



CITTÀ DI CARPI



DA VENIAM SCRIPTIS QUORUM NON GLORIA NOBIS
CAUSA, SED UTILITAS OFFICIUMQUE FUT

COLLEGIUM RAMAZZINI ANNUAL RAMAZZINI DAYS 2011

**28-30 OCTOBER 2011
CARPI, ITALY**

**SCHEDULE OF EVENTS
SCIENTIFIC PROGRAM
ABSTRACTS BY SESSION**

RAMAZZINI DAYS 2011
28-30 October 2011

ORGANIZED BY:

Collegium Ramazzini
Comune di Carpi
Istituto Ramazzini

UNDER THE AUSPICES OF:

INAIL
Regione Emilia-Romagna
Provincia di Modena
Azienda USL di Modena
NYS Laborers Health and Safety Fund

CHAIRPERSONS:

Enrico Campedelli, Mayor of Carpi
Philip J. Landrigan, President of the Collegium Ramazzini

SCIENTIFIC COMMITTEE:

Melissa McDiarmid, USA, Chair
Carol Rice, USA, Chair
Philip J. Landrigan, USA
Morando Soffritti, Italy
Henry Anderson, USA
Fiorella Belpoggi, Italy
Nachman Brautbar, USA
Massimo Crespi, Italy
Philippe Grandjean, USA
James Melius, USA
Karel Van Damme, Belgium

ITALIAN ORGANIZING COMMITTEE:

Kathryn Knowles, Collegium Secretariat
Susanna Tassinari, Conference Co- Manager
Erica Tommasini, Conference Co- Manager
Diane Woodford, Carpi Secretariat

RAMAZZINI DAYS 2011
SUMMARY SCHEDULE OF EVENTS

FRIDAY, 28 OCTOBER 2011

- 12:45-15:00 Memorial Luncheon and Tour of “Casa Maltoni”
San Lazzaro di Savena, Bologna
- 16:00 Conference check-in
Lobby, Hotel Touring
- 17:00-19:00 Meeting of the Executive Council (closed session)
Hotel Touring
- 19:00 Welcome aperitivo
Breakfast area, Hotel Touring
- 20:00 Dinner
Ristorante B&B, Hotel Touring

SATURDAY, 29 OCTOBER 2011

- 8:45 Guided tour of Parma for spouses/guests
Meet at the Hotel Touring
- 9:00-12:15 **Council of Fellows** (Fellows and Emeritus members only)
Town Hall of Carpi
- 12:30-13:45 Participant lunch
Ristorante B&B, Hotel Touring
- 14:00-17:40 **Scientific Session I: Work Of The Fellows**
Sala delle Vedute Foyer, Palazzo dei Pio
- 17:45-18:45 Free time
- 19:00-20:00 **Presentation of the Ramazzini Award and Ramazzini Lecture**
Sala delle Vedute, Palazzo dei Pio
- 20:00 Dinner
Coaches depart directly from Palazzo dei Pio for Locanda Ristorante l'Anatra
- 23:00 Return to hotels

RAMAZZINI DAYS 2011
SUMMARY SCHEDULE OF EVENTS

SUNDAY, 30 OCTOBER 2011

- 9:00-9:45 **Presentation of the Irving J. Selikoff Award**
Sala delle Vedute, Palazzo dei Pio
- 9:45-10:00 **Presentation of the exhibit “Chernobyl 1986-2011” by Golem Photography**
Sala delle Vedute, Palazzo dei Pio
- 10:00-10:30 Coffee
- 10:30-12:30 **Scientific Session II:**
"Nuclear Power: Present Realities and Implications for the Future"
Sala delle Vedute, Palazzo dei Pio
- 12:30-13:00 Discussion and Conference Closing
- 13:15 Farewell lunch
Ristorante B&B, Hotel Touring
- 20:00 Optional no-host dinner for Sunday night guests
(please rsvp with conference organization)
Pizzeria Re Artù

RAMAZZINI DAYS 2011
SCIENTIFIC PROGRAM

SATURDAY, 23 OCTOBER 2010

- 8:45 Guided tour of Parma for spouses/guests
Meet at the Hotel Touring
- 9:00-12:15 Council of Fellows Statutory Session (Fellows and Emeritus members only)
Town Hall of Carpi
- 12:30-13:45 Participant lunch
Ristorante B&B, Hotel Touring

SCIENTIFIC SESSION I: WORK OF THE FELLOWS

Chairs: Melissa McDiarmid, USA and Carol Rice, USA

Sala delle Vedute Foyer, Palazzo dei Pio

14:00-15:15 **Oral Communications part I**

- 14:00-14:15 RISK ASSESSMENT FOR CARBON NANOTUBES
Maria Albin, Sweden
- 14:20-14:35 DEREGULATION OF MICRO-RNAS (MIR-21, MIR146A AND LET-7A) INDUCED BY
DMBA IN CBA/CA MICE
István Ember, Hungary
- 14:40-14:55 LONG TERM HEALTH EFFECTS OF HUMANS EXPOSED TO PCBS AND PCDFS
Yue Leon Guo, Taiwan
- 15:00-15:15 WHEN POLITICS AND EVIDENCE COLLIDE: CANADA'S "ROGUE NATION" POSITION
ON ASBESTOS
Colin L. Soskolne, Canada
- 15:20-16:00 **Attended Poster Session**
- PHYSICAL ACTIVITY AND CANCER: KNOWLEDGE AND PRACTICE AMONG
NATIONAL CANCER INSTITUTE EMPLOYEES, CAIRO UNIVERSITY
Wagida Anwar, Egypt
- SENTIERI PROJECT: MORTALITY STUDY OF RESIDENTS IN ITALIAN POLLUTED
SITES
Pietro Comba, Italy
- HYDRAULIC FRACTURING: BENEFITS AND COSTS
Chris De Rosa, USA
- ALTERATIONS IN MICRORNA EXPRESSIONS IN PRIMARY HUMAN CERVICAL
CANCER
Katalin Gocze, Hungary (Fellow: István Ember)
- EXPRESSION CORRELATIONS OF NF κ B SIGNALING AND MIR EXPRESSIONS IN
PRIMARY HUMAN HEAD AND NECK SQUAMOUS CELL CARCINOMAS
Katalin Gombos, Hungary (Fellow: István Ember)
- EPIDEMIOLOGICAL ANALYSIS AND GENOMIC EVALUATION OF ESOPHAGEAL
AND GASTRIC CANCERS IN NORTHWEST HUNGARY
Krisztina Juhasz, Hungary (Fellow: István Ember)
- IMMUNOGENOTOXICOLOGY – NEW COMBINED BIOMARKERS FOR EVALUATION
OF HEALTH RISK AFTER EXPOSURE TO IONIZING RADIATION
Aleksandra Fucic, Croatia
- SURVEILLANCE OF OCCUPATIONAL HAZARDS IN TAIWAN
Yue Leon Guo, Taiwan
- TOXICLARO- TOXICOLOGY IN THE CLASSROOM
Birger Heinzow, Germany

RAMAZZINI DAYS 2011
SCIENTIFIC PROGRAM

THE EFFECT OF CHILDHOOD LEAD EXPOSURE ON SCHOOL PERFORMANCE

Daniel Hryhorczuk, USA

OCCUPATIONAL HEALTH PHYSICIAN AND PSYCHIATRIC DISORDERS: FROM HEALTH SURVEILLANCE TO FITNESS FOR WORK

A. Isgrò, Italy (Fellow: Roberto Lucchini)

OCCUPATIONAL FATALITIES IN SWEDEN DUE TO CANCER, CARDIOVASCULAR AND RESPIRATORY DISEASES

Bengt Järholm, Sweden

AN EXPOSURE INDEX ESTIMATION FRAMEWORK FOR SEGMENTS AND PARTICIPANTS IN THE NATIONAL CHILDREN'S STUDY (NCS)

Paul J. Liroy, USA

OXIDATIVE/NITROSATIVE STRESS MARKERS MEASURED NON-INVASIVELY IN SUBJECTS WITH CHRONIC 2,3,7,8-TETRACHLORO-DIBENZO-P-DIOXIN INTOXICATION

Daniela Pelclova, Czech Republic

A SENTINEL CASE SERIES OF CANCER PATIENTS WITH OCCUPATIONAL EXPOSURES TO ELECTROMAGNETIC NON-IONIZING RADIATION WITH SHORT LATENT PERIODS

Elihu Richter, Israel

MONGOLIA: PARTNERSHIP FOR CAPACITY BUILDING IN ENVIRONMENTAL HEALTH TO MEET RAPID ECONOMIC DEVELOPMENT

Ellen Silbergeld, USA

THE PROTECTIVE EFFECT OF TAMOXIFEN ON MAMMARY CARCINOGENESIS WHEN ADMINISTERED TO YOUNG FEMALE SPRAGUE-DAWLEY RATS TREATED WITH ONE SHOT OF γ -RADIATION

Luciano Bua, Italy (Fellows: Fiorella Belpoggi and Morando Soffritti)

THE EFFICACY OF LEUPROLIDE IN PROTECTING FEMALE SPRAGUE-DAWLEY RATS TREATED WITH β -RADIATION FROM THE ONSET OF MAMMARY CANCERS

Michela Lauriola, Italy (Fellows: Fiorella Belpoggi and Morando Soffritti)

THE PROTECTIVE EFFECT OF TAMOXIFEN ON MAMMARY CARCINOGENESIS IN γ -IRRADIATED 56-OLD FEMALE SPRAGUE-DAWLEY RATS

Marco Manservigi, Italy (Fellows: Fiorella Belpoggi and Morando Soffritti)

THE LIFE SPAN STUDY ON THE CHRONIC EFFECTS OF WORLD TRADE CENTER DUST AFTER INTRATRACHEAL INSTILLATION OF TOTAL PARTICULATE MASS TO SPRAGUE-DAWLEY RATS: FIRST OBSERVATIONS

Laura Falcioni, Italy (Fellows: Fiorella Belpoggi and Morando Soffritti)

IMMUNOHISTOCHEMICAL CHARACTERIZATION OF SPONTANEOUS LYMPHOMAS IN SPRAGUE-DAWLEY RATS: COMPARISON WITH THE HUMAN COUNTERPART

Daniela Chiozzotto, Italy (Fellows: Fiorella Belpoggi and Morando Soffritti)

SUCRALOSE (SPLENDA®) ADMINISTERED WITH FEED FROM PRENATAL LIFE THROUGH LIFE-SPAN, INDUCE LEUKAEMIA IN SWISS MICE

Morando Soffritti and **Fiorella Belpoggi**, Italy

RAMAZZINI DAYS 2011
SCIENTIFIC PROGRAM

- 16:00-17:35 **Oral Communications part II**
- 16:00-16:15 IARC MONOGRAPHS ON THE EVALUATION OF CARCINOGENIC RISKS TO HUMANS, VOL 102. NON-IONIZING RADIATION, PART II: RADIOFREQUENCY ELECTROMAGNETIC FIELDS
Kurt Straif, France
- 16:20-16:45 THE OUTBREAK OF ASBESTOS-CAUSED DISEASES IN CASALE MONFERRATO, ITALY
Benedetto Terracini, Italy
- 16:50-17:05 BERYLLIUM SENSITIZATION IN THE BUILDING TRADES NATIONAL MEDICAL SCREENING PROGRAM
Laura S. Welch, USA
- 17:10-17:35 OCCUPATIONAL HEALTH IN THE SOUTH AND SOUTH EAST ASIA REGION
Hemantha Wickramatillake, Sri Lanka
- 17:45-18:45 Free time

Presentation of the Ramazzini Award and Ramazzini Lecture

Sala delle Vedute, Palazzo dei Pio

- 19:00 Special Work of the Fellows Presentation
A DEADLY ASBESTOS FAMILY SAGA
Piergiorgio Natali, Italy
- 19:20 Opening addresses
Enrico Campedelli, Mayor of Carpi
Philip Landrigan, President of the Collegium Ramazzini
- The 2011 Ramazzini Award will be conferred upon
Morris Greenberg, UK
for his seminal contribution to occupational medicine in the United Kingdom and his career-long dedication to the health, safety and well-being of workers.
- 2011 Ramazzini Lecture
“Concerning the Collegium's Founding Fathers and its future”
- 20:00 Social Dinner
Coaches depart directly from Palazzo dei Pio for Locanda Ristorante l'Anatra
- 23:00 Return to hotels

SUNDAY, 30 OCTOBER 2011

- 9:00-9:45 **Presentation of the Irving J. Selikoff Award to Congresswoman Carolyn Maloney, US Representative for New York's 14th District**
to honor her steadfast and ultimately successful advocacy in support of the James Zadroga 9/11 Health and Compensation Act which guarantees health care to the men and women who responded to the attacks on the World Trade Center on September 11, 2001.
Sala delle Vedute, Palazzo dei Pio
- 9:45-10:00 **Presentation of the exhibit “Chernobyl 1986-2011” by Golem Photography**
Sala delle Vedute, Palazzo dei Pio
- 10:00-10:30 Coffee

RAMAZZINI DAYS 2011
SCIENTIFIC PROGRAM

SCIENTIFIC SESSION II:

"NUCLEAR POWER: PRESENT REALITIES AND IMPLICATIONS FOR THE FUTURE"

Sala delle Vedute, Palazzo dei Pio

Using nuclear fuel to generate electricity has great benefits to public health because it produces little CO₂ emissions, and from that perspective it is a good alternative to fossil fuels. However, using nuclear fuel also creates potential radiation risks to the population that cannot be quantified either in terms of probability or severity.

We have experience with three major nuclear disasters associated with generating electricity using nuclear fuel—Three Mile Island, USA; Chernobyl, Ukraine; and Fukushima, Japan. The cumulative uncertainty associated with these disasters have had major consequences, including an international review of nuclear safety and the announcement by both Switzerland and Germany that they will phase out their reliance on nuclear power in the next decade. The fact that even three months after the event, Tokyo Electrical Power Company is still struggling to control the core meltdowns at its Dai-Ichi plants adds to these concerns.

The Collegium Ramazzini will devote its special session for 2011 to the public health questions surrounding nuclear electricity generation. Three Mile Island, Chernobyl and Fukushima present very different events and provide a good cross-section of likely exposure scenarios associated with nuclear power disasters. We will take this evidence and prepare an objective analysis from a public health perspective. This analysis will form the basis for the preparation of a Statement from the Collegium Ramazzini about public health risks of nuclear power.

- 10:30-10:50 NUCLEAR POWER INDUSTRY OVERVIEW
Knut Ringen, USA
- 10:50-11:10 REVISITING THE CHERNOBYL DISASTER WITH A FOCUS ON CHILDHOOD THYROID
CANCER
Martin Cherniack, USA
- 11:10-11:30 CARCINOGENIC RISKS: EXPERIMENTAL DATA ON THE EFFECTS OF LOW
EXPOSURE TO γ RADIATION
Morando Soffritti, Italy
- 11:30-11:50 GEOSTATISTICAL INTERPOLATION: KRIGING AND THE FUKUSHIMA DATA
Erik Hoel, USA
- 11:50-12:10 HEALTH RISK ASSESSMENT: FROM CHERNOBYL TO FUKUSHIMA
David Hoel, USA
- 12:10-12:30 HEALTH EFFECTS ON WORKERS IN NUCLEAR PLANTS
Jim Melius, USA
- 12:30-13:00 Discussion and Conference Closing
- 13:15 Farewell lunch
Ristorante B&B, Hotel Touring
- 20:00 Optional no-host dinner for Sunday night guests
(please rsvp with conference organization)
Pizzeria Re Artù

RAMAZZINI DAYS 2011

WORK OF THE FELLOWS ORAL COMMUNICATIONS

RISK ASSESSMENT FOR CARBON NANOTUBES

M Albin*, M Bohgard**, M Hedmer*, P Gustavsson***, M Kanje***, J Rissler**

Departments of Occupational and Environmental Medicine*, Ergonomics and Aerosol Technology**, Cell and Organism Biology***, Lund University, Lund, Sweden.

Maria.Albin@med.lu.se

Background: The use of carbon nanotubes (CNTs) has increased substantially in recent years, and is expected to continue to increase strongly in the future. CNTs are a whole class of nanomaterials, which may contain contaminants, such as metals, from the manufacturing process; moreover they may be functionalized to obtain new properties. We reviewed exposure, toxicology and protective measures for the Swedish Work Environment Authority. A systematic search was performed.

Results: Inhalation appears to be the route of exposure that is associated with the greatest potential risk, since CNTs, in bulk form, have a very low density and produce a lot of dust during handling. The measured levels have typically been 0.1 mg/m³ or less, but higher concentrations have been reported. Furthermore, aligned in the airflow CNTs >1µm can penetrate deep into the lung and reach the alveolar region.

Both single-walled and multiple-walled CNTs may cause inflammation and fibrosis in the airways, lungs and pleura in laboratory animals. Some studies suggest that longer CNTs cause greater biological effects than shorter carbon ones. There are not enough long-term studies with repeated exposure in order to draw clear conclusions about the capacity of CNTs to cause lung cancer or mesothelioma. However, several studies indicate a genotoxic effect. The functionalization of carbon CNTs, i.e. attaching chemical groups to the tubes strongly affects the half-life period in the blood and may influence their biological effects.

Based on the effects on laboratory animals, the lowest dose observed to cause adverse effects on the respiratory airways (inflammation and slight granuloma) was 0.2 to 0.3 mg/kg bw, the lowest air concentration where this has been observed is 0.1 mg/m³. At higher levels, more severe pulmonary reactions were observed as well as cardiac effects. After exposure to doses of 0.06 mg/kg bw via tube-feeding, DNA damage occurred.

Conclusions: There are major gaps in knowledge regarding the health effects of CNTs. It is particularly important that long-term animal inhalation studies are conducted (including studies of functionalized CNTs), but more studies are also needed of the reproductive effects and effects of skin exposure. Human data is lacking.

There is a need for a standardized measurement methodology for the quantification of occupational exposure to CNTs. In order to distinguish CNTs from other airborne particles, analyses with scanning electron or transmission electron microscopy are required.

Today, there is not enough knowledge about either exposure levels or the health effects when handling CNTs. A precautionary principle should therefore prevail in the manufacture, handling and use of CNTs, as well as in the processing of materials containing CNTs. In practice this means that established safety and protection devices such as enclosures and process ventilation should be used, together with personal protective equipment such as respiratory protective equipment, protective gloves and protective clothing.

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS ORAL COMMUNICATIONS

DEREGULATION OF MICRO-RNAS (MIR-21, MIR146A AND LET-7A) INDUCED BY DMBA IN CBA/CA MICE

István Ember

Institute of Public Health, Faculty of Medicine, Pécs University, Pécs, Hungary

istvan.ember@aok.pte.hu

MiRNAs function as mediators of cell responses to extracellular signals by targeting genes involved in cell differentiation, proliferation and apoptosis. Deregulation of these short noncoding molecules play an essential role in tumorigenesis.

In our recent study we investigated the effect of 7, 12 – dimethylbenz(α)anthracene on the expressions of miR-21 oncomiR, miR-146a that is strongly linked to NF κ B antiapoptotic signal transduction and let-7a that functions as a tumor suppressor miRNA targeting the p53 signalling pathway. DMBA is a complete carcinogen capable of inducing various types of tumors such as lung cancer, lymphoma, leukaemia, spleen hemangiosarcoma, skin and breast cancer. MiRNA was isolated from liver, lung, kidneys and red bone marrows of CBA/CA H2^k mice after 24 hours of exposure and 1 week post-exposure. MiRNA expressions were analysed in LightCycler 480 real-time quantitative PCR system.

The expression level of miR-21, miR-146a and let-7a were significantly higher in the vital organs of the mice after 24 hours of DMBA exposure compared to those of the control animals. On the other hand a significant down-regulation of the miRNAs was seen 7 days after the DMBA exposure. To our knowledge, this is the first study of micro-RNA modulation caused by DMBA in non-malignant tissues.

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS ORAL COMMUNICATIONS

LONG TERM HEALTH EFFECTS OF HUMANS EXPOSED TO PCBs AND PCDFs

Yue Leon Guo, MD, MPH, PHD^{1,2}; Judith SC Shiao, RN, PHD³

¹Environmental and Occupational Medicine, ²Occupational Medicine and Industrial Hygiene, ³Nursing, National Taiwan University (NTU) College of Medicine and NTU Hospital, Taipei, Taiwan
leonguo@ntu.edu.tw

Yucheng (“oil-disease”) victims were approximately 1800 Taiwanese people exposed to polychlorinated biphenyls (PCBs) and their heat-degradation products, mainly polychlorinated dibenzofurans (PCDFs), from the ingestion of contaminated rice oil in 1978-1979. Using 2,3,7,8-tetrachloro-dibenzodioxin toxic equivalencies (TEQ) as the exposure index, the exposed people had serum levels at 577 ± 393 ppt TEQ lipid 15 years after the exposure. We have established an age-, gender-, and socioeconomic status-matched community referent group for long-term follow-up.

Increased mortality due to chronic liver diseases and cirrhosis in earlier years after the exposure, and that due to systemic lupus erythematus in later years were found in Yucheng people. Exposed women had chloracne, increased thyroid goiter, anemia, diabetes, and loss of memory functioning. Exposed men had chloracne, arthritis, and poorer sperm quality. Children of the exposed women were born with delayed growth, dysmorphic physical findings, tooth abnormalities, and increased otitis media as compared to their neighbors matched for gender, age, maternal age, parental education, and socioeconomic status. The Yucheng children achieved 32 out of 33 developmental milestones later than referents. Lower scores in both mental and psychomotor subscales of the Bayley Scale in ages of 12, 18, 24, and 30 months were observed. At the ages 4 and 5 years, the Yucheng children scored approximately 5 points (0.3 standard deviation) lower than their referents on the Stanford-Binet test. At the ages of 6 and 7 years, the Yucheng children scored approximately 5 points (0.4 standard deviation) lower on the Wechsler Intelligence Scale for Children, Revised (WISC-R). Yucheng children were found to have higher behavioral problems as compared to their referents between the ages of 3 and 11 years as assessed by Rutter’s Child Behavior Scale A.. After puberty, Yucheng young men born to exposed mothers had poorer sperm quality.

We conclude that previous exposure to PCBs and PCDFs caused health effects in humans and the second generation born to exposed women.

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS ORAL COMMUNICATIONS

WHEN POLITICS AND EVIDENCE COLLIDE: CANADA'S 'ROGUE NATION' POSITION ON ASBESTOS

Colin L. Soskolne, PhD (Epidemiology), School of Public Health, University of Alberta, Edmonton, Canada and Kathleen Ruff, Senior Human Rights Adviser, Rideau Institute, Ottawa, Canada

colin.soskolne@ualberta.ca

Canada has stood alone for several years among developed nations by maintaining the double-standard of mining and exporting asbestos while avoiding its use at home. In this paper, we explore the behavior of Canada in its intransigence on this double-standard.

The government of Canada maintains that asbestos can be used safely in developing parts of the world. There are no data to support this position. Indeed, the data show just the opposite. In its defense, the Canadian government has relied on scientists, funded by the asbestos industry, who claim that chrysotile asbestos (the only kind of asbestos mined for more than twenty years) is less hazardous than other forms of asbestos, and that breathing high levels of chrysotile asbestos (ten times higher than permitted in Western countries) causes no harm to health among people in developing countries.

Being the discipline that provides the scientific basis (i.e., the evidence) for public health policy formulation, the focus of epidemiology is on prevention. This paper focuses on the prevention goal that is targeted at the policy-level (i.e., primordial prevention).

Consistent with the mission of those working in public health, the role of the epidemiologist is to maintain, enhance, and promote health in communities worldwide. Thus, epidemiologists work to protect the public health interest above any other interest. But, what can be done when there is a clash between evidence and politics?

This is where the overlap between public health and human rights enquiry can be instructive. When political decisions clash with evidence, it is typically due to the distorting influence of powerful special interests. The greater the imbalance of power, the greater the danger that public health decisions, instead of being grounded in objective evidence, will be shaped by dominant political and economic vested interests.

Human rights imperatives run exactly counter to that distortion. They require that decisions be grounded in the principle that all human beings, by virtue of their humanity, are entitled to equal dignity and equal rights. Decisions must be made transparently and on the basis of evidence and, rather than serving the interests of the powerful, special attention must be paid to ensure that the rights of the most vulnerable are protected.

Non-compliance with the principle solidarity is arrogant and disrespectful; it presents a double-standard in breach of international norms that are foundational to ethical conduct. Hence the label "rogue nation" for Canada.

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS ORAL COMMUNICATIONS

IARC MONOGRAPHS ON THE EVALUATION OF CARCINOGENIC RISKS TO HUMANS, VOL 102. NON-IONIZING RADIATION, PART II: RADIOFREQUENCY ELECTROMAGNETIC FIELDS.

Robert Baan, Yann Grosse, Béatrice Lauby-Secretan, Fatiha El Ghissassi, Véronique Bouvard, Lamia Benbrahim-Tallaa, Neela Guha, Farhad Islami, Laurent Galichet, Kurt Straif, on behalf of the WHO International Agency for Research on Cancer Monograph Working Group
Head IARC Monographs, International Agency for Research on Cancer, World Health Organization, Lyon, France
straif@iarc.fr

In May 2011, a Working Group of 31 scientists from 14 countries met at the IARC in Lyon to assess the carcinogenic hazards from exposure to radiofrequency electromagnetic fields. The Working Group considered the radiofrequency segment of the electromagnetic spectrum (30 kHz-300 GHz) with respect to its possible carcinogenic hazards, and reviewed the following exposure categories: (a) occupational exposures to radar and microwaves, (b) environmental exposures associated with transmission of signals for radio, television and wireless telecommunication, and (c) personal exposures associated with use of mobile telephones (cell phones). The most important information came from studies on cell-phone use, discussed in some detail below.

The INTERPHONE study, a multicentre case-control study, is the largest investigation so far of mobile phone use and brain tumours, including glioma, meningioma, and acoustic neuroma. Comparing those who ever used mobile phones with those who never did yielded an odds ratio (OR) of 0.81 (95% CI 0.70–0.94). In terms of cumulative call time, ORs were uniformly below or close to unity for all deciles of exposure except the highest decile (>1640 hours of use), for which the OR for glioma was 1.40 (95% CI 1.03–1.89). A pooled analysis from Sweden comprised two very similar studies of associations between mobile and cordless phone use and glioma, meningioma, and acoustic neuroma. Participants who had used a mobile phone for more than one year had an OR for glioma of 1.3 (95% CI 1.1–1.6). The OR increased with increasing time since first use and with total call time, reaching 3.2 (95% CI 2.0–5.1) for more than 2000 hours of use. Ipsilateral use of the mobile phone was associated with higher risk for glioma. Similar findings were reported for use of cordless phones. Comparable results were presented in these two studies for acoustic neuroma, although the case numbers were substantially smaller than for glioma. A study from Japan also found some evidence of an increased risk for acoustic neuroma associated with ipsilateral mobile phone use. The Working Group concluded that the epidemiological studies overall provided *limited evidence* of carcinogenicity and classified Radiofrequency Electromagnetic Fields as “*possibly carcinogenic to humans*” (Group 2B).

RAMAZZINI DAYS 2011

WORK OF THE FELLOWS ORAL COMMUNICATIONS

THE OUTBREAK OF ASBESTOS-CAUSED DISEASES IN CASALE MONFERRATO, ITALY

Benedetto Terracini, Professor of Cancer Epidemiology (retired), University of Torino, Torino Italy
benedetto.terracini@fastwebnet.it

An Eternit plant has been active in the production of asbestos-cement in Casale Monferrato between 1905 and 1987. It is the major of the 4 Eternit plants involved in the on-going trial in court in Torino. Very few protective measures in the workplace were implemented. Also, the general population of the area was exposed to asbestos and asbestos-related materials, partly because of the emissions from the factory and mainly because the leftovers of the production were used for insulation in the households.

Over the last 30 years, scientists of the Cancer Epidemiology Unit of the University of Torino (including myself, Francesco Barone-Adesi, Daniela Ferrante, Corrado Magnani, Milena Maule, Franco Merletti and Dario Mirabelli) have investigated the epidemiological consequences of such a massive exposure to asbestos. Three lines of studies have been pursued.

1. A retrospective mortality cohort study of the workforce active in 1965 or hired subsequently, i.e. 2657 men and 777 women. During 1965-2008, in men, a total of 1717 deaths were recorded vs. an expected figure of 1281.8 estimated on the basis of regional statistics. Corresponding figures in women were 480 and 322.2. The average yearly excess of approximately 9-10 deaths in men and 3 in women was similar over the whole period of observation. The table reports the numbers of observed and expected cases for the major asbestos-associated causes of death.

	Men			Women		
	obs	Exp	obs-exp	Obs	exp	obs-exp
Lung cancer	272	120.5	151.5	14	7.1	6.9
Peritoneal cancer	46	1.7	44.3	23	0.9	22.1
Pleural cancer	124	3.9	120.1	53	0.8	52.2
Asbestosis	197	0.4	196.6	37	0.1	36.9

2. A population-based registry of incident mesotheliomas has been implemented in 1990 and has served the population of the (ex) Local Health Unit 76 of the Region Piemonte (approximately 100.000 persons). A total of 626 incident mesotheliomas were registered between 1990 and 2006, out of which 98 were ex Eternit workers. Among the latter, the annual average number of cases was in the order of 6-7 over the whole period of registration. On the contrary, the number of mesotheliomas diagnosed to residents in the area who never worked at Eternit increased from approximately 15 in the early 90s vs more than 40 in the new millennium. For residents in the area, the lifelong cumulative risk of developing a mesothelioma is in the order of 2-3%, i.e. 10 times higher than in the rest of Piemonte and 100 times higher than in populations never exposed to asbestos.

3. A cohort of 1781 women married to Eternit workers (excluding women who themselves had worked at Eternit) has been retrospectively assembled through the registrars of the towns of residence of the male Eternit workers. These women have been retrospectively followed up for mortality during 1965-2003 and for mesothelioma incidence during 1990-2001. The mortality study detected a total of 395 deaths (vs 389.3 expected), among which 21 were certified to be caused by pleural cancer (1.2 expected). The incidence study detected 11 newly-diagnosed mesotheliomas vs 0.4 expected.

In total, epidemiological studies identified 1145 asbestos victims. This is an underestimate of the actual number of victims of this tragedy, since the periods covered by the epidemiological studies did not match with the total period in which the lethal effects of exposure to asbestos took (and will still take) place. In addition, our studies excluded the occurrence of non lethal diseases, including cured lung cancers and pleural plaques.

RAMAZZINI DAYS 2011

WORK OF THE FELLOWS ORAL COMMUNICATIONS

BERYLLIUM SENSITIZATION IN THE BUILDING TRADES NATIONAL MEDICAL SCREENING PROGRAM

Laura S Welch MD, Janet Shorter RN, Knut Ringen, DrPH, Eula Bingham PhD

LWelch@cpwr.com

Introduction:

Chronic beryllium disease of the lung can be disabling or fatal, and treatment at an early stage may prevent disease progression. Screening workers with using BeLPT is generally accepted as a valid indicator of both exposure and probability of developing subsequent chronic beryllium disease.

The Building Trades National Medical Screening Program (BTMed) was established in 1996 to provide medical surveillance for construction workers who worked in the DOE atomic weapons complex; a BeLPT is included in the initial examination for all workers. A follow-back evaluation in 2004 found that a 62% of our participants with a single abnormal BeLPT were confirmed abnormal with a second test; while that rate is reported at 80% in other population studies. In addition, a smaller proportion of those sensitized were found to have CBD. Here we report on a 2011 follow-back survey.

Methods:

We attempted to contact all participants with beryllium sensitivity (BeS). BeS was defined as a confirmed abnormal BeLPT or an abnormal plus a borderline BeLPT. We conducted a structured interview by telephone that assessed whether the participant had had additional diagnostic evaluation, where that evaluation was performed, and the results. We requested permission to obtain medical records for all those who had had additional evaluation. We also asked if the worker had filed a claim for BeS or CBD with the Energy Employees Compensation Program, which provides payment for work-related illnesses caused by employment in US nuclear weapons facilities.

Results:

Among 13,500 workers who have received a BeLPT in the BTMed program, 168 individuals had BeS and were still alive. Among these 37 were lost to follow up and 1 refused an interview. Of the 130 individuals interviewed, 43 had no diagnostic testing for CBD; 81 had additional diagnostic testing of whom 62 went to a center with expertise in diagnosis of CBD and 19 went to a doctor not affiliated with one of those centers. Twenty four individuals reported a diagnosis of CBD; this represents 38% of those who went to a specialized center for evaluation. We will present additional details on referral patterns, and on the review of medical records obtained.

Conclusion:

When we started the screening program, nuclear weapons employers did not believe construction workers were at risk for CBD. We have found that these construction workers are at risk, although the absolute prevalence of sensitization and the rate of conversion to CBD among sensitized workers are lower than rates in other studies. Exposures may have come from contact with beryllium dust in place during repair and maintenance of DOE facilities. CBD prevalence in our population is estimated at fewer than 5 cases per 1000 workers screened. Findings from the current follow-back survey will be used to encourage enhanced Be control programs, and to improve communications and support to these workers through the BTMed program.

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS ORAL COMMUNICATIONS

OCCUPATIONAL HEALTH IN THE SOUTH AND SOUTH EAST ASIA REGION

Hemantha Wickramatillake

Head, Occupational Health Unit, University of Brunei Darussalam and Visiting Professor at Drexel University, USA

Hemanth_wickram@yahoo.co.uk

The occupational health burden in the South-East Asia Region (SEAR), covering both South and South East Asia remains largely uncharacterized. Countries in the region have witnessed major occupational health problems highlighted by the Bhopal disaster in India and the Kader Toy Factory fire in Thailand. However, workers of the region are exposed to a wider range of occupational hazards and risks including chemical, physical and biological hazards as well as inadequate ergonomic practice and high psychosocial stress. One of the major contributory factors can be the existence of a large informal sector. Also, most of the countries in the region are in the process of rapid economic development, a process that potentially amplifies the pre-existing traditional risks and introduces new occupational risks in the region. Occupational health is of major concern in the South and South-East Asia Region with a potential work force of about 560 million persons. Occupational health is inextricably linked to social and economic conditions as well as governed by globalization. Therefore, attaining the goal of occupational health for all will require a strategy to secure work conditions that protect and promote occupational health, especially among the vulnerable groups.

The vulnerable population of SEAR countries consisting of women, the poor, and children, are primarily employed in the informal sectors. They often lack the basic knowledge of hazards and personal protection and work for long hours in unsafe work conditions with little or no health care or insurance. Industries have to perceive occupational health as an investment for economic productivity from a healthy work-force. Thus, in this age of increased globalization where the market conditions often shift in favour of the employers and not the employees, workers' health has to be addressed in a broader context of a basic human right for bridging the gap in health inequity to alleviate poverty and achieve gender balance. Some countries in the region have much established occupational health systems than other developing countries in the region, serving the purpose.

RAMAZZINI DAYS 2011

WORK OF THE FELLOWS ORAL COMMUNICATIONS

A DEADLY ASBESTOS FAMILY SAGA

Pier Giorgio Natali, MD, PhD, Regina Elena National Cancer Inst. Rome University “G. d’Annunzio”,
Chieti, Italy
natali@ifo.it

“Asbestos dust was all over the room as grey snow: books left on the table, when removed, left their negative image“ writes Primo Levi in his book “The Periodic Table”, describing his working conditions when temporarily employed as a chemist in an asbestos mine in northern Italy in 1941. Hard to believe, what Levi described was the home environment where the children of Philippe S. and his wife L., three boys and a girl, grew up in Patrimonio, a small village in Cape Corse overlooking the Mediterranean Sea. Wrapped in the wild scents of the Mediterranean bushes of liquorice, myrtle, fennel and rosemary spread by frequent winds, the village is split by the main road which connects the west to the east coast of Cape Corse, where the busy harbor of Bastia is located. Since the late forties, the village was crossed daily by tens of trucks. They were carrying cracked asbestos rich rocks from the open sky mine of Canari, sited 30 km north of Bastia, to be shipped mainland to the fast growing French industry “Eternit”. As proudly commented by a contemporary chief inspector (Docteur G.M.) of the local Social and Public Health Affairs Office “the mine provides almost 100% of asbestos nationally and represents about 25% of continent production”. Philippe and his wife had set up a successful family business, he being a reliable butcher and she, an unmatched cook of succulent “figatelli” (medium roasted pork liver seasoned with laurel leaves, fennel flowers and black course-ground black pepper) she was preparing in a small tavern they opened at the ground level of their house facing the main road. Being halfway from Canari to Bastia, the tavern rapidly became the obligatory stop of the high calorie-consuming truck drivers, who enthusiastically interrupted their monotonous trip to enjoy figatelli and, most likely, local wine which has made Patrimonio famous among the wine producers and connoisseurs. At the first floor of the house, the four children during school months were doing their home work. Their daily unenthusiastic commitment was largely attenuated by the fun of writing and drawing fanny faces on the tables and the furniture covered by the grey powder the open trucks left parked on the road were releasing at any breath of wind. The dust was constantly cleaned up by mommy, most likely rather as a boring house duty than a concern about her and the family’s health. Why should it be different, since the Canari mine was reported in 1962 in the “Bulletin of historical and natural sciences society of Corsica” as the “third most florid industry of the isle after forestry and animal products”? Contrary to a later developed tourism industry, the asbestos extraction provided a time-limited modest wealth and a number of Corsican were bound to emigrate Philippe’s older two sons, A and B, emigrated in fact in search of better opportunities to Canada, where one became an engineer in a steel industry and the other, an operator in oil pipelines; the girl married and spent most of her life in Paris, employed as social assistant, the son D., with a solid pragmatic mentality, became an entrepreneur in restoration in Bastia, and opened a quite restful camping site on the shores near Patrimonio.

I have been visiting the campsite for the last 15 years during my summer vacations and D.’s very outgoing personality gifted me of a friendship of uncommon intimacy for two persons who met once a year. He mentioned during the endless evening chats, often focused on medical issues (I’m a doctor!!), that the two emigrated brothers have died of mesothelioma. I was surprised because for my judgment they did not have any occupational risk and were non-smokers; negligently, I did not inquire further. Four years ago at my arrival in Corsica, I found D, at the time 60 years old, in organizing his passing away since a mesothelioma was diagnosed in him in the winter and he was well aware of the prognosis. I felt disarmed, and besides manifesting my closeness, I inquired of him further. Thus, I became fully aware of his family story starting from childhood. His father died at 68 of an unspecified pulmonary “bad disease “, his mother died at 69 of mesothelioma; as I mentioned similarly happened to his two emigrated brothers, who passed away at 47 and 60. His sister died two years after D., at 64, of the same malignancy.

The mine operating since the early forties, had been closed in 1965 because of decreased productivity and surging health hazard awareness, but remained unprotected ever since, until two years ago. A project co-financed by the European Community has now begun to clean the area (nobody locally knows how) which overlooks the beautiful coastal D80 main road of Cape Corse. An association named ANDEVA has been established in 1996, providing information, legal and medical support to the potential victims of the mine,

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS ORAL COMMUNICATIONS

but only in February 2010 the Court for Social Affairs recognized the link between the extraction activity in Canari and asbestos-related pathologies. The government, initially reluctant to consider any compensation, in view that there was a work-related link, has granted to D. a monthly pension of 900 euro from the diagnosis to death for a total of 16.000 euro and 15.000 euro to the three surviving sons. In short, D.'s life, at the time of full productivity, was from the government's point of view, worth 31.000 euro. His widow is not eligible to any compensation. Only through a legal action supported by ANDEVA, the final reimbursement to D.'s family has been settled at 40.000 euro. His emigrated brothers did not receive any compensation. A still unsettled amount of money will be made available to the surviving daughter of D.'s sister. Conclusively this story tells us that a death token may be claimed also by non occupational exposure to asbestos ("The Tragic Legacy of Sania's White Death", Toronto Star, Nov, 1999), which should therefore always be considered in enforcing public health policies.

Thanks to Massimo Crespi who when kindly hosting me on his sailing boat was sadly impressed by the story and asked me to write a short note about. The latter is based on inquiries to D's surviving relatives, to people presently living nearby the mine and from an article appeared on the daily "Corse Matin" (Aug. 2011)

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS POSTER PRESENTATIONS

PHYSICAL ACTIVITY AND CANCER: KNOWLEDGE AND PRACTICE AMONG NATIONAL CANCER INSTITUTE EMPLOYEES, CAIRO UNIVERSITY

Shaimaa A Abd Al Geleel¹, Manar M Moneer¹, Enas A Elattar¹, Wagida A Anwar²

Biostatistics and Cancer Epidemiology Department, National Cancer Institute, Cairo University¹, Public Health and Community Medicine, Faculty of Medicine, Ain Shams University²

wagidaanwar@yahoo.com

Background: The epidemic of physical inactivity is an issue of global concern, the inverse dose response relationship of physical inactivity to poor health and mortality is independent of other major risk factors. Physical activity (PA) is hypothesized to reduce the risk of several chronic diseases and enhance longevity. Low levels of activities have been associated with some but not all types of cancers. Lack of PA is rated among the top ten leading causes of death in high income countries, approximately 60- 85% of the world population lead sedentary lifestyles. According to current estimates, physical inactivity causes around 2 million deaths globally every year.

Aim: To evaluate physical activity practice among workers (medical & nonmedical) in National Cancer Institute (NCI), Cairo University and to assess knowledge about different health benefits of physical activity and its role in cancer prevention and treatment.

Participants & method: A cross sectional study was conducted on 400 workers (207 medical and 193 non medical). Their level and pattern of physical activity were assessed using modified International Physical Activity Questionnaire version 8 and how did it varies with regard demographic factors, their knowledge about health benefits of PA and its relation to cancer prevention and treatment were studied. The PA level was estimated as metabolic equivalent task (MET minutes/week).

Results: The medical group of workers was significantly more knowledgeable about different health benefits of regular physical activity (PA), however there was lack of adequate knowledge about relation between PA and cancer prevention and its role in cancer treatment among the whole group. No significant difference between the medical and non medical workers as regard the activity level. The most common barrier to participate in regular PA among the whole studied group was no enough time. Significant variables affecting total score MET minute were age groups, work type, job hours per week, education level (years), presence or absence of children, sitting minutes/day. Only 23.5% of the whole studied groups participate in recreation and sport PA. The study concluded that there was lack of adequate knowledge about relation between PA and cancer prevention and its role in cancer treatment. The study recommended implementation of a health-related physical education program and lessons about benefit of PA activity. Additionally, suitable place and equipment should be established at the NCI to stimulate workers for PA participation.

Key words: physical activity – medical workers – knowledge – attitude – cancer prevention

RAMAZZINI DAYS 2011

WORK OF THE FELLOWS POSTER PRESENTATIONS

SENTIERI PROJECT: MORTALITY STUDY OF RESIDENTS IN ITALIAN POLLUTED SITES

Pietro Comba¹, Fabrizio Bianchi², Susanna Conti³, Francesco Forastiere⁴, Ivano Iavarone¹, Marco Martuzzi⁵, Loredana Musmeci¹, Roberta Pirastu⁶

¹ *Dipartimento Ambiente e connessa Prevenzione Primaria, Istituto Superiore di Sanità, Roma*

² *Consiglio Nazionale delle Ricerche, Istituto di Fisiologia Clinica, Sezione di Epidemiologia, Pisa*

³ *Ufficio di Statistica, CNESPS, Istituto Superiore di Sanità, Roma*

⁴ *Dipartimento di epidemiologia del Servizio sanitario regionale, Regione Lazio*

⁵ *World Health Organization Regional Office for Europe, Rome, Italy;*

⁶ *Dipartimento Biologia e Biotecnologie Charles Darwin, Sapienza Università di Roma*

pietro.comba@iss.it

SENTIERI Project (Mortality study of residents in Italian Polluted Sites, IPS) studies mortality of residents in the sites of national interest for environmental remediation. IPSs are located in the vicinity of industrial areas, either active or dismissed, or near dumping sites of industrial and hazardous waste or incinerators.

The Project included 44 out of the 57 sites comprised in the “National Environmental Remediation Programme”; they correspond to the largest national industrial agglomerates. For each site, characterization data were collected, classified and arranged in tables. A great part of collected data also came from the Environmental Remediation Programmes planned for the sites. These plans showed that characterization and risk assessment activities were mainly undertaken in private industrial areas, as they were considered the source of pollution. On the other hand, municipal and/or green and agricultural areas included in the IPSs were poorly studied. Therefore, it is difficult to assess the exposure conditions of the populations living inside and/or near the IPSs. The most probable population exposures come from the contamination of ground water utilized for irrigation, or industrial process emissions.

SENTIERI concerned 44 IPSs, each one including one or more municipalities. Mortality at the municipality level was studied for the period 1995-2002, using the following indicators: crude rate, standardized rate, Standardized Mortality Ratios (SMR), and SMR adjusted for an *ad hoc* deprivation index. Regional populations were used as reference for indirect standardization. The deprivation index was constructed using 2001 national census variables representing the following socioeconomic domains: education, unemployment, ownership of dwellings, overcrowding. Mortality indicators were computed for 63 single or grouped causes.

The presence of asbestos (or asbestiform fibres in Biancavilla) has been the rationale for recognizing six IPSs (Balangero, Emarese, Casale Monferrato, Broni, Bari-Fibronit and Biancavilla). In these sites, with the exception of Emarese, increases in pleural mesothelioma mortality were detected; in four of them, excesses were present in both genders. Among six more sites, in which other sources of environmental pollution in addition to asbestos were reported, mortality from pleural mesothelioma had increased in both genders in Pitelli, Massa Carrara, Priolo and Litorale Vesuviano. In the time span 1995-2002, a total of 416 extra cases of pleural mesothelioma were detected in the twelve asbestos-polluted sites.

Drawing conclusions on the association between *environmental exposures* and specific health outcomes might be difficult, if mortality increases are observed for diseases with multifactorial etiology, or multiple sources of different pollutant agents are present, even concurrently with air pollution deriving from densely populated urban areas. Though, at times it was possible to attribute an etiological role to *environmental exposure* associated with emissions and leaks from refineries, petrochemical plants and metal industries. This attribution can be fostered by the observation of increases in both genders and in different age classes, thus reasonably excluding a major role of occupational exposures. A role of emissions from refineries and petrochemical plants was then hypothesized with reference to increases in mortality from lung cancer and respiratory diseases in Gela and Porto Torres; a role of emissions from metal industries was suggested to explain increases in mortality and respiratory diseases in Taranto and in Sulcis-Iglesiente-Guspinese. An etiological role of air pollution in the increase in congenital anomalies and perinatal disorders was suggested in Falconara, Massa-Carrara, Milazzo and Porto Torres. A causal role of heavy metals, PAHs and halogenated compounds was suspected for mortality from renal failure in Massa Carrara, Piombino, Orbetello, Basso Bacino del fiume Chienti and Sulcis-Iglesiente-Guspinese. In Trento-Nord, Grado and Marano, and Basso Bacino del fiume Chienti increases in neurological diseases, for which an etiological role

RAMAZZINI DAYS 2011

WORK OF THE FELLOWS POSTER PRESENTATIONS

of lead, mercury and organohalogenated solvents is possible, were reported. The increase of non Hodgkin lymphoma in Brescia was associated with the widespread PCB pollution.

SENTIERI Project has assessed the overall mortality profile in all the IPSs combined. Mortality for causes of death with *a priori* Sufficient or Limited evidence exceeded the expected figures, with a SMR of 115.8% for men (90% IC 114.4–117.2, 2,439 extra deaths) and 114.4% for women (90% CI 112.4–116.5, 1,069 extra deaths). These excesses were also observed when analysis was extended to all the causes of death (i.e. with no restriction to the ones with *a priori* Sufficient or Limited evidence): for a total of 403,692 deaths (both men and women), an excess of 9,969 deaths was observed, with an average of around 1,200 extra deaths per year. Most of these excesses were observed in IPSs located in Southern and Central Italy.

It should be remembered that SENTIERI is a descriptive investigation aimed at assessing whether and how much the mortality of residents in polluted sites differ from that observed in the reference population. For an appropriate interpretation of the results, it should be noted that the observation of cause-specific mortality increases can point to an etiologic role of *environmental exposures*, characterized by varying degrees of scientific evidence. It should also be considered that a mortality pattern similar to the expected may reflect the absence of relevant exposures or the inadequacy of the analyzed outcome (mortality instead than incidence). Furthermore the time window selected for analysis might lead to an inappropriate account of induction-latency time.

The study results will be shared with the Ministries of Health and Environment, Regional Governments, Regional Environmental Protection Agencies, Local Health Authorities and Municipalities. A collaborative approach between institutions in charge of environmental protection and health promotion will foster, among else, a scientifically sound and transparent communication process with concerned populations.

Keywords: Italian Polluted Sites, geographical mortality, environmental health impact

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS POSTER PRESENTATIONS

HYDRAULIC FRACTURING: BENEFITS AND COSTS

Chris De Rosa, Thomas And Glouy Donadio and Anthony Bondoch
ctderosal@yahoo.com

In the pursuit of energy resources there has been an increased industry interest in the utilization of shale fields to extract natural gas on a global scale.

In North America, the Marcellus and Utica shale fields are notable examples where a drilling technology known as hydraulic fracturing (“fracking” has been employed. Concerns surrounding the use of this technology have led to moratoriums in Pennsylvania, Quebec, Texas, France and elsewhere. Despite the potential risks associated with hydraulic fracturing, its economic benefits have led to the leasing of land on an unprecedented scale.

Fracturing requires the use of approximately 1000 chemicals, two thirds of which are unknown based upon “proprietary interests” claimed by industry. The identity of the remaining chemicals is known based upon accidental spills. For 353 known chemicals the percent of those with 10 or more adverse health effects are identified. Potential health respiratory, hepatic, cardiovascular, mutagenicity, neurological and renal effects as well as cancer. Natural resource concerns entail the volumes of water and sands, along with chemical contamination of the environment.

In this paper we review fracking technology, its scope of application, the benefits as well as environmental costs and human health implications, including human displacement and disease.

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS POSTER PRESENTATIONS

ALTERATIONS IN MICRORNA EXPRESSIONS IN PRIMARY HUMAN CERVICAL CANCER

Katalin Gocze¹, Krisztina Kovacs², Marta Benczik³, Peter Gocze⁴, Istvan Ember¹

¹ Department of Public Health, University of Pecs, Hungary

² Department of Pathology, University of Pecs, Hungary

³ Genoid Laboratory, Budapest, Hungary

⁴ Department of Obstetrics and Gynecology, University of Pecs, Hungary

katag@hotmail.com

Background:

Cervical cancer is the second leading cause of death among female cancer patients in the world. Clinical manifestation and progression are very diverse and not easily predictable.

Aim:

Detailed analysis of cervical cancer cases in Southwestern Transdanubian Region of Hungary in concordance with HPV genotype, histological and clinical grading.

Objectives and methods:

After HPV-testing and genotyping we analyzed the expression of 8 different pre-microRNAs (miR-21, miR-27a, miR-34a, miR-146a, miR-155, miR-196a, miR-203, miR-221) in FFPE primary human cervical cancer samples with the help of Light Cycler 480 PCR System (Roche). Expression profiles were evaluated in conjunction to HPV status, histological and clinical grading. We carried out statistical analysis with IBM SPSS Version 19.

Results:

Significant alterations in miRNA expressions were observed in the case of miR-21, mi-27a, miR-34a, miR-155 and miR-221 in concordance with HPV status, histological and clinical grading.

Discussion:

Deregulated miRNAs can be candidate gene targets enabling a better understanding of the molecular mechanisms underlying the development of this tumor type and might even serve as possible predictive biomarkers in response to the urging need for an earlier diagnosis, a more precise prognosis and a successful, personalized therapy. The p53-induced miR-34a together with miR-21, miR-27a, miR-155 and miR-221 proved to be a useful marker in cervical cancer.

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS POSTER PRESENTATIONS

EXPRESSION CORRELATIONS OF NFκB SIGNALING AND MIR EXPRESSIONS IN PRIMARY HUMAN HEAD AND NECK SQUAMOUS CELL CARCINOMAS

Katalin Gombos¹, Gábor Pajkos² and Istvan Ember¹

¹Pécs University, Faculty of Medicine, Institute of Public Health, Pécs, Hungary

²Oncoradiology Center of Bács-kiskun County Hospital, Kecskemét, Hungary

katalin_gombos@yahoo.com

Background: Head and neck squamous cell carcinoma (HNSCC) is characterized by elevated constitutive activity or aberrant regulation of NFκB signal transduction. NFκB acts as a survival factor for malignant cells by its anti-apoptotic function and plays as an important link between inflammation and cancer.

Aims: Expression analysis of 12 miRNAs (miR-21, -27a, -34a, -93,-143, 146a, 148a, 155, 196a,-203, -205, 221) parallel with their predicted target mRNAs (Rel-A and p50 subunits of Nfkb1), the NFκB signal suppressors (Pparγ, Jnk1) and activator Ikk1 and Gadd45α as an NFκB downstream target.

Materials and methods: Freshfrozen and formalin fixed paraffin embedded samples of primary human head and neck squamous cell carcinomas were obtained from patients diagnosed at the Oncoradiology Center of Bács-Kiskun County Hospital between 2009-2010. After clinical and histopathology evaluation 65 squamous cell carcinomas at T3-T4 stage and 20 corresponding autologous normal skin tissues were selected for miRNA and mRNA expression analysis with Light Cyclor 480 PCR system.

Results: 92% of the HNSCC samples were found to express significant alteration on the miRNA panel (considering miR-146a, miR-21, miR-221, miR-205 and miR-27a) compared to the normal tissues. 73% of the miRNA overexpressing tumors were found to have altered mRNA expression of Rel-A, p50 and Pparγ.

Conclusions: Apart from the heterogenous genetic alterations leading to the formation of HNSCC, this group of tumors can be characterized by consistent and specific molecular changes and behave as a homogenous group in terms of gene expression. Focused analysis of miRNA regulators and their mRNA targets of the NFκB signaling pathway showed significant expression alterations in HNSCC III-IV stage tumors. MiRNA up-regulation was sensitive, and the over expression of the sequence specific Rel-A, the DNA binding p50 subunit and the down regulated Pparγ was characteristic for the late stage tumors. Parallel evaluation of miRNA and mRNA expressions connecting to a focused signaling pathway could enhance the sensitivity and specificity of molecular tumor characterization that could support cancer diagnostics and individual molecular target therapy.

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS POSTER PRESENTATIONS

EPIDEMIOLOGICAL ANALYSIS AND GENOMIC EVALUATION OF ESOPHAGEAL AND GASTRIC CANCERS IN NORTHWEST HUNGARY

K. Juhasz¹, E. Stanitz², I. Ember¹

¹Department of Public Health, University of Pecs, Hungary

²Markusovszky County Hospital, Szombathely, Hungary

krisztina.juhasz01@gmail.com

Background: Environmental factors play an important role in the pathogenesis of esophageal and gastric cancers, accounting for 6-34 % of cancer-related deaths in the world.

Aims: The epidemiological and functional genomics analysis of gastric and esophageal cancers diagnosed between 2005 and 2010 in the Oncoradiology Center of Szombathely.

Patients and Methods: 213 cases were analysed by geographic information system (GIS) according to tumour type, age, sex and exposure markers. 48 formalin fixed paraffin embedded (FFPE) cancer samples were analysed using quantitative real-time PCR for the expression levels of the following precursors of miRNAs: miR-21, miR-27a, miR-34a, miR-93, miR-143, miR-146a, miR-155, miR-196, miR-203, miR-205, miR-221 and miR-223.

Results: 113 cases over a 5-year period were analyzed. 29% was diagnosed as esophageal and 65% as gastric cancer. The sex distribution was 1:2 in favor of men. Most of the cases was localised to the capital of Northwest region of Hungary, Szombathely. More than 90% of the cases had a positive anamnesis for alcohol consumption and smoking. Quantitative analysis showed significant up-regulation of pre-miR-34a, pre-miR-21 and pre-miR-93 in the esophageal samples. In the case of gastric samples pre-miR-205 was found to be the most strikingly up-regulated miRNA.

Discussion: We try to demonstrate the complementary use of traditional and molecular epidemiology. Development of miRNA-based biomarker development can not lack parallel epidemiological evaluation of environmental exposure factors for thorough understanding of carcinogenesis.

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS POSTER PRESENTATIONS

IMMUNOGENOTOXICOLOGY – NEW COMBINED BIOMARKERS FOR EVALUATION OF HEALTH RISK AFTER EXPOSURE TO IONIZING RADIATION

Aleksandra Fucic, Institute for Medical Research and Occupational Health, Zagreb, Croatia

afucic@imi.hr

Evaluation of biological response of mammals to ionizing radiation (IR) exposure by integration of genome and non-genome parameters, hormonal and immunological disturbances, distant organ bystander effects and respecting impact of gender and age will significantly change evaluation of health risks and preventive measures. Most of these pathways might be recognized as crucial in carcinogenesis. Estimation of micronucleus (MN) frequency in mononucleated and binucleated lymphocytes recently got a lot of attention as it gives insight, if used with mitotic index, on significance of immunological status for genome damage interpretation. Disturbances of mitotic index and cytokine levels in subjects exposed to IR show the need of combining immunologic and genotoxicologic parameters in order to achieve a better understanding of health risks. Cytokine diversity, their role in number of biological pathways, interaction with hormones and pathological processes confirm their significance as a biomarker of exposure and effect. It is already known that in Hiroshima, Nagasaki and Chernobyl victims disturbances of CD 4, CD 8 T cells and interleukins are reported decades after exposure.

Combining data of genome damage and cytokine levels by introduction of immunogenotoxicology will significantly contribute in directing radiation protection measures. However, application of available radiation protection preparedness and protection systems in practice and biomonitoring of exposed populations are still within domain of political and economical decisions. Such social environment has to be changed but in the meantime education of the general population and non-governmental bodies will enable their more active role in case of nuclear accidents.

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS POSTER PRESENTATIONS

SURVEILLANCE OF OCCUPATIONAL HAZARDS IN TAIWAN

Judith SC Shiao, RN, PHD¹; Yue Leon Guo, MD, MPH, PHD^{2,3}

¹Nursing, ² Environmental and Occupational Medicine, ³Occupational Medicine and Industrial Hygiene, National Taiwan University (NTU) College of Medicine and NTU Hospital, Taipei, Taiwan

leonguo@ntu.edu.tw

Occupational hazards had gathered attention only in the past two decades in Taiwan. We took efforts in surveillance in order to quantify the severity of occupational hazards. Among all surveillance systems in Taiwan, two are considered successful and ongoing.

An example for surveillance of occupational injuries is the needlestick injury reporting systems maintained by the Center for Medical Employees Safety and Health (C-MESH). This reporting system uses a web-based reporting approach for all needlestick and body fluid exposure at 260+ hospitals in Taiwan. An annual incidence of 45 percutaneous injuries per 1,000 healthcare workers is estimated. Among the source patients of these injuries, 14% were seropositive for hepatitis B, 15% for hepatitis C, 0.7% for HIV, and 2.8% for syphilis. Direct cost can be estimated for all percutaneous injuries by using the data from this surveillance system as well.

An example for surveillance for occupational diseases is maintained by the Network of Occupational Diseases and Injuries Services (NODIS). The Network consists of 9 tertiary referral centers, 52 hospitals, and one coordination center. These institutions provide services to workers sustaining occupational diseases and injuries, and report these cases to the coordination center in an anonymous manner. Due to the establishment of this network, the number of reported cases with occupational diseases has increased from 2003 to 2010. Among the reported patients with occupational diseases, the most prevalent is musculoskeletal diseases, such as carpal tunnel syndrome, lumbar intervertebral disc disorder, and musculoskeletal diseases of upper limb. Lung and skin diseases are also important occupational diseases. The annual incidence of specific occupational diseases can be calculated in each industrial and occupational category, for forming preventive strategies. Clusters of specific diseases can be identified, allowing for epidemiological investigation.

Taiwan's experience establishing the above-mentioned surveillance systems for occupational hazards can be examples for newly developed countries.

RAMAZZINI DAYS 2011

WORK OF THE FELLOWS POSTER PRESENTATIONS

Toxiclaro- Toxicology in the Classroom

Birger Heinzow¹, Wayne Temple², Nida Besbelli³, Agneta Sundén⁴, Maizurah⁵ Omar, and Rahmat Awang⁵

1 State Agency for Social Services, Kiel, Germany and Univ. of Notre Dame Australia, Sydney School of Medicine

2 National Poisons Centre, Dunedin School of Medicine, University of Otago, New Zealand

3 World Health Organization (WHO), Department of Public Health and the Environment

4 United Nations Environment Programme (UNEP) Chemicals, Geneva, Switzerland

5 National Poison Centre, Universiti Sains Malaysia, Penang, Malaysia

Birger.Heinzow@lasd.landsh.de

Introduction

Pesticides are widely used in farming economies, especially in developing countries and economies in transition, where adverse effects caused by weeds, diseases and pests are of greater concern. It is essential to avoid exposures that pose risks of adverse effects to human health and the environment, not the least such exposures that are due to careless use and disposal of pesticides. Ignorance about the potential dangers that pesticides and other chemicals can pose is often the reason for inadequate handling and disposal. Infants and children are particularly vulnerable to pesticides and especially children living in farming areas often face high exposures that can lead to adverse effects.

Aims

It is the aim of this capacity building project: **Toxicology in the classroom (Toxiclaro)** to introduce within the natural sciences education the topics of chemistry, toxicology and risk assessment: a) to educate children on protecting themselves (and others) from the harmful effects of pesticides; b) to lay a foundation for a safety culture for the future.

Rather than addressing the user and the parents, this educational material aims at raising the awareness among children by providing basic educational information and material in environmental chemistry and health and toxicology. Thus chemistry/science teachers in the early years of secondary school can teach their students aged 9-15 to understand the action of toxic chemicals/pesticides, and the principles of safe handling, and to protect themselves and the environment from harmful effects.

Development and Progress

The material has been developed by a task group in a joint effort (1) involving IUPAC, WHO, UNEP and the Universiti Sains Malaysia. The training material conveys basic information about chemistry, risk assessment, pesticides, safe handling, and preventing contamination, protecting themselves and others from harmful effects, how pesticides could harm human health and the environment. The training material consists of several modules in a CD-ROM, booklet and flip charts for use in countries with different level of development (2).

A prototype computer animation package was developed at the Universiti Sains Malaysia based on a top-down research model that encompasses theories, models, and principles about the best instructional approach for this type of multimedia material. (3). It is structured like a house where the student can progress through several topics (rooms) related to toxicology and pesticides. A second level additional material on the horizontal menu provides basic information, a glossary, links and teacher aids and an experimental design for teaching the dose response principle in the classroom, making use of the suppression of seed growth by Cu-sulfate.

The project is presently being evaluated in accordance with the theory of learning by piloting this educational material and seeking critique, advice and comments from users (teachers and students). Therefore several test runs were conducted, in Malaysia and Argentina and are planned for Ghana. The pilot tests came up with several very valuable observations and recommendations to review and refine the existing material. Experimental amendments were made and the results were used for improvement of the computer animation and the addition of shorter animated stories. (4)

Conclusion

The development of educational courseware Toxiclaro has been successfully accomplished. The test runs were extremely well received and the creativity shown by the children and their teachers was impressive. The age group of 9-15 years was targeted since it is in the transition from guarded childhood to more

RAMAZZINI DAYS 2011

WORK OF THE FELLOWS POSTER PRESENTATIONS

independent youth and may be at higher risk, because of independent activities. Also this age group might be responsible to look after younger siblings and influence their behavior.

The animated computer version will be presented onsite.

We recommend disseminating and using the courseware and invite all those interested to make adjustments to individual countries or regions by translating it into native language. An English and Spanish edition is freely available.

The amended version of the Toxiclaro multimedia package can be found at:

http://www.prn.usm.my/toxicology_spanish/

http://www.prn.usm.my/toxicology_english/

References

1.) Temple WA. Teaching School Children About Pesticides and Health.

[Chem. Int 27, No. 5, Sep-Oct 2005](#)

2.) IUPAC Project: Training of school children on pesticides and health - "Toxicology in the classroom."

<http://www.iupac.org/web/ins/2004-045-1-700>

3.) Omar M. and Awang R. Toxicology in the Classroom. [Errore. Riferimento a collegamento ipertestuale non valido. www.iupac.org/publications/ci/2009/3106/4_omar.html](#)

4.) Awang R. "The Design and Development of a Multimedia "Toxicology in the Classroom" Courseware for Young Children. 7th Annual Congress of the Asia Pacific Association of Medical Toxicology, December 8-10, 2008, Chandigarh, India.

Contact:

Mrs. Agneta Sundén-Byléhn

Scientific Affairs Officer, UNEP Chemicals

11-13 Chemin des Anémones, CH-1219 Châtelaine, Geneva, Switzerland

Tel.: (+4122) 917 8193, Fax.: (+4122) 797 34 60

E-mail: Agneta.sunden@unep.org

Affiliations

1- State Social Services Agency/ Dept. for Healthcare - LAsD 34

Brunswikerstr. 4

D 24105 KIEL, Germany

Email: birger.heinzow@lasd.landsh.de

2- National Poisons Centre

Department of Preventive and Social Medicine

Dunedin School of Medicine, University of Otago

PO Box 913, Dunedin, New Zealand

3- World Health Organization (WHO)

European Centre for Environment and Health

Hermann Ehlers Strasse 10

D-53113 Bonn, Germany

and

Department of Public Health and the Environment

20 Avenue Appia ,

CH-1211 Geneva 27, Switzerland

4- United Nations Environment Programme (UNEP) Chemicals

11-13 Chemin des Anémones

CH-1219 Châtelaine Switzerland

Email: chemicals@unep.org

5- National Poison Centre

Universiti Sains Malaysia

11800 Penang, Malaysia

Email: prnnet@usm.my

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS POSTER PRESENTATIONS

THE EFFECT OF CHILDHOOD LEAD EXPOSURE ON SCHOOL PERFORMANCE

Anne Evens, PhD,¹ [Daniel Hryhorczuk, MD, MPH,](mailto:dhryhorc@uic.edu)¹ Bruce Lanphear, MD, MPH,³ Daniel Lewis, PhD,² Linda Forst, MD, MPH,¹ Deborah Rosenberg, PhD.¹

University of Illinois at Chicago¹, Northwestern University², Child & Family Research Institute, BC Children's Hospital and Faculty of Health Sciences, Simon Fraser University³

dhryhorc@uic.edu

Objective

This study examines the association between blood lead levels (BLLs) of children born in Chicago and their performance in Chicago Public Schools (CPS), as measured by their scores on the 3rd grade Illinois Standard Achievement Tests (ISAT).

Patients and Methods

We examined 58,650 children who were born in Chicago between 1994 and 1998, who were both tested for blood lead between birth and 2006 and enrolled in the 3rd grade at a CPS school between 2003 and 2006. We linked the Chicago birth registry, the Chicago Blood Lead Registry, and 3rd grade ISAT scores to examine associations between BLLs and school performance, especially for children with BLLs below 10 µg/dL, the Center for Disease Control's current level of concern.

Results

After adjusting for other predictors of school performance such as poverty, race/ethnicity, gender, maternal education and low birth weight or preterm birth, we found that BLLs less than 10 µg/dL, and, in particular, less than 5 µg/dL, were inversely associated with reading and math ISAT scores in 3rd grade children. The strength of the association between lead exposure and school performance was found to be comparable with other factors typically associated with decreased academic achievement. Finally, we found that children whose BLL increased by 5 µg/dL had an increased relative risk of failing the 3rd grade reading and math ISATs.

Conclusions

Early childhood lead exposure negatively affects children's academic abilities even at BLLs less than 5 µg/dL. Preventing lead exposure in early childhood is essential to improving school performance.

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS POSTER PRESENTATIONS

OCCUPATIONAL HEALTH PHYSICIAN AND PSYCHIATRIC DISORDERS: FROM HEALTH SURVEILLANCE TO FITNESS FOR WORK

A. Isgro, S. Zoni, S. Arnaboldi, J. Fostinelli, M. Oppini, E. Toninelli, R. Lucchini, L. Alessio
School of Occupational Medicine, University of Brescia, Italy
lucchini@med.unibs.it

Psychiatric disorders are a major cause of disability and can be considered the main cause (40%) in most developed countries. Various literature reports estimate that about 1/5 of the adult population is affected by one or more mental disorders and WHO projections for 2020 foresee a further increase.

Reintroducing and maintaining people at work after a period of mental illness is an important social objective, supported by ethical and clinical motivations. However, work itself can generate psychopathologies, the so-called stress-related illnesses.

According to the Italian legislative Decree n. 81 of 2008, the employer must assess any risk for safety and health, including work-related stress, that can potentially affect the employees. The assessment of health risk from occupational stress is facilitated by the health surveillance programs and the role of occupational physicians is to promote and maintain the highest degree of physical, mental and social well being of workers in all occupation. This task may be complex and problematic in critical situations.

This work aims to assess the impact of these diseases on society and on the workplace, considering the clinical and behavioural patterns of the various psychiatric disorders, with special emphasis on the most disabling forms, identifying all the possible effects on employment and their way of presentation, assessing the role of stress in the development or in the worsening of the psychiatric disorders, discussing and evaluating the role of the occupational physician in the management of workers suffering from psychiatric disease. For this purpose, data available from the literature and specific guidelines were considered. The cases of work-related mental disorders observed at the Occupational Health Clinic (OHC) of the University of Brescia, Italy from 2001 to 2010 were also analyzed. In this decade 205 cases were observed as referred by General Practitioners. These cases with potential work related mental illness were equivalent to the 4% of the total number of cases observed at the OHC within that period of time. Sixty –three cases (45%) were diagnosed as work – related psychopathology and 13 of these (9,3%) as job stress-related. In 50 cases (37,5%) a working condition characterized by repeated moral harassment and mobbing was considered as responsible for mental condition. The remaining 92 cases were diagnosed as non-work-related mental illnesses.

In the same period of time, 65 cases were referred by Company Doctors for work-fitness evaluation of workers with mental illness. The work fitness was restricted for one half of these cases and 7 subjects (11%) were considered unable to work. The work fitness was considered as unconditional for 40% cases.

These results show that the diagnosis of mental illness can hardly exclude workers from their job. The management of psychiatric disorders, especially in dangerous activities should involve the whole work organization, encouraging active participation of the workers and proper communication within the company. Adjustments of tasks in the workplace should be favoured in order to make “able” the “disable”. Improvements in guidelines are still needed to help the occupational physician in the management of workers in their employment.

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS POSTER PRESENTATIONS

Occupational fatalities in Sweden due to cancer, cardiovascular and respiratory diseases.

Bengt Järholm, Professor, Umeå University, Sweden
Christina Reuterwall, Ass prof, Umeå University, Sweden
Jennie Bystedt, physician, Sundsvall's Hospital, Sweden
bengt.jarvholm@envmed.umu.se

The objective is to estimate the proportion of mortality due to cancer, cardiovascular and respiratory diseases that can be attributed to occupational exposure. Exposure to carcinogens that in IARC categories I and 2A were considered, along with myocardial infarction, asthma, chronic obstructive lung disease, pneumoconiosis and hypersensitivity pneumonitis. The analyses were restricted to ages between 25 and 74 years. We used conservative estimates, when possible from national case-reference studies.

We estimated that, in total there were around 800 deaths in 2007 attributable to occupational exposures in this age group. The majority were myocardial infarction (N=463) attributable to job-strain (N=193), shift work (N=89) exhausts from motors and burning (N=152) and environmental tobacco smoke (N=29). In total 270 deaths of cancer were attributed to occupational factors, approximately half of them in lung cancer (N=134). Ninety percent of mesothelioma deaths were estimated to be attributed to occupational factors meaning a total of 56 cases (54 men and 2 women). There were 2 deaths from pneumoconiosis and no death due to hypersensitivity pneumonitis in this age group. There were 4 deaths due to asthma and 92 deaths due to chronic obstructive lung disease attributed to occupational factors.

Cardiovascular diseases contribute to a considerable proportion of the mortality related to occupational factors in the working population. Both psychosocial factors and exhaust gases from engines and combustion seem important. Estimations of attributable deaths may be a useful tool in setting priorities in preventive strategies.

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS POSTER PRESENTATIONS

AN EXPOSURE INDEX ESTIMATION FRAMEWORK FOR SEGMENTS AND PARTICIPANTS IN THE NATIONAL CHILDREN'S STUDY (NCS)

Paul J. Lioy¹, Christopher J. Brinkerhoff¹, Sastry

Isukapalli¹, Michael Dellarco², Philip J. Landrigan³ and Panos G. Georgopoulos¹

¹Environmental & Occupational Health Science Institute, EOHSI, 170 Frelinghuysen Road, Piscataway, NJ 08854, 732-445-0159, [NCS Queens Vanguard Center]

²National Institute of Child Health & Human Development, NICHD, 6100 Executive Blvd Room 5C01, [NCS Program Office]

MSC 7510, Bethesda MD 20892-7510,

³Mount Sinai School of Medicine, 17 East 102 Street, New York, NY 10029, 212-824-7018, [NCS Queens Vanguard Center]

plioy@eohsi.rutgers.edu

Description of Research to be presented

Typically, Exposure Indices (EIs) are designed to capture and summarize data, in a small set of numerical values/ranges, however, they can also be employed with a complex data set to characterize distributions of potential exposures to multiple contaminants. They are defined to evaluate exposure- health risks associated with common health endpoints, and take into account location-specific contaminant information on multiple media and exposure pathways.

The recently developed NCS-EI framework is designed to support formulation and testing of specific exposure based hypotheses for children in the NCS by maximizing the use of extant data in exposure estimation, and to rank different NCS locations in relation to potential for environmental exposures. This improves the efficiency of data collection and provides details on the location of major data gaps. This framework utilizes an Exposure Information System (EXIS) that has been developed by EOHSI to process and integrate diverse extant databases of environmental, demographic, behavioral, biological, etc. attributes at the Federal, regional, State, and local level. This was a major effort that took about 15 years. Within the EOHSI- EXIS, these data are supplemented by estimates from numerical model simulations of environmental quality and population exposures. Overall The EXIS has been designed to support and to take advantage of the MENTOR (Modeling ENvironment for TOtal Risk studies) and PRoTEGE (Prioritization/Ranking of Toxic Exposures with GIS Extension) systems.

Initial EI applications of MENTOR and EXIS within the NCS have focused on inhalation exposures potentially relevant to pregnancy outcomes such as low birth weight and pre-term birth rates, and are demonstrated (a) for the set of all NCS counties, and (b) for NCS study segments for Queens County, NY. They highlight the feasibility and utility of the EIs and also identify various challenges due to heterogeneities and gaps in data that can be overcome by site specific data and analyses. Systematic data analyses will help prioritize information collection efforts within the main NCS study.

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS POSTER PRESENTATIONS

OXIDATIVE/NITROSATIVE STRESS MARKERS MEASURED NON-INVASIVELY IN SUBJECTS WITH CHRONIC 2,3,7,8-TETRACHLORO-DIBENZO-P-DIOXIN INTOXICATION

Daniela Pelclova¹, Tomas Navratil², Zdenka Fenclova¹, Stepanka Vlckova¹, Kamila Syslova³, Marek Kuzma⁴, Petr Kacer³

¹Department of Occupational Medicine, 1stMedical Faculty, Charles University and General Teaching Hospital, Na Bojisti 1, 120 00 Prague, Czech Republic

²J. Heyrovský Institute of Physical Chemistry of AS CR, v. v. i., Dolejskova 3, 182 23 Prague, Czech Republic

³Institute of Chemical Technology, Technicka 5, 166 28 Prague, Czech Republic

⁴Institute of Microbiology, AS CR, v.v. i., Videnska 1083, 142 20 Prague, Czech Republic

daniela@pelclova.cz

INTRODUCTION: 2,3,7,8-tetrachloro-dibenzo-*p*-dioxin (TCDD), a highly toxic persistent environmental contaminant, is classified as a human carcinogen affecting any target organ. The mechanism of carcinogenesis by TCDD is unclear because TCDD shows a lack of direct genotoxicity. Experimental studies also support the role of oxidative stress in TCDD neurotoxicity and vascular dysfunction. The goal was to investigate markers of oxidative/nitrosative stress and inflammation using non-invasive methods in subjects who got ill due to severe occupational exposure to TCDD in the years 1965-1968.

METHODS: In 11 TCDD-exposed patients, and 16 controls, the analysis of following oxidative products of lipids, proteins and nucleic acids in plasma, urine and exhaled breath condensate (EBC) was performed: 8-*iso*-prostaglandin F_{2α} (8-isoprostane), 4-hydroxy-*trans*-2-nonenal (HNE), malondialdehyde (MDA), *o*-tyrosine (*o*-Tyr), 8-hydroxyguanosine (8-OHG), 8-hydroxy-2'-deoxy-guanosine (8-OHdG), 5-hydroxymethyluracil (5-OHMeU). In addition, nitric-oxide-tyrosine (NO-Tyr) and leukotriene (LT) B₄, C₄, D₄, and E₄ were detected by liquid chromatography-mass spectrometry/mass spectrometry (LC-ESI-MS/MS). TCDD was measured by HRGC/HRMS, body lipid content by densitometry.

RESULTS: Mean TCDD plasma level in 2010 was 175±162 pg/g lipids (population level about 2 pg/g), total TCDD content in the body 5.16±4.62 mg. In the EBC, 10 from 12 markers (all except LT D₄ and LT E₄), were significantly increased in the patients (p<0.05). In the urine, 7 markers were significantly higher than in the controls (p<0.05): 8-isoprostane, MDA, HNE, LT C₄, LT E₄, *o*-Tyr and NO-Tyr. In plasma, only NO-Tyr and 8-OHG were elevated (p<0.05).

CONCLUSIONS: NO-Tyr was increased in all matrices in dioxin-exposed patients. EBC is not limited to lung disorders as the markers of oxidative stress and inflammation were elevated in EBC of patients with normal lung functions. TCDD-induced oxidative stress and inflammation markers can be detected non-invasively in the EBC and urine in the follow-up of the highly-exposed patients. Their prognostic value, however, needs to be elucidated.

ACKNOWLEDGEMENT: IGA NS10298.

RAMAZZINI DAYS 2011

WORK OF THE FELLOWS POSTER PRESENTATIONS

A SENTINEL CASE SERIES OF CANCER PATIENTS WITH OCCUPATIONAL EXPOSURES TO ELECTROMAGNETIC NON-IONIZING RADIATION WITH SHORT LATENT PERIODS

Yael Stein MD, Or Levy-Nativ MSc, Elihu D Richter MD MPH
 Hebrew University-Hadassah, Jerusalem, Israel
elihudrichter@gmail.com

Abstract:

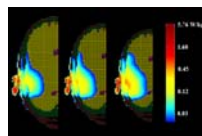
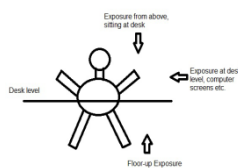
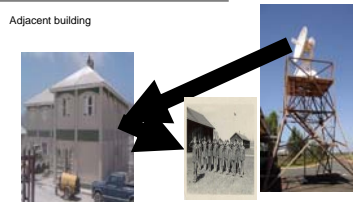
Background and Aims: We have reported groups of workers with high exposures to Non-Ionizing Radiation and short latent periods for cancer. We present a sentinel case series (n=47, 40M, 7F) of self-referred cancer patients with occupational exposures to EMF. Our aim was to report ages of first diagnosis/latency and tumour type and exposures

Methods: We categorized patients with regard to types of radiation, far or near field exposure and direct body contact, age of diagnosis and latency. For some we had data on frequencies, for others we provided assessments

Results: 15 patients developed cancer with latent periods < 5y and 12 patients with latent periods between 5y and 10y. The remaining 20 patients had longer latent periods In the <5y latency group there were 8 hematolympathic cancers and 9 solid tumours – testis, head & neck (including brain) and GI tract. In both the <5y and 5-9y latency groups there were patients exposed to intense levels of EMF, to several frequencies of EMF, or to EMF in combination with IR or other exposures. There were patients with direct body contact, or were in direct line of focus from point sources, or worked in small, electronically dense environments. In the >10y latency group there were more patients with intermittent exposures or exposures at older ages

Conclusions: The fact latent periods for Testes were very short, HL longer and Solid still longer suggests a coherent and biologically plausible pattern of latency in relation to the onset of exposure to RF and other agents. The findings state the case for (1) more careful modelling of exposure sources and penetration into the body, (2) preventive and protective measures based on control of exposure at source, barriers, and personal protection and (3) exploring low-exposure-low risk relationships for latent periods <10 y

TRANSMISSION AND EXPOSURE:
 Bounceback from surfaces of buildings → exposure to personnel in vicinity



Gandhi & Kang, Phys. Med. Biol., 47, 1501-16, 2002

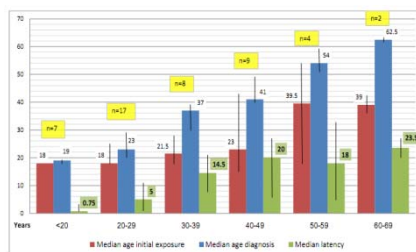
yael.stein@mail.huji.ac.il . elihudrichter@gmail.com

Implications for further work:

We suggest that the intensity, direction and depth of penetration of electromagnetic non-ionizing radiation are physical variables which should be investigated regarding the possibility of development of cancer in different body tissues in relation to source, geometry of exposure and penetration. There is a need for an exposure assessment matrix which takes into consideration hypothesized situations of exposures and their effect, using MRI-based models developed by Gandhi & Christ.

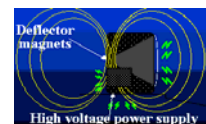
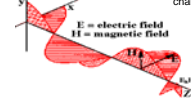
Age group	n patient	MF	Dis d	N tumour	Age bx (m.y)	Age initial Exp (m.y)	Diagnoses
<20	7	6M/1F	1	7	15y (15-19)	18	Hematolympathic
20-29	17	16M/1F	5	20	25y (20-29)	18y (18-25)	5 hematolympathic: 4 testis, 7 head & neck, 2 GI tract, 1 breast cancer, 1 skin
30-39	8	7M/1F	0	9	37y (30-39)	21.5y (18-28)	3 hematolympathic: 2 testis, 2 head & neck, 1 liver, 1 lung
40-49	9	7M/2F	1	10	41y (40-49)	25y (15-43)	3 hematolympathic, 5 head & neck, 1 breast
50-59	4	3M/1F	0	4	54y (51-59)	38.5y (18-54)	1 hematolympathic, 1 lung, 1 head & neck (bone), 1 bone
60-69	2	2M	1	5	62.5y (60-63)	59y (38-42)	2 head & neck, 1 kidney, 1 prostate, 1 GI tract
Total	47	40M/7F	6	58	39y (18-63)	19y (14-54)	23 Hematolympathic: 6 Testis, 17 Head & neck (6 brain, 4 bone, 3 endocrine), 4 GI tract, 2 Breast, 2 Kidney & prostate, 1 skin, 1 bone

47 patients with cancer and RF/MW and other exposures: Median ages of initial exposure, diagnosis, and latency



THERE ARE TWO FIELDS IN AN ELECTROMAGNETIC WAVE

The electric and magnetic fields are both perpendicular to the direction of travel. They travel together at very close to 300 million meters per second in air or vacuum (slower in water and tissue). The strengths of the electric and magnetic field change periodically.



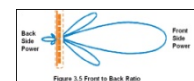
Median and average latencies for different tumour types within each age group

Age at Diagnosis			
<20y			
Totals, patients	7	Average: 0.83 (0.417-1.67)	Median: 0.75 (0.417-1.67)
Totals, for Solid tumours	0	Average: NA	Median: NA
Totals, Non-solid tumours	7	Average: 0.83 (0.417-1.67)	Median: 0.75 (0.417-1.67)
20-29y			
Totals, patients	17	Average: 5.35 (1.5-11)	Median: 5 (1.5-11)
Totals, for Solid tumours who testis (Head & neck (including brain), breast, GI tract)	8	Average: 5.187 (1.5-11)	Median: 4.5 (1.5-11)
Totals, Vesticular tumours	4	Average: 3.875 (2.5-6)	Median: 3.5 (2.5-6)
Totals, Non-solid tumours	5	Average: 6.5 (3-9)	Median: 7 (3-9)
30-39y			
Totals, patients	8	Average: 14.83 (8-21)	Median: 14.5 (8-21)
Totals, for Solid tumours who testis (Head & neck (including brain), liver)	3	Average: 15.667 (10-21)	Median: 16 (10-21)
Totals, Vesticular tumours	2	Average: 3.875 (2.5-6)	Median: 3.5 (2.5-6)
Totals, Non-solid tumours	3	Average: 13.667 (8-20)	Median: 13 (8-20)
40-49y			
Totals, patients	10	Average: 19 (8-27)	Median: 20 (8-27)
Totals, for Solid tumours (Head & neck (including brain), breast)	6	Average: 18 (8-27)	Median: 18.5 (8-27)
Totals, Non-solid tumours	4	Average: 20.5 (17-25)	Median: 20 (17-25)
50-59y			
Totals, patients	4	Average: 14.7 (5-33)	Median: 18 (5-33)
Totals, for Solid tumours (Bones (head & neck, vertebral column), lung)	3	Average: 14.7 (5-33)	Median: 6 (5-33)
Totals, Non-solid tumours	1	Average: 30 (NA)	Median: 30 (NA)
60-69y			
Totals, patients	2	Average: 23.5 (20-27)	Median: 23.5 (20-27)
Totals, for Solid tumours (Brain, kidney)	2	Average: 23.5 (20-27)	Median: 23.5 (20-27)
Totals, Non-solid tumours	0	Average: NA	Median: NA

Median latency periods by type of organ			
Tumour type	n = patients	Median Latency (y, r)	Median Latency (y, r)
Hematolympathic	19	7 (0.417-30)	7.5 (0.417-30)
Testis	6	5 (2.5-18)	5 (2.5-18)
Head & Neck (total)	14	13 (2-27)	12 (2-28)
Brain (& meninges) only	9	11 (2-27)	10 (2.5-28)
Head & Neck Other	5	13 (4-25)	7 (2 (4-25))
Other Organs (GI tract, lung, breast, liver, kidney, prostate, skin, bone)	8	7 (1.5-33)	12.5 (1.5-33)
Total	47 patients	6y (0.4167-33)	9y (0.4167-33)

NEAR FIELDS ARE FOUND NEAR ENERGY SOURCES

Near fields exist wherever there is electricity. A voltage will create an electric field. Current flow will create magnetic field. Electric and magnetic field can exist in different places. Electric field at any given place could be strong when the magnetic field is weak, and vice versa. These "near fields" drop off rapidly with distance.



RADIATION HAS ANTENNAS HAS "NULLS" AND "LOBES"

Notice the supposedly highly directional antennas, such as dishes, horns, and Yagis have radiation popping out towards the sides and rear flanks. These "side lobes" could be a safety concern for super high powered sources.

References:

Richter ED, Ben-Michael E, Berman T, Laster R, Westin JB. Cancer in Radar Technicians Exposed to RF/MW: Sentinel Episodes; Intl Journ Occ and Env Health.2000; 75: 187-193.
 Richter ED, Berman T, Levy O. Brain cancer in young radar workers with induction periods < 10 y. Arch Environ Health. 2002 57(4):270-272
 Szmitkowski S. Cancer morbidity in subjects occupationally exposed to high frequency (radiofrequency and microwave) electromagnetic radiation. Sci Total Environ. 1996; 180: 9-17.
 Grayson JK, Lyons TJ. Brain cancer, flying and socioeconomic status: a nested case-control study of USAF aircrew. Aviat Space Environ Med 1996b; 67(12):1152-54.
 Robinette CD, Silverman C, Jablon S. Effects upon health of occupational exposure to microwave radiation (radar). Am J Epidemiol. 1980 Jul;112(1):39-53.
 Degraeve E, Autier P, Grivegne e AR, Zizi M. All-cause mortality among Belgian military radar operators: A 40-year controlled longitudinal study. European Journal of Epidemiology (2005) 20: 677–681
 Gandhi & Kang. Some present problems and a proposed experimental phantom for SAR compliance testing of cellular telephones at 835 and 1900 MHz. Phys Med Biol. 2002 May 7;47(9):1501-18.
 Christ A, Kaniz W, Hahn EG, Honegger K, Zeffner E, Neufeld E, Rascher W, Janka R, Bautz W, Chen J, Kiefer B, Schmitt P, Hollenbach HP, Shen J, Oberle M, Sczerba D, Kam A, Guag JW, Kuster N. The Virtual Family--development of surface-based anatomical models of two adults and two children for dosimetric simulations. Phys Med Biol. 2010 Jan 21;55(2):N23-38.

RAMAZZINI DAYS 2011

WORK OF THE FELLOWS POSTER PRESENTATIONS

MONGOLIA: PARTNERSHIP FOR CAPACITY BUILDING IN ENVIRONMENTAL HEALTH TO MEET RAPID ECONOMIC DEVELOPMENT

Ellen Silbergeld, PhD¹, Chimedsuren Ochir, MD MPH²

¹Johns Hopkins University, Bloomberg School of Public Health, Baltimore MD USA

²Health Sciences University of Mongolia, School of Public Health, Ulaanbaatar MONGOLIA

esilberg@jhsph.edu



Mongolia, a strategically important democratic country in Central Asia, is undergoing rapid economic development since the decision to exploit its extraordinary mineral and fossil fuel resources. As shown in the map, Mongolia possesses large deposits of many important metals (including gold, copper, tungsten, manganese, and the rare earth metals), along with coal and natural gas reserves.

After a prolonged national debate and consultation with national and international stakeholders, the government has signed two major licenses to develop mines for copper and gold at Oyu Tolgoi and caol at Tavan Tolgoi, both in the Gobi region of the country.

The national government has also set a high priority on the development of capacity in research and practice in public health as well as in occupational and environmental health. Over the past five years, major capacities have been developed in environmental monitoring and analytic chemistry. The country has also participated in several cycles of the WHO STEPS health survey to gain an understanding of present and future priorities for disease prevention. As part of this process, the Minister of Health requested that the School of Public Health at the Health Sciences University of Mongolia (seek a partnership with Johns Hopkins School of Public Health (JHSPH_ to develop capacity in training and research to create the cadre of researchers and practitioners needed to ensure that resource development does not endanger health. These two institutions together have obtained funding from the NonCommunicable Disease Research and Training Program of the the Fogarty International Center, NIH.

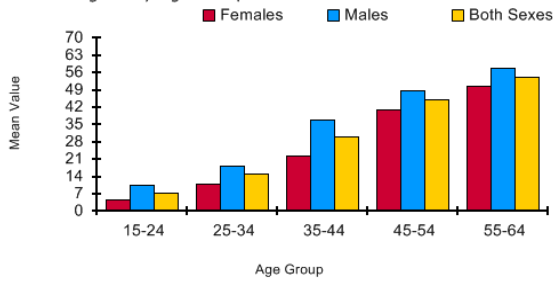
In developing this project, Mongolia School of Public Health and JHSPH assessed available information on health priorities in Mongolia. This research demonstrated that cardiovascular disease is the leading cause of mortality and morbidity in Mongolia, and that rates are increasing

In addition, economic development is driving major socioeconomic changes in Mongolia. Prior to 2000, the Mongolian economy was dominated by herder agronomy and the production of textiles and leather goods from animals (including cashmere). Since 2000, there has been a major internal migration of the population from rural areas into the capital city of Ulaanbaatar, with major consequences for public health. Migrants live in unincorporated areas of the city, predominantly in traditional felt tents with no access to urban services in areas such as drinking water, sanitation, electricity, education, or health.

RAMAZZINI DAYS 2011

WORK OF THE FELLOWS POSTER PRESENTATIONS

Blood Pressure, Raised
 ≥ SBP 140 and/or DBP 90 mmHg
 Mongolia by Age Group



Source: Public Health Institute of the Ministry of Health, Mongolian STEPS survey on the prevalence of noncommunicable disease risk factors 2006, 2006 (<http://www.who.int/infobase> IIRef: 102580)

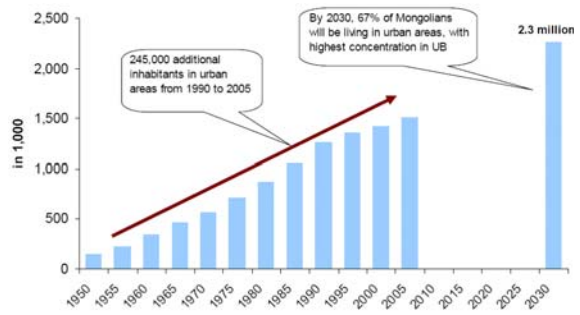
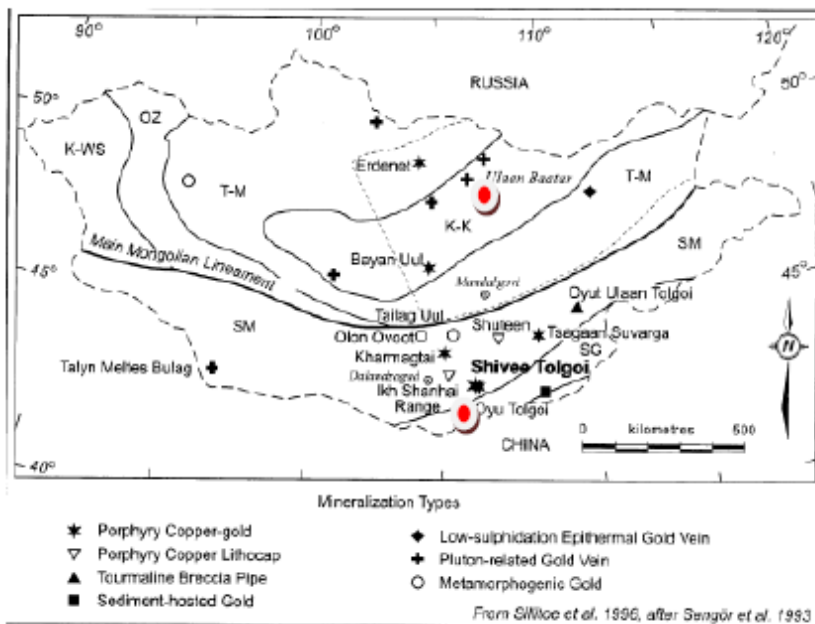


Figure 1. Map of mineralization in Mongolia. The capital Ulaanbataar and the Oyu Tolgoi region are circled. <http://www.infomine.com/index/pr/Pa101728.PDF>



RAMAZZINI DAYS 2011
WORK OF THE FELLOWS POSTER PRESENTATIONS

THE PROTECTIVE EFFECT OF TAMOXIFEN ON MAMMARY CARCINOGENESIS WHEN ADMINISTERED TO YOUNG FEMALE SPRAGUE-DAWLEY RATS TREATED WITH ONE SHOT OF γ -RADIATION

Bua L., Chiozzotto D., Tibaldi E., Panzacchi S., Soffritti M., Belpoggi F.

Cesare Maltoni Cancer Research Center, Ramazzini Institute (CMCRC/RI), Bologna, Italy

bual@ramazzini.it

In the framework of the integrated experimental project performed at the CMCRC/RI on γ -radiation carcinogenicity, the efficacy of Tamoxifen (TAM) on the chemoprevention of mammary cancers in irradiated female Sprague-Dawley rats, was studied. TAM is a well known drug used in oncology mainly for its antioestrogenic activity both in primary hormonotherapy in male breast cancer and in postsurgical adjuvant therapy for mammary cancer in women. In our laboratory, it was demonstrated that the antioestrogen TAM had a strong inhibiting effect on mammary cancer in females rats, even after the interruption of the treatment (1, 2). These findings were of particular interest for clinical purpose since mammary tumours in our animal model can be considered human equivalent for histopathological pattern, incidence and age-equivalent distributions. The aim of the present study was to evaluate the protective effects of TAM on mammary cancer in female Sprague-Dawley rats exposed to of 3 Gray γ - radiation at 6 weeks of age. Three groups of 200 females were treated with TAM, suspended in water, and administered by stomach tube at the dose of 3.3 mg/b.w. (10X of the dose woman equivalent), once daily, 6 days/week lasting for 16 weeks or for the life span. In the 2 groups dosed with TAM for 16 weeks, the treatment started 2 weeks before irradiation or immediately after. For the group treated with TAM for the lifespan, the treatment started after the irradiation.

References

1. Maltoni C, Minardi F, Pinto C, et al. Results of three Life-Span Experimental Carcinogenicity and Anticarcinogenicity Studies on Tamoxifen in Rats. *Ann N Y Acad Sci* 1997; 837: 469-512.
2. Minardi F, Soffritti M, Bua L, et al. Chemoprevention of mammary cancer: experimental contributions. *Eur J Oncol* 2001; 6(3): 277-285. (In Italian)

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS POSTER PRESENTATIONS

THE EFFICACY OF LEUPROLIDE IN PROTECTING FEMALE SPRAGUE-DAWLEY RATS TREATED WITH γ -RADIATION FROM THE ONSET OF MAMMARY CANCERS

Lauriola M., Tibaldi E., Falcioni L., Bua L., Pérez Hernández J., Soffritti M., Belpoggi F.
Cesare Maltoni Cancer Research Center Ramazzini Institute (CMCRC/RI), Bologna, Italy
lauriolam@ramazzini.it

Leuprolide, a gonadotropin-releasing hormone (GnRH) analog, acts as luteinizing hormone-releasing hormone (LH-RH) agonist-antagonist. It has been widely used in oncology to induce reversible chemical castration for patients with metastatic prostate cancer who prefer nonsurgical options. Several studies have provided evidence that, besides its inhibition of pituitary functions, Leuprolide may exert direct antiproliferative effects on tumour cells. The efficacy of Leuprolide in the chemoprevention of mammary cancer was studied within the framework of a large project started in 1986 at the CMCRC/RI, to evaluate the efficacy of a series of agents considered eligible for the chemoprevention of mammary tumours. In order to study the protective effect of this GnRH-analog on mammary glands, after tumour induction by ionizing radiation, 56-week-old female Sprague-Dawley rats were previously total body exposed to γ -radiation at 3 Gray dosage (administered "una tantum") and then treated with Leuprolide. The drug was administered in water suspension by subcutaneous injection at the dose of 0.0625 mg/Kg b.w. (1X woman equivalent), one injection every 4 weeks for 40 weeks. At the end of the treatment with Leuprolide, the females still alive were sacrificed. The results of the experiment are presented and discussed. The preliminary available data indicate that Leuprolide has a protective effect of 54.8% on mammary benign tumours and of 61.1% on malignant mammary cancers in irradiated rats. Leuprolide, like other drugs with hormonal activity, showed a strong chemopreventive effect on mammary tumours, and its use should be carefully considered for this purpose.

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS POSTER PRESENTATIONS

THE PROTECTIVE EFFECT OF TAMOXIFEN ON MAMMARY CARCINOGENESIS IN γ -IRRADIATED 56-OLD FEMALE SPRAGUE-DAWLEY RATS

Manservigi M., Manservigi F., Lauriola M., Ginesi G., Bua L., Soffritti M., Belpoggi F.
Cesare Maltoni Cancer Research Center Ramazzini Institute (CMCRC/RI), Bologna, Italy
maservigi@ramazzini.it

At the CMCRC/RI an integrated experimental project on the effect of γ -radiation on mammary carcinogenesis and of the possible antitumour effect of some drugs co-administered, was performed. Our previous studies showed that TAM was able to strongly inhibit mammary carcinogenesis, even at far lower doses than those currently used in clinical trials (dose of 20-40 mg/day) (1). The aim of this experiment was to test the protective effects of TAM on mammary cancer in female Sprague-Dawley rats exposed to 3 Gray γ -radiation one off at the age of 56 weeks. TAM, suspended in water, was administered by gavage at the dose of 0.1 mg/Kg b.w. (1/3 of the dose woman equivalent), 6 days/week for 40 weeks starting after the exposure to γ -radiation. At the end of the treatment with TAM, the females still alive were sacrificed. The animals were submitted daily to observation, weighed and clinically controlled periodically. During clinical examinations, it was registered that TAM reduced the incidence of palpable mammary tumours in animals co-treated with γ -radiation, compared to those treated only with γ -radiation. Histopathology confirmed that the antioestrogen TAM was able to reduce the onset of malignant mammary tumours in our experimental conditions. The efficacy of TAM in protecting from malignant mammary tumours induced by γ -radiation at a such low concentration makes the drug an eligible tool for breast cancer chemoprevention and opens a debate on reviewing TAM therapeutic dosage, in order to benefit from its healthy properties without severe side effects.

References

1. Minardi F, Soffritti M, Bua L, et al. Chemoprevention of mammary cancer: experimental contributions. *Eur J Oncol* 2001; 6(3): 277-285. (In Italian)

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS POSTER PRESENTATIONS

THE LIFE SPAN STUDY ON THE CHRONIC EFFECTS OF WORLD TRADE CENTER DUST AFTER INTRATRACHEAL INSTILLATION OF TOTAL PARTICULATE MASS TO SPRAGUE-DAWLEY RATS: FIRST OBSERVATIONS

Falcioni L., Bua L., Chiozzotto D., Manzoli I., Gambarotto D., Belpoggi F., Soffritti M.
Cesare Maltoni Cancer Research Center Ramazzini Institute (CMCRC/RI), Bologna, Italy
falcionil@ramazzini.it

Ten years have passed since the terroristic attack to the Twin Towers and Pentagon building on September 11th, 2001. Acute environmental exposures after the World Trade Center (WTC) destruction were associated with significant adverse health effects, such as bronchial hyperreactivity, persistent cough, and asthma. In order to evaluate the chronic long-term health effects of the disaster, a continuing follow-up of all exposed people (i.e.: firefighters, police, EMS, rescue workers, volunteers, community residents, etc.) was started. At present, the federal government doesn't classify cancers as WTC attack-related, but this decision is being periodically re-evaluated in light of ongoing research (1). It is well known that long term carcinogenic bioassays on rodents can predict potential carcinogenic effects of chemical and physical agents. In this regard, a long-term carcinogenicity bioassay on the total particulate mass present in the WTC dust was conducted at the CMCRC/RI to determine the potential lifetime consequences of the exposure experienced by individuals immediately after the collapse and fires caused by the terroristic attack. The tested WTC material is a complex mixture of coarse particle (95%) and contains pulverized cement, glass fibres, asbestos, lead, polycyclic aromatic hydrocarbons, polychlorinated biphenyls and polychlorinated furans and dioxin (2). Our test system consisted of 8-week-old male and female Sprague-Dawley rats. To mimic human WTC dust aerosol, test matter was suspended in sterile saline and administered by intratracheal instillation to rats (100 animals/sex). A group of 200 animals (100 males and 100 females), instilled with saline only, served as the control. A dose volume of 0.2 mg/0.2 ml in the first week of treatment, 0.3 mg/0.2 ml in the second week, 0.5 mg/0.2 ml in the third week were instilled respectively once/day for 3 consecutive day/week; on the fourth week, four different instillation of 0.5 mg/0.2 ml were performed, once/day for 4 consecutive days. A third group of rats (40 males and 40 females) were tested with the same WTC materials administered by intraperitoneal injection at the dose of 25 mg suspended in 1 ml steril saline. The animals were kept under observation until spontaneous death. They were clinically checked every 2 weeks and weighted every week for the first 13 weeks, every 2 weeks until 110 weeks, than every 8 weeks awaiting the end of biophase. No significant differences were observed in body weight, in survival or behaviour between WTC dust-treated rats and control animals. At death, they were submitted to complete necropsy. Early observations related to pulmonary long-term chronic effects, with particular regard to lung tumours, among the animals instilled with WTC material, will be reported.

Acknowledgements

We thank Dr. Paul J. Liroy who kindly provided the tested material.

References

1. Thorpe LE, Friedman S. Health Consequences of the World Trade Center Disaster. JAMA, 2011; 306(10): 1133-4
2. Landrigan PJ, Liroy PJ, Thurston G, et al. Health and Environmental Consequences of the World Trade Center Disaster. EHP 2004; 112(6): 731-9.

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS POSTER PRESENTATIONS

IMMUNOHISTOCHEMICAL CHARACTERIZATION OF SPONTANEOUS LYMPHOMAS IN SPRAGUE-DAWLEY RATS: COMPARISON WITH THE HUMAN COUNTERPART

Chiozzotto D., Tibaldi E., Panzacchi S., Belpoggi F.

Cesare Maltoni Cancer Research Centre Ramazzini Institute (CMCRC/RI), Bentivoglio, Bologna, Italy
servizi@ramazzini.it

Malignant lymphoblastic diseases are a heterogeneous group of neoplasms that arise from reticuloendothelial and lymphatic systems: based on the cell line, a lymphoid, myeloid and histiocytic type can be identified. Lymphoid neoplasms in humans are referred to the classification of WHO, based on biochemical, molecular, histopathological, and cytological criteria established by REAL. WHO/REAL classification divide into 3 broad categories the numerous forms of neoplastic disorders of lymphoid nature: B cell lymphomas, Hodgkin's disease and T-cell, and NK-cell lymphomas. Hodgkin's lymphoma develops mainly in cervical lymph nodes; histological pattern is characterized by the presence of multinucleated cells, called Reed-Sternberg, and abundant inflammatory tissue. Hodgkin's lymphoma represents about 30% of all lymphomas. The remaining 70% is generally indicated with the term "Non-Hodgkin's lymphoma" and includes a very heterogeneous group of neoplasms that comes from malignant degeneration of different immune system cells. The 25-35% of them involve extranodal sites, in particular the stomach, skin and intestine, but also the salivary glands, thyroid, lungs, thymus, liver, spleen and dura mater. In industrialized countries, it is estimated that 17.3 new cases of Non-Hodgkin's lymphoma, per 100,000 population, are diagnosed each year, representing about 2% (cumulative risk standardized by age, 0-74 years) of all cancers. To complete the pathological diagnosis and to obtain a targeted and effective therapy, immunohistochemical studies are performed to discriminate the various types of lymphoma. A panel of antibodies against proteins specifically expressed by T or B cells is usually chosen to establish the cellular origin of the neoplasia: e.g. the B immunophenotype can be investigated through the expression of markers like CD23, CD5, CD10, CD43, bcl-6 and CD79a, while T cells can be verified with the reactivity to CD3, CD4, CD8 proteins. Experimental animals models that reproduce situations that occur in humans, are usually used to better study some diagnostic and biomolecular aspects. The colony of S-D rats used by CRCCM for more than 35 years has been proved to have a susceptibility to cancer very close to the human one. Referring to the RITA nomenclature, internationally adopted for experimental toxicological studies in rodents (rats and mice), lymphoblastic, lymphoimmunoblastic and lymphocytic lymphomas are the most frequent neoplasias in our animal model, comparable for the neoplastic and biological characteristics to human counterparts: while the last two subclasses are present in both rat and human classification, lymphoimmunoblastic lymphoma refers to diffuse large B cell lymphoma, usually involving also the lung. The experimental approach to demonstrate malignancy in lymphoid disease is based on the concept that cancer growth is monoclonal, in contrast to the polyclonal expression in reactive hyperplasia. To characterize the immunohistochemical pattern of these neoplasms specific markers, for each cell line, are available: the B phenotype can be investigated through the expression of Bcl-2, Bcl-6, CD45, CD79a and the analysis of the ratio Kappa/Lambda light chains for clonality; the T phenotype may be described using anti-CD3, anti-CD4, anti-CD8 antibodies, whereas the nuclear enzyme TdT can be investigate in early lymphoid cells. Our main interest is directed to the characterization of lymphomas of difficult diagnosis, that may involve extranodal site such as the lung. This characterization is ongoing at our laboratory.

RAMAZZINI DAYS 2011
WORK OF THE FELLOWS POSTER PRESENTATIONS

SUCRALOSE (SPLENDA®) ADMINISTERED WITH FEED FROM PRENATAL LIFE THROUGH LIFE-SPAN, INDUCE LEUKAEMIA IN SWISS MICE

Soffritti M., Manservigi F., Manservigi M., Tibaldi E., Falcioni L., Lauriola M., De Angelis L., Belpoggi F. Cesare Maltoni Cancer Research Centre Ramazzini Institute (CMCRC/RI), Bentivoglio, Bologna, Italy
soffrittim@ramazzini.it

Sucralose (Splenda®) is an artificial sweetener approximately 600 times as sweet as sucrose (table sugar). It is manufactured by the selective chlorination of sucrose, which substitutes three of the hydroxyl groups with chloride and its molecular formula is $C_{12}H_{18}Cl_3O_8$. Sucralose is widely used in more than 80 countries as a non-nutritive sweetener. Currently the annual global demand for sucralose is about 600 tonnes with an annual growth rate of 20%. About 75% of the demand comes from the USA and Europe (CCM International Ltd 2011). Sucralose is widely used in beverages and foods and in blends with acesulfame-K and aspartame. In a recent report summarizing the genotoxicity studies in vitro and in vivo, all results were evaluated as negative (Brusick et al 2010).

Long-term carcinogenicity bioassays conducted by the industry producing the sweetener indicated that sucralose administered in feed to Sprague-Dawley rats and Swiss mice did not show carcinogenic effects in either species (Mann et al., 2000; Mann et al., 2000).

The weaknesses of the industry bioassays become readily apparent when considering that: 1) in the rat study, all animals had, at all doses, significant ($p < 0.001$) decreased body weight compared to controls, and the incidences of benign and malignant tumours were lower in all treated groups compared to the controls; and 2) in the mouse study the animals treated at the highest dose had significant ($p < 0.01$) decreased body weight and lower incidence of malignant tumours compared to the controls and the other treated groups. It is noticeable that concerning malignant lymphomas in females, the incidences were 17%, 32%, 29%, and 12% in animals treated respectively with 0, 0.3, 1.0 or 3.0 % ppm of sucralose in the feed.

For these reasons we began a first experiment in 2005 testing sucralose on Swiss mice (Exp BT 6012). In this study, the feed with sucralose (with a purity of 99.4%) was administered ad libitum (at the concentrations of 16,000; 8,000; 2,000; 500; 0 ppm to simulate a daily assumption of 2,000; 1,000; 250; 62.5; 0 mg/Kg b.w. respectively) to groups of 120 – 200 male and female Swiss mice from prenatal life (12th day of gestation) until spontaneous death. Mean daily drinking and feed consumption were measured per cage and body weight was periodically measured individually. Upon death the animals underwent to complete necropsy.

First results indicate that sucralose induces a dose-related increased incidence of leukaemias in males ($p \leq 0.01$) and in particular at the doses of 16,000 ($p \leq 0.01$); 8,000 ($p \leq 0.05$) and 2,000 ($p \leq 0.01$).

RAMAZZINI DAYS 2011 **SCIENTIFIC SESSION II**

NUCLEAR POWER INDUSTRY OVERVIEW

Knut Ringen, USA

Objectives: This presentation is based on a White Paper, *From Three Mile Island to the Future: Improving Worker Safety and Health In the U.S. Nuclear Power Industry*, March 14, 2011, commissioned by the President's Blue Ribbon Commission on America's Nuclear Future, (BRC)(available at www.brc.gov, commissioned papers). In the US, 104 nuclear reactors generate about 20% of the electricity supply. We were asked to review the risks of the entire nuclear fuel cycle from before Three Mile Island (1979) and anticipating future developments, in comparison to risks from other sources of electrical power generation. Subsequently we also have examined some aspects of the Fukushima Daiichi disaster.

Methods: We relied on the following data sources for this study: industry performance indicators, NRC, OSHA and MSHA inspection data, radiation monitoring data on workers in the civilian nuclear industry, occupational fatality, injury and illness data, and interviews with over 100 decision-makers representing utilities, maintenance contractors, regulators, unions and environmental activism.

Findings: The nuclear industry is very safe. For all indicators examined, the nuclear industry has reduced its risks by more than 90% since Three Mile Island. Risks to workers are more than 80% lower than in alternative sources of industry. However, there have been many near misses that could have led to catastrophic disasters over the years, and there are added uncertainties from the rapidly aging nuclear facilities and nuclear workforce. The main risks faced by the industry are: uncertainty, overconfidence, complacency/negligence and risk taking.

Discussion: It is hard to envision how the US can meet its energy and CO-2 reduction objectives without continued reliance on nuclear power. Other sources that do not produce CO-2 emissions (wind, solar, geothermal) are currently much too inefficient to produce the needed electricity capacity. Nuclear energy should be judged on the basis of its relative risks compared to other sources of energy, for workers, the public, energy security and climate change. All our major sources of energy -- nuclear, coal, hydro and petroleum -- require the most careful management of very high risks. In assessing the relative risks of nuclear power, the following questions should be debated carefully:

- How do you balance a very good safety record against a Fukushima Daiichi disaster?
- How do you balance the likely greater safety to workers in nuclear plants against the potential greater risk to the general public?
- How do you balance nuclear energy against other sources of energy given the likely severity of an adverse nuclear event?
- How do you balance the likely greater climate change benefits of nuclear energy against nuclear safety risks?
- How do you balance the benefits from nuclear power against possible nuclear weapons proliferation risks?

RAMAZZINI DAYS 2011

SCIENTIFIC SESSION II

REVISITING THE CHERNOBYL DISASTER WITH A FOCUS ON CHILDHOOD THYROID CANCER

Martin Cherniack, USA

The Chernobyl nuclear event in April 1986 effected large areas in Belarus, Ukraine and Russia with the principal risks to children associated with food contaminated by I^{131} . In Belarus, the most effected country, more than 24,000 village children received radiation doses to the thyroid in excess of 2 Gy. In 1986 two childhood thyroid cancer cases were surgically treated and registered in Belarus; by 1991, incidence had increased almost 30-fold, producing the greatest radiation-related identified cancer risk since World War II. There was intensive international interest. In 1994-1995, the American NCI initiated two 30-year prospective cohort studies for exposed children (70,000 in Belarus and 15,000 in Ukraine). Compared with the ABC study of 45 years later, there was an enormous resource pool: direct radiation measurements on >600,000 people taken within weeks of the incident; the availability of high resolution Ultrasound (US) and subsequent active screening of several hundred thousand children; cancer registries in Belarus, Ukraine and Russia; and the active engagement of multiple international research teams. Despite magisterial dose reconstruction, and several important observations on iodine deficiency, KI administration, and risk, accomplishments have been modest compared with post-Hiroshima and Nagasaki Life Span Study (LSS). Sustainability has not occurred, and many decades of unneeded thyroidectomy are a likely consequence.

The effects of political upheaval and the delays from circuitous negotiations between governments and multiple international institutions were underestimated, particularly in Belarus. However, the factors resulting in an unrealized public health research objective, following a disaster, may be more generalizable, particularly when domestic resources are inadequate. For one thing, the combination of public anxieties and limited evidence for thyroid cancer risk, associated with previous nuclear exposure, supported initial scepticism around the Belarussian case reports. In 1992, the IAEA report from the International Chernobyl Project concluded that there would be no measurable impact on cancer incidence from Chernobyl. A second consideration involves the unleashing of wide-scale dose measurements in the absence of extensive quality control or selection strategy. This was followed by a similarly wide-scale US screening for thyroid cancer a decade after the event. The result was a substantial selection bias towards an older urban-based demographic and the screening of a large non-clinical population with a sensitive pre-clinical diagnostic technique. Accordingly, most thyroid cancer cases have been diagnosed in less exposed populations whose age at exposure and gender distribution differs markedly from the initial cases. The reliance on case control and ecologic studies places a particular reliance on accurate dose estimation. The tiering of measurements – ‘measured’, ‘passport’, ‘inferred’ – blends direct measurement with ecological presumptions and with resulting estimates to controls that were often equivalent to those from cases. The reliance on established study designs lead to a failure of imagination. The LSS were also disorganized in their first years and American epidemiologists and health physicists were similarly ignorant of Japanese culture.

The United States was the major source of the post-Chernobyl thyroid research effort. American investigators had fared much better two generations earlier in Japan in the setting of more limited epidemiological sophistication. The American prospective cohort study design was flawed in several basic ways: 1) unfamiliarity with the social translocations that followed 1991, 2) unrealistic optimism on the utility of available direct measurements in lieu of a more traditional geographic approach, 3) the decision to work with unstable local institutions rather than setting up a single identifiable authority and identity, and 4) a scale of operations that was well beyond the allocation of very modest resources. Finally, it may be that the Alex Langmuirs and Gilbert Beebes of 1948 were a more effective breed than their successors from the professional radiation effects bureaucracy.

RAMAZZINI DAYS 2011

SCIENTIFIC SESSION II

CARCINOGENIC RISKS OF γ RADIATION: EXPERIMENTAL DATA ON THE EFFECTS OF LOW EXPOSURE

Morando Soffritti, Italy

It is well known that exposure to ionizing radiation increases the risk of cancer and that the level of such risk may change in relation to dose, age, exposure during prenatal life, sex, exposure to other carcinogenic agents.

Epidemiological studies on the Japanese atomic bomb survivors have shown an increased cancer risk among people exposed to low dose of γ radiation (≤ 10 rads). However the most common form of exposure of the general population is from chronic or fractionated low-dose radiation. For this reason, scientific research has developed a special interest to follow workers of nuclear industry, medical radiation workers, and persons exposed to multiple diagnostic radiological examinations. However, epidemiological and experimental studies are still insufficient/inadequate to quantify the dimension of the carcinogenic effects of the exposure to low dose of ionizing radiation, particularly with reference to individual sites/types of cancers.

In light of this insufficiency, an integrated project of mega-experiments to evaluate the carcinogenic effects of exposure to low dose of γ radiation on large groups of male and female Sprague_Dawley rats was planned at the Cesare Maltoni Cancer Research Center of the Ramazzini Institute.

In this project, rats were exposed to gamma radiation at different dose levels and in 4 different situations, namely: 1) post-natal exposure exposing animals to one shot at 6 weeks of age or the same doses fractionated in 10 shots, 1 every 4 weeks); 2) exposure during embryonic life; 3) exposure of male breeders before mating; and 4) administration of irradiated feed starting from embryonic life lasting until spontaneous death. The 4 mega-experiments, begun simultaneously, encompassed all the offspring of each litter (10,511, males and females) born from 4,000 breeders. During the presentation, the results of the carcinogenic effects on groups of 416, 619, 1046 and 1051 male and female rats (overall 5213) exposed at 6 weeks of age to one shot of 300, 100, 10 or 0 rads respectively, and kept under observation until spontaneous death will be reported.

Once the evaluation of all mega-experiments is completed, quantitative risk models can be developed, in particular to compare chronic versus acute exposures. Moreover, once the basic risks are determined in these rodent studies, the results can be integrated with human epidemiology such as the A-bomb cohorts for a better understanding of the cancer risks from environmental nuclear disaster exposures like in Chernobyl.

RAMAZZINI DAYS 2011
SCIENTIFIC SESSION II

HEALTH RISK ASSESSMENT: FROM CHERNOBYL TO FUKUSHIMA

David Hoel, USA

A comparison of the Chernobyl and Fukushima environmental radiation levels will be discussed. The relationships between environmental levels and doses to the individual with corresponding health risks will also be considered. For Chernobyl the liquidators have been well studied. They have cancer risks similar to those expected from high levels of low LET radiation. The primary health issue to the public from the Chernobyl exposures has been thyroid disease resulting from childhood exposures to the short-lived radioisotopes of iodine.

GEOSTATISTICAL INTERPOLATION: KRIGING AND THE FUKUSHIMA DATA

EG Hoel, USA

A brief review of geostatistical interpolation techniques (e.g., Kriging) will be provided. A discussion of these methods and their application to the Fukushima airborne ionizing radiation data, as well as measured soil, and food-based radioisotopes will be given. The talk will conclude with a brief tour of a public web site that allows users to interactively visualize the geostatistical interpolations in a temporal manner.

HEALTH EFFECTS ON WORKERS IN NUCLEAR PLANTS

Jim Melius, USA

A brief review of available health data on nuclear plant workers including weapons plants will be presented including information on exposure trends and on the US program to compensate workers formerly employed at nuclear weapons facilities. Implications of these data for future nuclear facility operation will be presented.