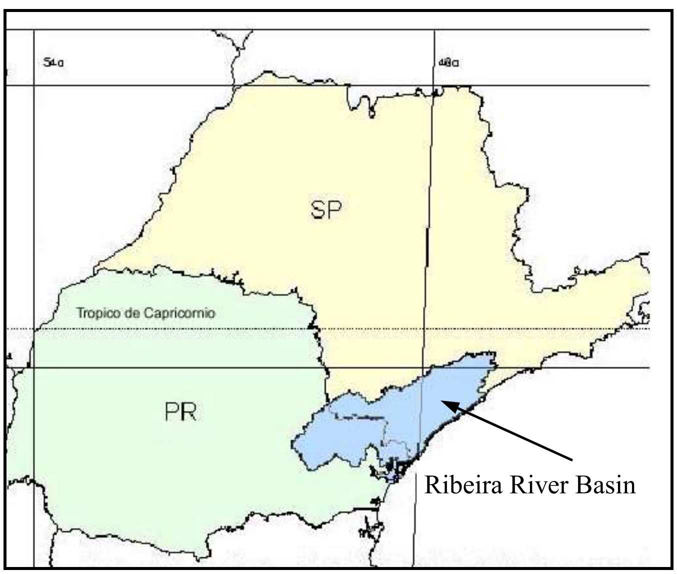

Figure 2. The Hydrographic Basin of the Ribeira River.

dL. The median of blood lead level in the area close to the lead refinery was 11.25 µg/dL with a range from 1.80 to 37.80 µg/dL. The percentages of children with blood lead levels greater than or equal to 10 µg/dL were 59.6 percent. In the other mining areas and control group the median was 4.40 µg/dL and 1.8 µg/dL, respectively. There were significant differences in median blood lead levels in all studied groups (Table 1). For adults, the median blood lead level in the area close to the refinery, far from the refinery, and control group were 8.80, 2.80, 1.80 µg/dL, respectively. Significant differences in medians were found in the three studied groups (Table 2).

Lead concentrations in tap water showed levels below quantification limits (equal to 0.001 mg/dL), and does not seem to be an important contribution to the total lead burden of the studied population. Analysis of lead obtained in the areas close to the refinery showed high levels on average (26.0 to 915.6 µg/g). Elhelu *et al.* (1995) showed that soil lead levels ranging from 50 to 150 ppm pose a significant risk to young children and pregnant mothers.

In this study, among the variables associated with the blood lead levels, the most important was the area of residence. The lead refinery was shut down at the end of 1995, approximately 3 1/2 years prior to the beginning of this study, and there were no remediation activities at the site since then. The high blood lead levels found in children living close to the refinery (around 2 km distant), seems to indicate that, despite the end of industrial activities in place, it is possible to have a residual contamination in the area.

In a logistic regression analysis, 3 of the variables studied were independently associated with high blood lead levels in children. For residential area (close to or far from lead refinery), the ODDS Ratio (OR) was equal to 10.38 (4.86 to 23.25 ; 95% CI). For the variable "former father's occupational lead exposure", the OR was 4.07 (1.82 to 9.24; 95% CI). For gender, OR was 2.60 (1.24 to 5.62, 95% CI). The other variables (age, former residence at the refinery

VARIABLE	n	Median[a]	Values[a]			Percentile[a]			p^b
			min.	-	max.	25th	-	75th	
RESIDENTIAL AREA									<0.0001
Exposed population: mining area near the lead refinery	94	11.25	1.80	-	37.80	6.60	-	14.00	
Exposed population: mining area far from the lead refinery	201	4.40	1.80	-	29.40	3.00	-	6.40	
Nonexposed population	39	1.80	1.80	-	8.20	1.80	-	1.80	

TABLE 1– Comparing blood lead levels among exposed and nonexposed children (n=334) aged 7-14 years old, Ribeira valley, Brazil

[a]µg/dL [b] Kruskal-Wallis test

VARIABLE	n	Median[a]	Values[a]			Percentile[a]			p^b
			min.	-	max.	25th	-	75th	
RESIDENTIAL AREA									<0.0001
Exposed population: mining area near from the lead refinery	101	8.80	1.80	-	48.70	4.60	-	14.90	
Exposed population: mining area far from the lead refinery	209	2.80	1.80	-	24.20	1.80	-	4.50	
Nonexposed population	40	1.80	1.80	-	6.90	1.80	-	1.90	

TABLE 2– – Comparing blood lead levels among exposed and non-exposed adults (n=350) aged 15-70 years old, Ribeira valley, Brazil

[a]µg/dL [b]Kruskal-Wallis test

village, daily consumption of milk, of garden vegetables and fruit from home backyards) did not show any association with blood lead levels (Paoliello et al, 2002).

Residential area close to the lead refinery, male gender, age, smoking habits, and alcohol consumption were positively associated with blood lead level in adults, although the variables were not adjusted

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EDITOR'S COMMENTS AND GUIDELINES FOR AUTHORS

We would like to publish the newsletter twice a year, but can only do so if we have enough articles, so please keep sending them. Remember that this is a Newsletter, not a refereed journal, and also that we are limited to 16—20 pages.

Articles should:

- Typically be a maximum of two pages of Times Roman 12 point text and/or figures and tables.
- May be edited to fit them into the space available in the Newsletter or for clarity.
- Should not have been published previously, although summaries of previously published articles may be acceptable — please let me know if this is the case.
- Lists of references should be kept short, and longer lists should be obtainable from the author, preferably by being posted on the net.
- Preferably in Word 2000 format, although I can I can handle a number of other formats.
- I can handle a number of graphics formats, although I do have problems with some of them. Word graphics format seems to give the least problem.

In addition to full articles, I am interested in receiving short news items: book reviews, accounts of conferences & workshops, etc., upcoming meetings, and, **especially**, interesting short pieces of news and information.

Dr. David C. Elliott, Newsletter Editor

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