

H. Boeing

## Nutritional Epidemiology: It's role in nutritional science and future perspectives

One of the most important discoveries of nutritional science during past years regards the fact that nutritional factors are involved in many biological mechanisms which are linked to chronic diseases. The evidence of a diet-disease relationship was generated by different nutritional scientific disciplines. Important contributions came from basic biochemistry, animal experimentation, and metabolic studies. However, the complexity of the pathogenesis of most chronic diseases usually does not allow us to relate results from experiments directly to human disease risk, in particular, since most of the experimental findings are derived from animals, or *in vitro* systems.

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### Definition of nutritional epidemiology

The study of disease risk in humans is the subject of epidemiology, a relatively young scientific discipline. In one of the first textbooks of epidemiology Lilienfeld (6) defined epidemiology as: "*The study of the distribution of a disease or a physiologic condition in human populations and of factors which influence this distribution*". Subsequently, several epidemiologists extended this 'narrow' definition of epidemiology by adding other mostly preventive aspects. The dictionary of epidemiology (5) lists

under epidemiology: "*The study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to control of health problems*". Nutritional epidemiology deals with diet as a potential determinant of diseases and is therefore an exposure defined subdiscipline of epidemiology similar to occupational or environmental epidemiology. Exposure is a generic epidemiological term and refers in the context of nutritional epidemiology to the amount of a factor to which a group or individual is exposed (5).

The major aim of nutritional epidemiology is to understand the relation of diet and disease risk. This is done by relating dietary exposure to disease occurrence using different study designs and research tools. In the long run, the summary of such findings will elucidate causal principles explaining morbidity in populations. However, it is far from clear whether the specific exposure observed to be associated with increased or decreased risk reflects the correct biological mechanisms. The correct biological meaning of epidemiological results can only be clarified according to the current knowledge which itself is depending on basic science.

Other scientists often reduce nutritional epidemiology to dietary assessment. It is true that dietary assessment and all related methodological issues such as measurement error play an important role in nutritional epidemiology. Meanwhile, nutritional epidemiology has a variety of dietary measurement instruments available, which are investigated in detail and tested for validity and reliability. In practice, there is hardly an area to find which shows such a continuous effort in understanding the performance of the exposure assessment methods as in nutritional epidemiology. Partly these efforts are owed to the complexity of diet. Research already showed that not only food, food constituents, and supplements but also food preparations, food additives, and contaminants are linked with disease risk.

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Dr. H. Boeing  
Department of Epidemiology  
German Institute of Human Nutrition  
Arthur-Scheunert-Allee 114-116  
D-14558 Bergholz-Rehbrücke  
Germany

A new area of research into nutritional epidemiology was opened by using biomarkers as a tool for assessment of exposure and early disease. Biomarkers have the advantage that they reflect biologically meaningful mechanisms. However, only a few parameters have been identified so far that can replace dietary assessment methods. Despite the current lack of biomarkers for dietary intake, their use in individual based epidemiological studies will open new areas of research. For instance, the endocrine levels in blood, and the concentration of xenobiotics and other metabolic parameters, can now individually be assessed and applied in risk analyses.

## Methods of nutritional epidemiology

Epidemiology is particularly helpful for experimental scientists to test their research results in a broader context of free-living individuals and risk of the chronic diseases as endpoint. Such testing of experimental hypotheses is a strength of epidemiology and deserves a close interaction between experimental science and epidemiology. 'Molecular Epidemiology', for instance, is describing this development and also covers new fields such as molecular genetics.

In the past, case-control studies dominated the research approach. Such studies include diseased and healthy subjects and evaluate the dietary habits in the past and before the disease occurred. It was frequently shown that such retrospective assessment of exposure is of limited value in the case of nutrition and is especially prone to recall bias. Such recall bias induces measurement error and will generate biased results if differentially occurring between study groups. In addition, the selection of the control group in a case-control study may not represent the dietary habits of the population from which the cases arose. Therefore, case-control studies are not considered as the preferred study design in nutritional epidemiology.

Cohort studies are now the preferred study design in observational nutritional epidemiology (2). Such studies usually comprise several ten-thousands of participants. In this design the current usual nutritional habits are measured at a baseline examination in unaffected subjects and the cohort is followed over time for new diseases. For each nutritional factor, disease risk over time will be calculated and compared. It is easy to include in cohort studies the collection of blood or other biological material. The collection of biological material is usually done at the baseline examination because at that time period the study subjects are not affected by major chronic diseases. Therefore, the biological material will be a meaningful source of information regarding the preclinical situation. The biological material is stored for future use and will only be analysed for those with new diseases and age and sex matched controls from the cohort population. The analysis of cohort studies for disease risk requires a suffi-

cient number of new cases of the disease of interest, usually more than 100. It can take decades before the required number of new diseases occurs in a cohort study in particular if the study population is small and/or the disease rare.

Intervention studies with supplements or changing habitual food pattern are derived from the classical experimental study design and are considered as the type of study that prove preventive measures. Similar as in other epidemiological study designs disease risk is calculated and compared for the experimental (intervention) and the control arm of the study. Only positive evidence of a link between intervention and reduced disease risk coming from such studies allows prevention on a large scale. Such a study is currently underway in the US, in which dietary measures such as reduction of fat and increase of fruit and vegetable will be investigated whether they can reduce the risk of breast cancer, cardiovascular diseases and osteoporosis (<http://www.nhlbi.nih.gov/nhlbi/whi1/>). More than 45 000 women participate in this study named 'Womens Health Initiative', which will need about 9 years of follow-up for definite results. Recently, other major intervention studies were able to show that supplementation of a substantial amount of  $\beta$ -carotene and tocopherol per day for many years in smokers did not influence Coronary-Heart-Disease mortality, but even increased the risk of lung cancer in case of  $\beta$ -carotene (1). These findings were obtained despite our (previous) conviction that antioxidants are beneficial because of the many studies showing that they scavenge radicals and prevent oxidation. This example of a non-positive effect demonstrates well that conclusions regarding prevention of diseases need solid epidemiological data and the full spectrum of epidemiological and experimental approaches.

Currently the most important nutritional epidemiological data base in Germany is a large cohort study conducted by the Department of Epidemiology at the German Cancer Research Center in Heidelberg and the Department of Epidemiology at the German Institute for Human Nutrition Potsdam-Rehbrücke (7). This cohort comprises about 53 000 study participants (25 500 in Heidelberg and 27 500 in Potsdam) and is part of the EPIC cohort, a European-wide project with more than 460 000 study participants and a particular focus on nutrition and cancer (3). In the German EPIC-Study from nearly all study participants biological material was collected during the baseline examination from 1994 to 1998 and is stored in liquid nitrogen. The Potsdam group especially will exploit their cohort for many disease endpoints. Other prospective data with dietary measurements are available from the MONICA-Study Augsburg which includes about 1 400 study participants with 7-day food records and about 14 000 with a short list of food consumption frequencies (4).

## Training in methodological epidemiology

There are different ways to become a nutritional epidemiologist. One way is practising nutritional epidemiology supplemented with additional courses offered by summer schools. Another way is going through an official academic training in epidemiology.

In the US, academic training in epidemiology is organized by the Schools of Public Health. In contrast to the Schools of Medicine, the Schools of Public Health have their focus on the entire population rather than on individual patients. A School of Public Health is usually organized in departments representing scientific disciplines such as Biostatistics, Epidemiology, Nutrition, Health Care, International Health, etc.. The training of epidemiology takes place in the Department of Epidemiology and includes master and PhD-degrees. The internet pages of the American Association of Schools of Public Health lists 31 accredited Schools of Public Health (<http://asph.org/listsph.htm>). Some of the Schools indicated departments of 'Epidemiology' as well as of 'Nutrition'. These schools are also centers of nutritional epidemiology: University of Massachusetts, Harvard University, University of North Carolina, Loma Linda University, and University of California, Berkeley. At the School of Public Health, University of Minnesota, the department of epidemiology is offering a study of Public Health Nutrition.

In Europe the situation is not as clear as in the US. Formal training in epidemiology can be obtained in several countries with different concepts. In the UK and the Netherlands the training is similar to the US. Other countries allow persons to study Public Health directly, in which epidemiology is a subject among others. In Germany, 6 universities (München, Bielefeld, Hannover, Bremen, Berlin, Dresden) are offering a two-year postgraduate study in Public Health. These studies are multidisciplinary, including epidemiology, and provide a Magister of Public Health degree. Due to the recent

establishment of such studies the scientific profile of each faculty is not so clear yet. München and Bremen declare to have a specialization in epidemiology. However, in none of the German Institutes of Public Health a link to nutritional science exists. On the other hand, none of the 7 German Institutes of Nutritional Sciences has established a particular professorship in nutritional epidemiology only. Nutritional epidemiology is also not a major subject in the curriculum of diploma studies for nutritionists.

In 1985 the German Academic Exchange Organization (DAAD) decided to establish a specific program that supports the training of German scientists in epidemiology. In the following years more than 200 scientists including nutritionists were trained as epidemiologists nearly exclusively in the Anglo-Saxon countries and are mostly now working in Germany. This program was stopped in 1996, a period in which the first German Public Health studies were fully established.

## Conclusion

Science just recently started to understand the conditions and requirements under which diseases occur and can probably be prevented. It is now clear that diet will be one of the most important factors in chronic disease development. It was shown that nutritional epidemiology has, together with other disciplines of nutritional science, the potential to substantially contribute to elucidating the exact role of dietary factors. This contribution of nutritional epidemiology is not restricted to particular epidemiological approaches or study designs, but has to be adequate to the research question. In some areas, such as disease risk in humans and prevention of chronic diseases, epidemiology is the only approach that can give proof of scientific hypotheses. The scientific community needs to acknowledge this fact by providing resources for academic training and research opportunities.

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