Gene-environment interactions in obstructive pulmonary diseases

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From conception onwards there is continuous interaction between the human being and the environment that sometimes leads to the development of complex diseases. The significant increase in chronic respiratory diseases observed in recent decades raised awareness of this interaction, and after intense research it is now generally acknowledged that their aetiology involves a complex interplay between the genetic background and multiple environmental exposures. Technological advances in the field of genetics, including completion of the Human Genome Project and implementation of genome-wide association analysis, have led to a rapid increase in the number of suggested susceptibility genes for asthma and other environmentally induced chronic respiratory diseases. This "explosion of knowledge" which has resulted from increasing evidence of the role genetic factors play in disease pathogenesis and the tremendous evolution in the field of clinical genetics, may discourage the respiratory clinician from pursuing "new knowledge".

The aim of the series presented in the current and following issues of the journal "PNEUMON" is to provide a detailed overview of the role of gene-environment interactions in obstructive respiratory diseases. Greek colleagues with expertise in the field, with the contribution of Professor Holloway in the asthma section, provide a comprehensive overview of the effects of these interactions in the development of pulmonary diseases[1], and specifically asthma[2], chronic obstructive pulmonary disease (COPD)[3] and obstructive sleep apnoea-hypopnoea syndrome[4].

Currently genome-wide association study (GWAS) is the most popular technique used to investigate the genetic basis of complex diseases[5]. Such studies represent an advanced approach for exploring the totality of genes associated with disease prevalence. The results of such studies are expected to elucidate causal pathways or pathogenetic mechanisms, to aid in the identification of sensitive individuals, and to contribute to the formulation of methods of disease prevention and treatment[1,2]. It should be noted, however, that in studies of disease, meticulous phenotypic classification of the cases with that disease and careful selection of an appropriate disease-free control group are essential, along with attention to adjustment issues for the enormous number of multiple comparisons. These are all critical steps that when not addressed could challenge the validity of the study results[6,7].

When researchers examine environmental risks they tend to concentrate

on a particular category of exposures, treating different risk factors separately. This approach is evident in our own series[1-4]. Although the aim of the studies included here was to determine the interaction between environment and genetics, concrete environmental risk factors were isolated and examined separately, while the assessment of the "total dose" has mainly been based on questionnaires. In reality, people are exposed to several environmental risk factors concurrently and the effects are not necessarily additive. The joint effects of different environmental risks are needed to present a full picture of the population burden of environmental risk, and greater reduction in disease may be obtained by effecting coordinated reduction in several environmental risks that act jointly on that disease. Imprecision in the measurement of interaction between genes and environment has the potential to under- or overestimate the real effects and lead to erroneous conclusions. It is not yet clear how accurately the balance of environmental exposures under study (pollution, diet, occupation, infections, etc.) reflects the real effects of "the environment" on our genes in leading to the development of chronic disease. After realization of the desperate need we have for determining the environmental equivalent of GWAS, that is, methods for the determination of an individual's environmental exposure with the same precision as we have for the individual's genome, Christopher P. Wild[8] suggested "…that there is need for an "exposome" to match the "genome"… At its most complete, the exposome encompasses life-course environmental exposures (including lifestyle factors), from the prenatal period onwards." As pointed out by Rappaport and Smith[9] all these exposures contribute to a greater or a lesser degree to the development of chronic diseases and "should be investigated collectively rather than separately". The development of the appropriate exposure indices and of the tools necessary for their precise measurement is a major challenge because, unlike the genome, the exposome is continuously evolving throughout the lifetime of an indivitual[10,11].

The journey for the discovery of the "exposome" has just started…

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