

SECTION OF ENVIRONMENT (ENV)

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ENVIRONMENT, INCLUDING LIFESTYLE, ENCOMPASSES MANY MAJOR CAUSES OF HUMAN CANCER, INCLUDING TOBACCO USE, ALCOHOL DRINKING, OCCUPATIONAL EXPOSURES, ENVIRONMENTAL POLLUTANTS AND RADIATION.

IARC is well placed to address these important questions because of its ability to coordinate large-scale studies, which take advantage of the heterogeneity of cancer and cancer risk factors across human populations. IARC can also integrate epidemiological and biological techniques and contribute to programmes aimed at reviewing and evaluating the evidence of carcinogenicity of specific agents and interventions. Studies of the effects of ionising radiation are important for elucidating mechanisms of carcinogenesis, and can provide the scientific basis for radiation protection of the general public, patients and occupationally-exposed populations. In particular, uncertainties persist with regard to the health consequences of low doses and low dose rates, and host factors that can modify radiation-related cancer risk.

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RESEARCH IN THE LIFESTYLE AND CANCER GROUP (LCA) COMPLEMENTS THAT IN OTHER SECTIONS ACROSS IARC BY AIMING AT IDENTIFYING THE ENVIRONMENTAL CAUSES OF HUMAN CANCER AND THEIR INTERACTIONS WITH GENETIC FACTORS (BOFFETTA ET AL., 2008A; BOFFETTA ET AL., 2009A). IT ALSO AIMS TO CONTRIBUTE TO THE METHODOLOGICAL DEVELOPMENT OF THE FIELD OF MOLECULAR AND GENETIC EPIDEMIOLOGY, AND OF CANCER PREVENTION RESEARCH, IN PARTICULAR IN THE FIELD OF TOBACCO CONTROL. THE FOCUS IS ON CANCERS OF THE LUNG, THE UPPER AERODIGESTIVE TRACT, THE PANCREAS AND THE KIDNEY, AND ON LYMPHOMA. THE PROGRAMME CONSISTS OF MULTICENTRIC INTERNATIONAL STUDIES CARRIED OUT IN COLLABORATING CENTRES, THE COORDINATION OF NETWORKS OF INVESTIGATORS, THE USE OF EXISTING RESOURCES SUCH AS CANCER REGISTRY DATA, AND THE PREPARATION OF THE *IARC HANDBOOKS OF TOBACCO CONTROL*.

Different types of study design are used (case-control, cohort, record linkage), and all field studies include a biological component. During 2008–9 the group completed a series of analyses of risk factors for cancers of the lung, the upper aerodigestive tract (including the oral cavity, pharynx, larynx and esophagus) and the kidney, the colorectum, the breast and of lymphoma, based on large-scale case-control studies coordinated by the former Gene-Environment Epidemiology (GEE) Group and conducted in previous years in Europe and Latin America. Extensive genotyping of samples collected in these studies has been conducted by the GCS and GEP groups.

The full exploitation of this material will take several years; results reported during 2008–2009 include causes of cancer in France (Boffetta *et al.*, 2009b), UV radiation exposure and the risk of malignant lymphoma and multiple myeloma (Boffetta *et al.*, 2008b), various second primary cancers (Chuang *et al.*, 2008a; Chuang *et al.*, 2008b; Maule *et al.*, 2008), and risk factors for hypopharyngeal, laryngeal and breast cancers in India (Chuang *et al.*, 2008a; Chuang *et al.*, 2008b; Heck *et al.*, 2008; Mathew *et al.*, 2008; Mathew *et al.*, 2009; Sapkota *et al.*, 2007; Sapkota *et al.*, 2008). Results of analyses conducted in these studies on the effect of genetic variants on the risk of lung and head and neck cancer are contained in the report from the GEP group.

The work of the Group in the epidemiological studies described above has been extended to the coordination of international consortia, with the following goals: fast and coordinated replication of new findings; pooling of data for analysis for which large populations are needed, typically for gene-environment interactions; and setting standards for future epidemiological research. In

particular, during 2008–2009 the Group played a key role in coordinating consortia of studies of lymphoma (InterLymph), lung cancer (ILCCO) and head and neck cancer (INHANCE); important results were reported on the effect of tobacco and alcohol interactions, marijuana, involuntary smoking, and family history of cancer on head and neck cancer in the INHANCE Consortium (Berthiller *et al.*, 2009; Hashibe *et al.*, 2009; Lee *et al.*, 2008; Negri *et al.*, 2009). In addition, the group continues to be actively involved in a consortia of investigators involved in molecular and genetic epidemiology of pancreatic cancer (PANC4) and squamous cell carcinoma of the esophagus (ESC3). Finally, the group has been collaborating on projects within the Asia Cohort Consortium, comprising ongoing and new prospective studies in Asia and the Pacific region.

Another important area of research for the Group is the field of diet and nutrition and their association with various cancers. The Group was successful in obtaining pilot funding from the World Cancer Research Fund (WCRF) to study the feasibility of establishing a large-scale study on dietary and lifestyle factors and the risk of esophageal cancer in Kashmir, India, a high-risk region lying within the Asian Esophageal Cancer Belt. In addition, the group has been active in the European Prospective Investigation into Cancer and Nutrition (EPIC), a large cohort of over 520 000 subjects with dietary information and biological samples. In this respect, the group has conducted a study of vitamin D receptor polymorphisms (Jenab *et al.*, 2009a) as well as blood vitamin D levels and risk of colorectal cancer, showing a strong inverse risk association (Jenab *et al.*, 2008).

In order to address the conclusions of the 2007 WCRF expert report (World Cancer Research Fund, 2007), which called for further epidemiologic research on the potential association of fruits and vegetables with reduced cancer risk, the Group was involved in studies based on EPIC to examine the association of these important food groups with the risk of colorectal (van Duijnhoven *et al.*, 2009) and pancreatic (Vrieling *et al.*, 2009) cancers. In addition, the Group led a comprehensive analysis for fruit and vegetable intake and the risk of all cancers, showing a small but significant reduction in total cancer risk with higher consumption (Boffetta *et al.*, submitted).

In an effort to identify future horizons for the field of dietary biomarkers, the Group led a comprehensive review of this topic (Jenab *et al.*, 2009b). The review highlighted a need for discovery of new dietary biomarkers, and in view of this the Group led a large collaborative grant application with the objective of identifying metabolomic profiles specific to different foods, dietary patterns and lifestyle habits.

The Group is leading a comprehensive review and meta-analysis of alcohol consumption and cancer risk, focused primarily on the dose effects of lower intake levels and on cancer sites for which previous reports have been inconclusive (Baan *et al.*, 2007; World Cancer Research Fund, 2007). The first publication from this project shows an increased risk of pancreatic cancer for consumption of 3 or more drinks per day (Tramacere *et al.*, submitted).

Another important area of work for the Group was its support to the establishment of prospective studies of cancer in populations in transition. In addition to the cohort study in the Russian Federation described in the GEP



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group, the prospective study established in the Golestan province of Northeastern Iran, an area with very high incidence of esophageal cancer, has been successful. Analyses of risk factors of esophageal cancer and other major

outcomes include socioeconomic status, high temperature beverages, tea drinking habits, tooth loss and oral hygiene, dietary habits, BRCA2 mutations and opium use (Abnet *et al.*, 2008; Akbari *et al.*, 2008; Hakami *et al.*, 2008; Islami *et al.*, 2009a; Islami *et al.*, 2009b; Islami *et al.*, 2009c; Nasrollahzadeh *et al.*, 2008; Pourshams *et al.*, 2009).

In the field of occupational cancer, a case-control study of lung cancer among European asphalt workers, aimed at clarifying whether the increased risk detected in the historical cohort phase of the study is due to exposure to bitumen fumes, exposure to other agents in the asphalt industry, or to confounders such as tobacco smoking and exposures in other industries, has been completed. The results are expected to be published in 2010–11.

For the SYNERGY project, ten case-control studies on lung cancer have been pooled to study the joint effects of selected occupational carcinogens (asbestos, PAH, chromium, nickel and crystalline silica) and tobacco smoking. A job-exposure matrix is currently being developed on the basis of measurements provided by major exposure databases of participating countries. The large dataset will also allow the investigation of many open questions in lung carcinogenesis, regarding occupational and other exposures. A close collaboration with ILCCO is anticipated, and the first results are expected in 2010.

During 2008–2009, with respect to tobacco prevention, the Group hosted one meeting (31 March–5 April 2008) of international experts to evaluate the evidence on the effectiveness of smoke-free legislation on reducing exposure to secondhand smoke, health effects and smoking behaviour, with the summary of the meeting's main conclusions published in *Lancet Oncology* in July of the same year (Pierce & Leon, 2008). The Group also completed the publication of two

volumes in the IARC series of Handbooks of Cancer Prevention on Tobacco Control; specifically, Volume 12 on *Methods for Evaluating Tobacco Control Policies* (IARC, 2008) and Volume 13 on *The Effectiveness of Smoke-free Policies* (IARC, 2009). Requests for partial translations of volume 12 into German and Japanese were received and granted. In addition, the Group coordinated a complete session on the main Handbook's findings on smoke-free policies at the 14th World Conference on Tobacco or Health, held in Mumbai in March of 2009. The Handbooks on Tobacco Control and concomitant dissemination efforts will support the implementation of WHO's Framework Convention on Tobacco Control. At present, planning for Volume 14 in the Handbooks series on *The Effectiveness of Tobacco Taxes in Controlling Tobacco Use* is proceeding, with the expert meeting scheduled for 17–22 May 2010 and the outline for the volume and corresponding authors already identified; publication of the volume is expected in 2011.

During the biennium, the Group has established preliminary contacts with researchers at the University of Sana'a and at the National Oncology Center in Sana'a, Yemen, and developed a preliminary study protocol to jointly plan and undertake a case-control study of lifestyle factors and aerodigestive tract cancer, with emphasis on the possible etiological role of khat chewing in oral, pharyngeal and esophageal cancers. This study will be the first to document if there is an association between khat use and upper digestive tract cancer in a country with a high incidence of oral cancer.

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RADIATION GROUP (RAD)

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THE SCOPE OF THE WORK IN THE RADIATION GROUP ENCOMPASSES BOTH IONISING AND NON-IONISING RADIATION.

The main objective of the research on ionising radiation is to provide answers to some of the outstanding questions in radiation protection and radiation carcinogenesis, specifically the shape of the dose–response relationship at low doses, the effects of different types of radiation, and individual variability in cancer risk and genetic susceptibility to cancer.

An unprecedented increase in the use of sources of non-ionising electromagnetic fields in occupational and environmental settings has brought public concerns about possible health risks associated with their use. At IARC, work has mainly focused on exposure to the radio frequency (RF) radiation emitted by mobile telephones.

IONISING RADIATION

Case–control studies of haematological malignancies and thyroid cancer among Chernobyl liquidators from Belarus, Estonia, Latvia, Lithuania and Russia have been finalised. The two studies included 107 cases of thyroid cancer and 117 cases of malignancies of lymphoid and hematopoietic tissue, and 904 controls. For all haematological malignancies combined, the Excess Relative Risk (ERR) per 100 mGy was 0.60 (90% confidence interval (CI): -0.02–2.35) (Kesminiene *et al.*, 2008). The corresponding estimates for leukaemia

excluding chronic lymphoid leukaemia (CLL), and for CLL were 0.50 (90% CI 0.38–5.7) and 0.47 (90% CI n.d.–7.6), respectively. A significantly elevated risk was observed for thyroid cancer, similar to that obtained in the recent studies of thyroid cancer following exposure to iodine-131 in childhood; the ERR per 100 mGy was 0.38 (95% CI 0.10–1.09) (Kesminiene *et al.*, submitted).

The **GENE-RAD-RISK** project was established to formally evaluate whether pathogenic alleles in DNA repair and damage recognition genes have an increased risk of breast cancer following exposure to ionising radiation, even at low doses. A multi-national study (France, Italy, the Netherlands and the UK) of pre-menopausal breast cancer risk is underway in populations chosen on the basis of their high prevalence of radiation exposure (childhood cancer and Hodgkin lymphoma survivors) and/or high prevalence of known mutations in susceptibility genes (BRCA1 and BRCA2 mutation carriers). More than 600 cases of breast cancer have been identified to date in the cancer survivor and Hodgkin lymphoma cohorts, and nearly 1500 cases in the mutation carrier cohorts. Data collection and dose reconstruction have been completed, and analyses are expected to be completed in early 2010.



Courtesy of J. Seppala, Turku University Hospital, Finland

Diagnostic radiation represents an indispensable, sometimes life-saving, tool in modern medicine. However, the growing use of diagnostic X-rays and of relatively high-dose techniques (CT scans, interventional procedures) is a topic of concern in radiological protection, especially in children and adolescents. The increasing use of paediatric diagnostic exposures is therefore a unique opportunity to address the possible health effects of low doses of radiation in an a priori particularly sensitive population. The **Child-Med-Rad** project is aiming to assess the feasibility of establishing trans-national cohorts suitable for long-term follow-up and to make recommendations concerning future research needs. The countries included in this project at the outset are: Denmark, Finland, France, Germany, the Netherlands, Spain, Sweden and the UK. Scientists from Australia, Canada, Israel, Japan, Korea, and the USA and from the WHO (Geneva) are also involved as experts to ensure that planned studies are fully harmonised with other existing or planned activities around the world.

Despite numerous studies, the exact consequences of the Chernobyl accident remain a matter of debate, and the future

direction of health research has been subject to wide differences of opinion. The **Agenda for Research on Chernobyl Health (ARCH) project** is conducting a 'scoping study' of all relevant research to determine where research efforts are most needed and to advise on the potential value of proposed studies to public-health decision making. The main output of ARCH will be a strategic research agenda (SRA) for short-, medium- and long-term research on the health consequences of the accident. The development of a sound SRA necessitates the coordinated efforts of a critical mass of experts with knowledge of the accident's impact on human health. Project partners are dispersed throughout Europe, including the three most affected countries, Belarus, the Russian Federation and Ukraine.

NON-IONISING RADIATION

The **INTERPHONE Study**, a series of multinational case-control studies established to determine whether mobile telephone use increases the risk of cancer and, specifically, whether the radio-frequency radiation emitted by mobile telephones is carcinogenic, has now been completed. Separate studies have

been carried out for acoustic neurinoma, glioma, meningioma and tumours of the parotid gland. These studies used a common core protocol and were carried out in Australia, Canada, Denmark, Finland, France, Germany, Israel, Italy, Japan, New Zealand, Norway, Sweden and the UK. Details of the study protocol and procedures have been published (Cardis *et al.*, 2007). A manuscript presenting the results of the international analyses of the relation between mobile phone use and risk of glioma and meningioma has been submitted for publication.

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