

### 1991 META-ANALYSIS OF ASBESTOS-RELATED DISEASE AMONG SKILLED CRAFTSMEN IN VARIOUS OCCUPATIONAL SETTINGS.

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A number of epidemiology studies have evaluated the risk of asbestos-related disease for different categories of workers who were potentially exposed to asbestos in non-manufacturing occupations over time. In this presentation, we provide an extensive review of the available literature on this topic, and present the methodology and key findings of a meta-analysis of asbestos-related disease among skilled craftsmen in various occupational settings. Our initial review of the literature included over 100 published and unpublished studies that were identified during various search efforts. Studies were included in a meta-analysis based on an evaluation of study and control populations, source of mortality data, diagnostic methods, exposure classifications, time period of exposure, latency period, and possible confounders. The different crafts evaluated were insulators, pipefitters and plumbers, boilermakers, carpenters, electricians, laborers, millwrights, sheet metal workers, and welders. Separate analyses were also performed for study setting (shipyard vs. non-shipyard) and disease outcome (mesothelioma vs. lung cancer). The results of each analysis yielded relative risk (RR) estimates and 95% confidence limits. Our findings indicated that, not surprisingly, the greatest risk of asbestos-related disease was historically observed among workers with the most potential for asbestos exposure, such as insulators or crafts employed in Naval shipyards, and workers with the longest duration of exposure. Elevated relative risks were also observed for some other crafts in non-manufacturing occupations, such as in the construction industry, where sprayed asbestos or insulation removal activities often occurred. Despite some limitations, the results of this analysis were generally consistent with prior estimates of asbestos exposure for various craftsmen in different occupational settings.

### 1992 CHARACTERIZATION OF RISKS TO WELDERS DUE TO EXPOSURES TO ASBESTOS IN WELDING ROD FLUX.

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Due to its unique chemical properties, chrysotile asbestos was formerly incorporated into a wide variety of products, including the outer covering, or "flux" of certain classifications of general arc welding electrodes. The purpose of this analysis was to review the historical exposure and epidemiology information relevant to asbestos in welding rods and assess whether mild steel welders are at increased risk of developing asbestos-related diseases as a result of welding rod use. We found that studies that have attempted to measure airborne asbestos directly in welding rod fumes found no measurable fibers; this is likely due to the fact that the fibers degrade at the high temperatures present in the welding arc. In addition, "worst-case" use simulation studies, specifically intended to generate airborne flux particles, reported that airborne concentrations were undetectable or very low. The airborne concentrations generated were always below the current OSHA permissible exposure limit (0.1 f/cc TWA), and the lifetime doses associated with "worst-case" use were found to be far below plausible thresholds for mesothelioma and lung cancer. The epidemiology literature is complicated by the fact welders often experienced significant "bystander" exposure to amphibole-containing insulation. We have reviewed over 65 studies of asbestos-related disease that either specifically examined welders or included welding as a job category. Of these, roughly 40% concluded that welders are not at an increased risk of developing mesothelioma or lung cancer; approximately 60% concluded that there is an increased risk of one or both diseases. Of these latter studies, 1). there was almost always clear evidence of significant insulation exposure, and 2). none of the authors attributed the disease to exposures to asbestos in welding rod flux. We conclude that the weight of evidence indicates that welders were not historically at risk of developing asbestos-related diseases as a result of welding rod use.

### 1993 CATEGORIZATION OF ASSOCIATIONS BETWEEN EXPOSURE TO THE HERBICIDES USED IN VIETNAM OR THEIR CONTAMINANTS AND HEALTH OUTCOMES.

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Between 1962 and 1971, United States military forces sprayed herbicides over Vietnam. Because of ongoing uncertainty about the long-term health effects on Vietnam veterans of the herbicides sprayed, Congress passed the Agent Orange Act of 1991. That legislation directed the Secretary of Veterans Affairs to request the National Academy of Sciences, a non-profit organization that provides independent, objective advice on scientific issues, to perform a comprehensive review and evaluation of scientific and medical information regarding the health effects of ex-

posure to Agent Orange, other herbicides used in Vietnam, and the various chemical components of those herbicides, including dioxin. The first comprehensive review was published in 1994 and biennial updates have integrated all subsequent relevant peer-reviewed information. In assessing the evidence for an association of exposure to the herbicides or their components with a health outcome, the committee responsible for the report reviews the available literature and categorize the evidence as 1) sufficient for an association; 2) suggestive of an association; 3) inadequate or insufficient to determine whether an association exists; or 4) suggestive of NO association. In addition, conclusions regarding the biological plausibility of the health effects and the risk to Vietnam veterans are made. The latest of reports, Veterans and Agent Orange: Update 2006, will be released in March 2007. The assessments in the reports are used by the Department of Veterans Affairs to make policy decisions regarding compensation to veterans for service-related illnesses. The methods used by the committee, as well its most recent conclusions, will be discussed.

### 1994 CHILDHOOD CANCER AND PESTICIDES: POSSIBLE GENE-ENVIRONMENT INTERACTIONS.

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**Introduction:** Growing evidence supports the association between pesticide exposure and pediatric acute lymphoblastic leukemia (ALL). Studies of the association of pesticides with ALL have been limited by ecological study designs, reliance on self-reported exposures, and lack of biological measurements.

**Study Question:** Does the interaction between environmental factors (pesticides) and genetic polymorphisms lead to childhood cancer.

**Methods:** Genomic DNA was extracted and SNP analysis conducted for GPX1, COMT, PON1, GSTM1 and GSTT1. Urine specimens were analyzed for pesticide content using Tandem Mass Spectrometry.

**Results:** Metabolites of organophosphorus pesticides (OP) had elevated levels in cases compared to controls. Overall, for most compounds these correlations were not statistically significant. Genetic polymorphisms in several genes for xenobiotic metabolizing enzymes indicated that cases were more likely to be impaired in their ability to detoxify OP relative to controls. The odds ratios for the three PON1 genotypes increase with the increase in the number of copies of mutant gene. For mothers the OR for GG vs. AG is 2.08 [95% CI: (0.41, 11.79); p=0.51], while the OR for GG vs. AA is 4.58 [(0.81, 28.31); p=0.10], indicating a trend of increasing risk with increasing number of copies of the A allele. The trends in the OR for children were similar: OR for GG vs. AG is 1.41 [95% CI: (0.21, 11.08); p>0.99] while OR for GG vs. AA is 3.33 [(0.32, 37.60); p=0.48].

**Conclusions:** The results of this pilot study suggest that cancer cases were more likely to be impaired in their ability to detoxify OP relative to controls.

### 1995 FAMILIAL INTERSTITIAL PNEUMONIA (FIP) IS PHENOTYPICALLY AND GENETICALLY HETEROGENEOUS.

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The Idiopathic Interstitial Pneumonias (IIPs) are complex conditions, with limited treatment options and unknown etiology. A whole genome microsatellite screen for Familial Interstitial Pneumonia (FIP, the familial form of IIP), revealed multiple linkage peaks on chr 10 with a maximum LOD score of 2.1. To determine if either phenotypic classification or environmental exposures could better define the linkage peaks, ordered subset analysis (OSA) was conducted. In the presence of genetic heterogeneity, OSA uses family level covariate data to define a more homogeneous subset of families that maximize linkage. The 83 families were divided into 2 phenotypic classifications: 40 homogeneous families where all cases were diagnosed with the idiopathic pulmonary fibrosis type of IIP and 43 heterogeneous families where more than one type of IIP was observed within each family. Smoking (proportion of cases that ever smoked in a family) and age of onset (average age of diagnosis for cases in a family, and youngest age of diagnosis in a family) were also investigated as covariates using OSA. On chr 10, an early age of onset was found to increase evidence for linkage amongst all families (LOD 2.1 to 3.2) and the homogeneous families (LOD 1.9 to 3.7, p=0.01 at the more centromeric peak), while cigarette smoking was found to be suggestive of an increase in linkage amongst all