

ciated with increasingly severe asthma both acutely and in terms of chronic morbidity. Reducing exposure to a relevant allergen decreases chronic severity in controlled clinical trials.

In population studies, specific IgE is detected in from 80–90% of asthmatic children by skin prick tests or by serologic tests. The pattern of specific IgE reflects environmental exposure usually including house dust mite, cat, dog, rodent, cockroach, mold and pollens. The pattern seen in a individual or a particular population reflects patterns of chronic exposure. For example, in dry or cold climates or on US inner cities, the rate of sensitization to house dust mite is low, while in maritime climates it is very high. Sensitization to ragweed pollen is rare in Europeans because the plant is indigenous to North America and almost unknown in Europe. These patterns then may lead to investigation of exposure sources. For example, mold is a common target of specific IgE, but environmental sources of exposure to these important allergens have not yet been discovered. In another example, the frequency of IgE antibody to cat and dog is unrelated to environmental exposure in homes; this paradox has led to immunologic hypotheses to explain the lack of association and to more extensive search for other exposure sources. Thus, in the sense that IgE is a marker for exposure reflects the exposure dose and is important in the pathophysiology human disease, it is an important biomarker in asthma and other respiratory disease.

326 GENOMICS AND METABOLOMICS: NEW GUIDES FOR HEALTH AND DEVELOPMENT

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The knowledge and tools of genomics (DNA micro-arrays, bioinformatics) are dramatically changing life sciences research, with early successes in pharmacology identifying targets, validating efficacy and recognizing individual variation in drug responses. The tools of genomic revolution are now merging with more traditional analytical technologies to provide the means to understand how complex environmental inputs including genetics, toxins, pathologies and metabolism affect individual health from a global perspective and yet in molecular detail.

The developments of genomics is transforming the concept of improving health. Nutrition need no longer pursue a reductionist pursuit of one potentially critical reaction whose dysregulation is diagnosed by one ideal biomarker. Rather, nutrition is becoming an integrative science in which a significant fraction of all regulated genes proteins and metabolites can be studied as a system. While the invention of DNA arrays precipitated the change in perspective, several techniques developed over the past to measure metabolites (e.g., fatty acids, amino acids, hormones) are being industrialized to highly parallel throughput. Automated separation techniques coupled to mass spectrometry make high throughput metabolite analyses possible. In fact, because the numbers of genes and activated enzymes involved in each metabolic situation are huge relative to the number of metabolites access to metabolites as end-points will be the easiest way to understand gene functions. Quantitative analyses of lipids in tissues and accessible body fluids provides an example of the power of metabolomic approaches for identifying the integrative effects of genetic predisposition to dysfunction and for guiding pharmacologic and nutritional interventions to recover function and yet minimize side effects. Addressing conditions such as diabetes, have proven the principles and now these techniques are being used to tackle more complex problems related to diseases of completely unknown cause such as Autism.

327 INCREASED INFLUENCE OF GENETIC VARIATION ON PARAOXONASE GENE EXPRESSION IN NEONATES

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Effects of functional polymorphisms in the coding region of a gene normally remain constant throughout the life of an individual. Effects of polymorphisms in the promoter region of a gene, which may affect the level of transcription, may vary unless the same transcription factors interact with the promoter in the same way throughout life. Paraoxonase-1 (*PON1*) is an example of a gene with common polymorphisms both in the promoter (-909, -162, -108) and the coding region (M54L, Q101R). Its product, PON1, is found bound to HDL and protects both HDL and LDL from oxidation. PON1 has arylesterase activity and protects against cholinesterase inhibition by cleavage of organophosphate oxons.

The five *PON1* genotypes as well as *PON1* enzymatic activities were determined for maternal (N=412) and cord blood (N=231) as part of a study of the effects of organophosphate pesticide exposure on neurodevelopment. The population contained similar numbers of Caucasians, Caribbean Hispanics and African-Americans. *PON1* enzymatic activity was strongly dependent upon the promoter alleles in both maternal and cord blood. For example, *PON1* activities for position -909 C/C, C/G and G/G mothers were 14.1, 133 and 116 arylesterase U/ml, (ANOVA, p<0.001), whereas the same *PON1* activities for the respective cord bloods were 46.7, 35.7 and 20.6 U/ml (p<0.001). The trends were independent of race/ethnicity. Thus, not only do neonates have reduced capacity to detoxify organophosphates compared to adults, but this lower capacity is more strongly influenced by genotype than in adults. Because the five polymorphisms in *PON1* occur in a short stretch of DNA, they were tested for linkage disequilibrium. Significant linkage disequilibrium was found between the -909 alleles and M54L for Caucasians and Hispanics. Linkage between the -909 alleles and Q191R was not significant. Additional significant linkage disequilibrium was observed between the -909 alleles and the other polymorphic promoter alleles as well as between the -909 allele and a polymorphism in the linked gene *PON2*.

Agriculture

330 USE OF LABORATORY GENERATED DUST AS PROXY EXPOSURE INDICATOR IN AGRICULTURAL FIELD OPERATION

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Agricultural workers are prone to exposure to mixed dust of inorganic and organic compounds. Diverse working conditions and operations in agriculture make direct measurements of the mixed dust exposure difficult. This study was conducted to develop a new dust generation system to determine possible exposure potency indicators of soil samples. The dust generator consists of a blower, a rotating chamber and a settling chamber. The rotating chamber has inner baffles to provide sufficient agitation of the samples while the chamber is rotating. A blower provides air into the rotating chamber, and the suspended dust is moved to the settling chamber through a perforated pipe. A small fan inside the settling chamber helps maintain suspension of the dust. Various size fractions of dust are sampled on filters suspended in the chamber via outlet ports and attached pumps. Air pressure is released through a filter plate mounted on the wall of the settling chamber. The following operating conditions were used to optimize results for dust sample: 300 g soil sample, blower choke 1/4 open, sampling time of 3 minutes, rotation speed of 16 rpm. To evaluate the characteristics of dust from the generation system, we collected dust samples from agricultural fields while the soil was prepared for planting. Bulk soil samples were collected from the fields where dust samples were collected. Analytical results using X-ray diffractometry (XRD) for mineralogical composition, and scanning electron microscope energy-dispersive X-ray spectra indicated that mineralogical and elemental characteristics of laboratory-generated dust and agricultural field dust are similar. It was observed that soils with higher silt and clay percentages produced more dust than soils with higher sand content. Soil with higher moisture content produced less dust than the same soil at lower soil moisture content. The results suggest that the new dust generation system can provide valuable information about soil dust characteristics.

331 STUDY OF IMMUNE EFFECTS IN CORN FARMERS WITHIN THE AGRICULTURAL HEALTH STUDY

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When compared to the general population, farmers have an increased risk of non-Hodgkin's lymphoma (NHL). Factors that contribute to this excess risk have not yet been identified. While several epidemiologic studies have observed an increased risk of NHL among farmers who are exposed to certain pesticides (i.e., phenoxyacetic acids, organophosphates, organochlorines, and triazines), these studies have not been conclusive. In addition, a clear mechanistic association between farming or pesticide exposure and subsequent development of cancer has not been identified. It has been hypothesized that altered immune function may be an indicator of increased potential for the development of immunologically-based diseases such as NHL. Therefore, research into immunologic perturbations due to farming activities and exposures holds some promise in discerning disease mechanisms and in identifying specific etiologic agents for immunologically-based diseases such as NHL. Few such studies have been conducted. We have recently launched a study of immune effects in corn farmers within the Agricultural Health Study (AHS) cohort. The main objective is to evaluate the changes in immune function throughout the growing season. Farmers and control subjects will be contacted just prior to planting (March-April) to be enrolled in the study. Biological sampling before and after planting and application of preemergent pesticides including atrazine will allow examination of short-term biological effects associated with specific pesticide exposures and general planting activities (e.g., tillage). The first postemergent application of chlorpyrifos will also be monitored, in order to evaluate short-term biologic effects associated with this organophosphate insecticide exposure. Mid-season, post-harvest, and off-season samples will be collected to allow evaluation of overall immune effects of farming activities during one growing season. Pesticide exposures (e.g., atrazine, organophosphates, and potentially 2,4-D or carbamates) will be primarily assessed by measurement of the parent compound or its metabolites in urine, and by empirical exposure modeling based on supplementary information on farming activities and work practices. Immune function will be assessed by means of multiple assays including complete blood cell- and differential cell counts, direct measurement of cytokines, immunoglobulins, and autoantibodies in plasma, and functional assays involving stimulation of cultured lymphocytes to measure proliferation and cytokine production. Farmers will serve as their own self-controls, and a selected control group will provide a means for external comparison. By presentation of our study design and preliminary field experience, we hope to stimulate discussion regarding effective conduct of such mechanistic studies in exposed populations.

332 MORTALITY AMONG A COHORT OF FEMALE FARM RESIDENTS IN NEW YORK STATE

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A retrospective cohort study of mortality among 6,405 female farm residents who are New York Farm Bureau members or members' spouses or relatives was conducted from 1980 through 1993. Similar to the previous findings for New York State male farmers, the female farm resident cohort experienced significantly lower mortality rates for all causes including malignant neoplasms compared to rural non-farm female residents. The findings suggest that farmers of both genders had favorable habits with respect to several life-style factors, and they therefore agree with results from other studies on farmers.

333 AGRICULTURAL CHEMICAL EXPOSURE AND BIRTH DEFECTS IN THE EASTERN CAPE, SOUTH AFRICA.

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Introduction: A case - control study was conducted in the rural area of the Eastern Cape, South Africa, to investigate the association between pesticide exposure and the prevalence of congenital malformations in agricultural workers. A total of 89 cases and 178 controls were interviewed. Data from the Register of the Department of Paediatrics at the Cecilia Makiwane Hospital were analysed with regard to birth defects. The cases were those who were diagnosed with selected defects during the first year of their lives. Controls were