Third Informal Consultation on Long Term Studies (LTS) on Environmental Threats to the Health of Children in Developing Countries and Industrialized Countries.

Cuernavaca, Mexico.
20-24 November 2004.
Report

1. The Third Informal Consultation on Long Term Children Studies (LTCS) on Environmental Threats to the Health of Children in Developing Countries, convened by the World Health Organization (WHO) was hosted by the Ministry of Health of Mexico in Cuernavaca, Mexico, 20-24 November 2004. The meeting was organized by WHO with the support of the United Sates Environmental Protection Agency (USEPA) jointly with the National Institute for Child Health and Development (NICHD) of the National Institutes of Health (NIH) and the Centers for Disease Control (CDC) in the USA. The local organizer was the Directorate of Health Planning and Development, at the Ministry of Health in Mexico. The meeting took place at the Hosteria "Las Quintas" in Cuernavaca, Mexico, that offered good facilities for a "retreat-type" meeting, allowing fruitful plenary sessions and working groups as well as informal discussions among participants. The meeting was covered with WHO funds (provided by USEPA) and CDC and NICHD/NIH funding, plus the contribution of the local organizers.

2. Participants from Australia, China India, Egypt, Guatemala, Mexico, South Africa, Uruguay and USA already conducting or embarking on LTS were present. The group included representatives of the Ministry of Health (Mexico), the Pediatric Hospital of Mexico - F. Lopez, the National Institute of Public Health and the National Institute of Ecology in Mexico, and representatives from the International Pediatric Association (IPA), CDC, NICHD/NIH, USEPA, WHO/HQ and PAHO. (See participants list, Annex A, and agenda of the consultation, Annex B).

3. The overall purpose of the consultation was to follow up developments on the planning and implementation of long-term (longitudinal) cohort children studies (LTCS) on environmental health since the Glion (Oct. 2003) and PAHO (Aug. 2004) consultations, and prepare a core set of hypotheses for inclusion in LTCS. Specific objectives of the consultation were:
   a) To review activities undertaken since the PAHO meeting (2nd Consultation)
   b) For participants to provide a brief report on new activities, developments and progress since the 2nd Consultation held in PAHO (August 2004).
   c) For the participants at the Global Forum 8 to report on the outcome of the two Panel Sessions organized on LTCS and the Millennium Development Goals.
   d) To develop and discuss hypotheses in selected areas: pregnancy outcome, growth and development, respiratory disease, neurodevelopment and reproduction.
   e) To review and discuss the latest versions of the position paper on international long term studies to study child health and the environment

f) To review the draft brochure and video on the need for long term studies of child health and the environment
g) To discuss how to incorporate child environmental health issues into existing studies
h) To plan the next steps

4. Dr Carlos Santos-Burgoa (Mexico), Director General de Planeación y Desarrollo en Salud, Subsecretaría de Innovación y Calidad, Secretaría de Salud, Mexico, host of the event, opened the first session of the meeting (Saturday, 20 November) welcoming everyone to Cuernavaca and explaining the purpose of this event. He accepted to Chair of the Consultation in association with Dr. Adolfo Correa (CDC). Dr Thea De Wet (South Africa) acted as Rapporteur, with the assistance of Mr. E. Mazursky (Intern at USEPA).

.

5. Dr Jenny Pronczuk (WHO/HQ) thanked Dr. Carlos Santos-Burgoa and his team from the Mexican Ministry of Health, for hosting and organizing the meeting. She conveyed the apologies of colleagues who were unable to participate: Drs. C. Choprapawan (Thailand), N. Ribas (Spain), D. Grande (Brazil) and P. Landrigan (USA). She also transmitted the invitation of Dr. Choprapawn to organize sessions on the international initiative on LTCS at the World Epidemiology Congress that will take place in Bangkok, Thailand, from 21 to 25 August 2005. Dr.s T. De Wet and A. Correa mentioned the coming international environmental epidemiology event in South Africa, that may provide a good opportunity for presenting the initiative. Dr. R. Etzel, representing the International pediatric Association (IPA) thanked the organizers for the invitation, as she sees this initiative has a larger potential for success if pediatricians in different countries are aware of the importance of these studies and able to contribute.

6. DR. pronczuk gave an overview on the technical activities developed by WHO was given: (i) preparing national profiles to assess the state of children and the environment; (ii) promoting collaborative research between countries; and (iii) developing a training package for health care providers and implementing capacity-building activities. In addition, WHO is promoting the use of the Pediatric Environmental History, the setting up of Pediatric Environmental Health Centres and is also providing technical assistance to Member States.

7. Dr Danuta Krotoski (NICHD/NIH) briefed the meeting on the outcome of the Global Forum for Health Research (GF8) that was held in Mexico City from 16-20 November 2004 (http://www.globalforumhealth.org). Some of the important issues highlighted by presentations at the meeting included the need for holistic information on the health status of children and the need to communicate and cooperate with the communities on children's health issues. Two posters were presented: one on LTCS and how they may contribute to achieving the MDGs (prepared by J. Pronczuk and D. Krotoski on behalf of the Working Group on LTCS, that provided very useful comments), and another one on Persisten Organic Pollutants and Endocrine Dirsuption (prepared by J. Pronczuk and T.

Damstra from WHO). Two sesions were organized on Children's Health and the Environment. During the first session (Wednesday 17 November), chaired by Drs. J. Pronczuk and C. Santos Burgoa, participants from Guatemala (Dr. Ruben Grajeda, INCAM), Thailand (Dr. J. Pronczuk on behalf of Dr. Chanpen Choprapawan), D. Krotoski (National Children's Study) presented their experience on child health and environment studies. The presentations included a short video prepared by Dr. Thea De Wet on child health and the environment. Six papers were presented during the second session (Friday 19 November), chaired by Dr D. Krotoski and Prof. P. Sly (Australia, on behalf of Dr. T. Damstra). On the final day of the GF8 (Saturday 20 November) a number of speakers stressed in the plenary the need to focus on children's health—not on research about determinants of adverse health outcomes (as they are well-known), but in other areas of importance, such as useful interventions.

8. Dr Adolfo Correa (CDC) presented background information on the importance of promoting collaboration in the development and implementation of longitudinal studies on the impact of the environment on children's health and development in both industrialized and developing countries. He pointed out that there are a number of child cohorts currently in operation or planned that should consider incorporating environmental health factors and pooling information on child health and the environment in the future. In order to pool data effectively a set of common hypotheses is required. The advantages of collaboration between countries include the potential to: (a) make use of existing expertise and instruments; (b) minimize duplication of efforts; (c) promote capacity building; (d) use standard methods for assessments of exposures and outcomes; (e) increased comparability across studies; and (f) allow for pooling of data to examine rare outcomes. Dr. Correa highlighted the priority exposures and outcomes: pregnancy outcomes, birth defects, neuro-behavioral, development and cognitive functioning, developmental respiratory diseases, asthma, acute respiratory diseases, physical growth, endocrine disruptors, sexual development and reproductive behavior, plus the specific causes of morbidity and mortality.

9. Dr Correa stressed that "harmonized" hypotheses would be very useful to collect information on specific outcomes, such as: (a) pregnancy (b) neurodevelopment (c) respiratory diseases (d) growth and physical development, as these are considered of the interest of both developing and industrialized countries. Four different work groups were tasked to look at the risk factors and outcome measures and then to: (a) identify gaps; (b) prioritize issues; (c) develop draft hypotheses; (d) identify potential measures of outcomes and exposures in relation to life stages (e) identify potential data gaps; and (f) propose pilot studies that would be needed. This was followed by a lively discussion.

10. Prof Peter Sly (Australia) pointed out that the development of the immune system should be considered too, as it underlies many of the problems relating to child health and the environment. Susceptibility increases because of immune problems i.e. children whose immune system matures slower are more at risk.

11. Dr Santos-Burgoa (Mexico) suggested a number of questions that need to be considered. such as the importance of looking at the interaction of a number of factors which are significant in developing countries: nutrition, access to financial resources, ethical issues, and the challenge to anticipate changes in the future of a longitudinal project, for example, new technology and the potential to find new bio-markers. The question posed was whether current hypotheses would be sufficient. It was remarked that we need to address current issues with our eyes on the future, keeping the sampling and storage challenges in mind.

12. Dr Correa pointed out that we need hypotheses to help us frame the study, that we should keep policy implications in mind from the outset of studies, and that we should be able to write up early outcomes e.g. pregnancy outcomes. Dr Sly concluded the discussion by pointing out that hypotheses and outcomes should be proposed for each life stage, and that careful consideration should be given to the collection of appropriate samples for each stage.

13. Dr Carolyn Salafia (USA) gave a stimulating presentation on the potential to develop novel methods of placental measures that can help clarify how fetal exposures may lead to poor neuro-developmental outcome. The placenta is an ideal tool for identifying the 'fetal origin of disease'. The technology for measuring, photographing and sampling placentas should be taken into consideration in LTS.

14. Dr Sly presented the hypotheses on the environmental impact on the development of asthma and respiratory diseases in children, that were developed in the context of a collaborative research study undertaken between paediatricians in India and Australia. Ms. F. Flack (Australia) responded to a number of questions raised by the audience.

15. Dr Santosh Bhargava (India) gave a presentation on Outcome and Survival of Birth Cohort in Delhi (1969-2004). The data from the study had raised several issues and concerns about existing beliefs over what a "healthy" child is. India is currently undergoing a nutritional transition. While under nutrition remains a problem, over weight and obesity are emerging as new challenges. Dietary changes are expected to lead to an epidemic of adult diseases, including diabetes, hypertension, dyslipidemia, and cardiovascular disease. Dr Bhargava suggested studying linear physical growth of children and looking at those children with low ponderal index or weight at birth and the upward trajectory of their body mass index (BMI) relative to the whole study population through childhood and adolescence. Intervention studies could be done and the impact of that measured on the development of diabetes and cardiovascular disease.

16. Prof Thea de Wet (S. Africa) presented the final draft of the video *Child Health and the Environment: A Research Priority.* The video was developed to present

in a visual manner the importance of long term studies of children's health and the environment around the world. Copies of this draft were made available to participants for personal use. The main audience for the video are donors, decision-makers and potential project participants. Copies will be distributed after final approval from the WHO (Dr Pronczuk to pursue).

17. Dr Terry Dwyer (Australia), the new director of the Murdoch Children's Research Institute joined the working group for the Sunday 21 Nov. session. His presentation stressed the importance of global collaboration in terms of the opportunities for data pooling and the sharing of knowledge and experience. Combining large data sets from children's cohort studies involving up to 500,000 subjects is of particular importance when studying rare outcomes such as childhood cancer and type-1 diabetes. A number of large child cohort studies (active or in planning) have indicated an interest in participating, for example, the US National Children's Study (100 000), the Norwegian Mother and Child Cohort Study (100 000), the Danish National Birth Cohort (100 000), ALSPAC in Bristol (14 000), and the Tasmanian Infant Health Survey (10 000). Completed studies that could possibly be included are the Jerusalem Perinatal Cohort Study (92 000), the NCPP (50 000), the Child Health and Development Studies (20 530), Northern Finland birth cohorts (9479 & 12231), and the Greek national perinatal survey (11 000). A working group is being set up to develop collaboration in this area. It involves the National Cancer Institute (NCI), the National Children's Study (NCS) of the USA and key cohort investigators. This group will look more carefully at the comparability of exposure data, encourage necessary collaborative input and recruit new studies to the collaboration scheme. (Dr. T. Damstra from WHO will be informed about this initiative).

18. Four working groups were organized on Monday 22 to discuss and prepare draft hypotheses on the:
    a) Impact of environmental factors on children's growth and development (Participants: Song LI, J. Gabriel Gay, R. Kamal, Santosh Bhargava)
    b) Impact of environmental factors on children's neurodevelopment and cognitive behavior. (Participants: D. Krotoski, A. Carroll, T. De Wet, A. Cebrian, L. Rivero)
    c) Impact of environmental factors on developmental respiratory diseases, asthma, and acute respiratory diseases. (Participants: R. Etzel, J. Pronczuk, R. Rosa, L. Rojas, E. Mazursky, J.I. Santos Preciado)
    d) Impact of environmental factors on pregnancy outcomes (including the consideration of birth defects and cancer) (Participants: C. Salafia, A. Correa, S. Flores, E. Mazursky, R. Grajeda, L. Lopez Carrillo).

19. On Tuesday 23 November the hypotheses were presented and discussed in plenary session. Some of the issues raised included:

- Under children's growth and development the importance to stress prematurity due to environmental internal and external factors and potential outcomes such as retinopathy, hearing defects and chronic lung disease.

- The environmental factors on children's neurodevelopment and cognitive behavior were considered in detail and the working group stressed the importance and complexity of measurements, definitions and ethical issues.
- The group dealing with developmental respiratory diseases, asthma, and acute respiratory diseases decided to include also otitis media, infant apnea and tuberculosis in their considerations.
- The environmental factors on pregnancy outcomes included the consideration of internal environmental factors (in utero) and also external factors.

After discussions on each hypothesis it was agreed that the next steps is to complete, assemble, edit and circulate the hypotheses for comments among the participants. Further work will have to be done through tele-conferencing and possibly in a face-to-face small meeting around March or May 2005 (Mr. E. Mazursky will work on this with Drs. A. Correa and D. Krotoski). The group suggested a list of experts and special advisors from different parts of the industrialized and developing world that could be approached for advice on respiratory outcomes, neurobehavioral issues, growth and nutrition, pregnancy outcomes.

20. A plan of action for 2005 was discussed and agreed. Advantage will be taken of a number of events that are taking place in 2005 and that may offer an opportunity for presenting the international LTCS initiative and discussing the hypotheses: World Congress of Epidemiology in Bangkok (August 2005) and International Congress of Environmental Epidemiology (September 2005), as well as other meetings taking place in USA (Washington DC) and potentially in Argentina.

Plan of Action for 2005		
Date	**Activity**	**Who? When?**
Nov 2004	Finalizing rough hypotheses	Cuernavaca WGs
Jan 05	Completion and initial editing	Correa, Mazursky, Krotoski
Feb 05	Review and completion by WGs	E-mail/Teleconferencing
Mar 05	Expert review	Experts in specific areas
April 05	Pooling meeting (big studies)	Washington DC
May 05	Peer review and approval	Small WG (Washington DC)
Aug 05	Conference	Small WG (Bangkok)
Sept 05	Conference	WG (Johannesburg)
Nov 05	Publication of hypotheses	
Nov 05	Meeting in Latin America?	

21. A number of key issue remain to be addressed and discussed, such as:
(a) measurements (including equipment, laboratory support, questionnaires, instruments to measure development outcomes, and psychosocial well-being)
(b) terminology and definitions (agreement on the terminology and glossry, with definitions on specific diseases, syndromes and parameters)
(c) study protocols
(d) informatics considerations (including questionnaire design and data management)

(e) ethical issues
(f) biostastical issues.

22. Dr Pronczuk adjourned the consultation, thanking Dr Carlos Santos-Burgoa for hosting the consultation in Mexico and the Mexican government for supporting the organization of the meeting. Special thanks were given to Dr. Lilia Rivero Rodriguez and Ms. Adrenalina Cebrián Gómez, and other members of the organizing team for providing excellent support to the meeting. Drs A. Correa and D. Krotoski took the opportunity to thank the organizers and stressed that this 3rd. Consultation on LTCS offered excellent results, and the work ahead is both challenging and promising.