Meetings

Air Pollution and Health

Health hazards caused by air pollution were discussed at the 7th annual Air Pollution Medical Research Conference in Los Angeles, 10–11 February 1964. The conference featured reports on acute episodes of community air pollution, studies of long-term effects of air pollution, experimental human exposure studies, experimental animal and plant research, new methods for evaluating biologic significance of air pollution, mechanisms of infiltrative lung disease, and epidemiologic methods for studying chronic respiratory diseases.

In a lecture on "The Natural History of Respiratory Tract Mucus: Secretion, Transport, Disposition" Lynne Reid (Brompton Hospital, London) described the base-line activity of the cells secreting mucus in the respiratory tract. In the absence of stimuli such as London smog, infection, and cigarette smoke, secretion amounting to about 100 milliliters per day is thought to occur. The presence of various irritants can lead to hypersecretion and can eventually lead to hyperplasia. Chronic bronchitis is characterized by hypertrophy of the mucous gland layer, as estimated by the gland-to-wall ratio. A condition similar to chronic bronchitis can be produced in rats by exposure to sulfur dioxide. The cells secreting mucus were studied by staining for mucopolysaccharide before and after subjecting the section to neuraminidase. After the addition of radioactive sulfate to tissue culture, autoradiography can be used to study secretory activity.

Epidemic asthma in New Orleans occurred again during 1963, according to Weill *et al.* (New Orleans). Previous studies had implicated air pollution from a burning dump, and measures to control this condition had been undertaken. It was hoped that the comparison of the 1963 data with those of 1962 would show a decrease in the sharpness of the asthma episodes if the burning dump were in fact a major contributor to the asthma attacks. But, contrary to what had been expected, the outbreak peaks were higher, more frequent, and there was a generally higher incidence of daily admissions. Sixty percent of the affected patients reacted with positive skin tests to one or more atmospheric sample extracts. Of the patients studied only 31 percent were cigarette smokers.

Greenburg and Field (New York) studied asthma admissions to hospitals in New York, and found abrupt increases in the fall months which were unassociated with high air pollution levels or pollen or mold counts. Data suggest that an abrupt onset of cold weather is associated with increased asthma attacks. Booth *et al.* (Cincinnati) examined asthma admissions for metropolitan hospitals in Washington, D.C., Philadelphia, Chicago, Evanston, Charleston, Norfolk, New York City, and New Orleans. While seasonal trends were observed, there was no evidence of epidemics similar to those in New Orleans.

Cassell *et al.* (New York) described two acute air pollution episodes in New York City. One occurred in November and December 1962, and was associated with increased frequency of chronic cough in a population under weekly surveillance. The other, in October 1963, was associated with increased eye irritation but not with cough. Greenburg and Field also studied these two episodes. During the December 1962 episode in New York City they found an increase in upper respiratory infections at five old-age homes. They found no measurable change in morbidity from other causes during the two incidents of air pollution. These findings suggest that New York City is experiencing air pollution episodes both of an oxidizing (Los Angeles) type and of a reducing (London) type. Data from student nurses related the oxidant level to eye irritation (Hammer *et al.*, Los Angeles). No association in this group between cough or sneeze and the oxidant level was shown.

In a discussion on long-term-effects of air pollution, Phelps (Fort Belvoir, Virginia) reported on a follow-up of military personnel who first developed a respiratory disease while in the Tokyo-Yokohama area. Of 244 cases who were returned to the United States, 64 percent still had abnormal pulmonary function in 1962, and emphysema was present in some. Of 40 subjects who had been back in the United States for 2 or more years, 30 still had cough, wheezing, and shortness of breath. Most subjects still had significant decreases in the forced expiratory volume, and a few had actual increases in their residual volume measurements. All but one of these were cigarette smokers. Anderson and Ferris (Vancouver, British Columbia and Boston) compared respiratory surveys of two small communities; one had significant air pollution and the other had none. Survey methods were very similar and in both cases over 95 percent of the sample was surveyed. Most of the differences in respiratory rates could be explained by differences in age and cigarette smoking. When corrections were applied, there were no important differences between these two communities. Pulmonary function results, corrected for age and smoking categories, were somewhat higher in the area with low air pollution. Reasons other than air pollution might explain the findings with respect to pulmonary function. Holland *et al.* (London), using the standardized respiratory survey and with data from outside plant telephone workers, compared the prevalence of respiratory findings in London, in rural England, and in the eastern United States. Persistent cough and phlegm in comparable groups were more frequent in London compared with rural areas and least frequent in the eastern cities of the United States. This gradient was confirmed by the mean value of the 1-second forced expiratory volume, and by the volume of sputum. The effects of smoking were prominent in all areas. Deane and Goldsmith (Berkeley), using comparable methods and populations in Los Angeles and San Francisco, found that symptoms among workmen in Los Angeles were more frequent, but pulmonary function tests did not show significant differences between the two California communities. Test results of symptom fre-

quencies and pulmonary function for Los Angeles and San Francisco combined were nearly identical with the findings of Holland *et al.* in cities of the eastern United States. Denson *et al.* (New York), using comparable methods, studied postmen in New York City and found test values of pulmonary function to be very slightly lower than Holland's data for outside-plant phone workers. Frequency of respiratory symptoms in postmen was very similar to Holland's findings for outside plant workers. Denson reported a lower frequency of respiratory symptoms in nonwhite populations. This contrasts with the higher frequency of asthma attacks among nonwhite groups reported in studies of Greenburg and Field. Denson found that the respiratory absentee rate was higher among persons with low pulmonary function.

Cederlof (Stockholm) reported on comparisons of monozygotic twins with respect to various symptom categories, smoking habits, and places of residence. Smoking of cigarettes was associated with increased prevalence of cough and bronchitis, stomach disorders, back troubles, and pains in the chest. There were no demonstrable differences for angina pectoris and shortness of breath. There was virtually no effect on symptoms in the twin populations when one of the twins lived in an urban area and one in a rural area. Horton, reporting for Zeidberg *et al.* (Nashville) presented a statistical study of mortality from cardiovascular disease in Nashville, in relation to socio-economic factors and air pollution. An inverse relation between socio-economic class and cardiovascular mortality was observed when statistical control of air pollution levels was used. Of the pollutants studied, a consistent association was noted for suspended particulate matter in relation to cardiovascular mortality.

In discussing human exposure, Smith (Riverside, California) told how he exposed college students to the photochemical product, peroxyacetyl nitrate, while they were exercising. He observed an increase in uptake of oxygen during the exposure. Battigelli (Pittsburg) studied the effects of diluted diesel exhaust on the mechanical properties of the lung with a body plethysmograph in human subjects. Exposures of 1-hour duration did not produce significant changes in airway resistance or pulmonary compliance either at the time of exposure or later. The concentrations were sufficient to produce marked lacrymation. Hallett (Duarte, California) compared the acute effects of ozone with those of cigarette smoke in human subjects. Ozone exposures between 1 and 3 parts per million for up to half an hour produced changes which were more definite than those produced by smoking one cigarette. A greater proportion of subjects reacted to the ozone. The effects observed were on ventilatory function and diffusion capacity. Nadel *et al.* (San Francisco) reported on inhalation of sulfur dioxide at 4 to 6 parts per million for 10 minutes. This led in each of seven healthy subjects to a decrease in the ratio of conductance to thoracic gas volume. One subject with a most marked change began to cough severely and became dyspneic and wheezed. Supplementary studies on cats indicated the bronchoconstriction during acute inhalation to be dependent upon intact parasympathetic pathways. He showed that the body plethysmograph can be used as an exposure chamber and for monitoring airway resistance and lung volume.

Experiments with animals were described by Friberg (Stockholm). He reported on studies of ciliated epithelium in the rabbit trachea, initial work on the generation and monitoring of uptake and clearance of inhaled particles in rabbits, and the methods for measuring the proportional absorption of sulfur dioxide in the lung. At high concentrations 95 percent of sulfur dioxide is absorbed in the upper airway and 98 percent in the airway and lungs. At lower concentrations, the proportions are 40 and 80 percent, respectively. Buckley and Balchum (Los Angeles) reported on oxygen uptake by lung homogenate and other organs of guinea pigs after acute and chronic exposure to nitrogen dioxide. In both groups of animals they found insignificant increases in the oxygen uptake of the lung homogenate and significant increases in oxygen uptake by the spleen and kidney. No important changes in lactic dehydrogenase were observed. Liver homogenate showed an increase after acute exposures but a decrease after chronic exposures; the decrease was not significant. In other exposures of guinea pigs to nitrogen dioxide, Balchum and Buckley showed that circulating antibody to normal lung proteins developed. Exposures were to 5 parts of nitrogen dioxide per million, 4 hours a day, 5 days each week. Another group was exposed for a longer period. Apparently the titers increased with the duration of exposure and with the magnitude within the day. Gross *et al.* (Pittsburgh) reported on the production of chronic pulmonary fibrosis in rats after exposure to between 0.5 and 4 parts of phosgene per million. They were able to trace the evolution of fibrosis from thickening of the respiratory bronchiole to peripheral extension involving the alveolar ducts and the alveolar sacs. These reactions are in marked contrast to the acute pneumonitis occurring after higher levels of exposure. Residual changes can be identified as late as 3 months after exposure. Aldehydes and other potential cross-linking agents were formed in the lung of the rabbit after in vivo exposure to ozone (Buell, Berkeley). Thin-layer chromatography was used to analyze the resulting hydrazones. Ozone also appeared to affect the ground substance of lung.

Reactions of vegetation were described by a group from the University of California, Riverside. Ordin studied reactions of cell walls to peroxyacetyl nitrate and ozone. The agents appear to inhibit the synthesis of cellulose. Dugger reported on the effect of peroxyacetyl nitrate on inhibiting photosynthetic phosphorylation and on the formation of NADPH. This could be prevented by ascorbate. The exposure only causes inhibition in the light. Mudd reported on the effects of peroxyacetyl nitrates on the enzymes, pancreatic ribonuclease, glucose-6-phosphate dehydrogenase, and malic dehydrogenase. Both peroxyacetyl nitrate and ozone can oxidize reduced forms of nicotinic adenine dinucleotides. The oxidation product is reactive when peroxyacetyl nitrate is used but not when ozone is used. The effect of sulfhydryls was also noted.

Estes and Pan (Galveston) described effects of photochemical reaction products on the activity of glutamic dehydrogenase. The inhibition was more rapid with a glutamate substrate than for the reversed reaction; the opposite occurred when formaldehyde was used to produce inhibition. It was suggested that formaldehyde and glutamic dehydrogenase form a product serving as an electron donor.

In discussing techniques used for monitoring biological reactions, Epstein (Boston) compared the photodynamic toxicity of polynuclear com-

pounds with their carcinogenicity and presented data on the photodynamic toxicity of atmospheric pollutant samples. Photodynamic toxicity is studied by dark incubating, motile ciliates, paramecia, or tetrahymena, with polynuclear compounds to which they are resistant in the absence of light. Subsequent long-wave ultraviolet irradiation, however, leads to severe toxic effects on the organism. Crocker *et al.* (San Francisco) presented data on the effects of carcinogenic hydrocarbons on cell multiplication in organ cultures from trachea of suckling rats. Hydrocarbons, such as 7,12-dimethylbenz[α]-anthracene, benz[α]pyrene, and 3-methylcholanthrene were studied at different concentrations. DNA synthesis in basal cells increased before columnar cells had changed in appearance. Metaplastic epithelium replaced differentiated epithelium in a pattern dependent on the hydrocarbon used. Withdrawal of hydrocarbon permitted differentiated cells to reappear while basal cell hyperplasia persisted. Mueller (Berkeley) studied the effects of gas and particulate matter in automobile exhaust on tissue culture cells in vitro. The growth-stimulating property appeared to be associated primarily with the particle phase and was independent of changes resulting from ultraviolet irradiation. Rounds and Bils (Pasadena), studying air pollutant effects on tissue cultures, concluded that all cell types tested showed partial but reversible inhibition in oxidative activity during treatment with sodium nitrate (simulating NO_2 exposures). Morphologic changes, including reversible changes in the shape of nucleus, the cytoplasm, and ultrastructure of mitochondria, occurred in alveolar wall cells.

Nusbaum *et al.* (Los Angeles) reported on the trace metal studies in bone in relation to air pollution exposure. Calvarium and rib samples revealed no correlation between lead levels and the duration of previous residence in Los Angeles. Specimens from males had significantly greater lead concentrations than those from females. Twelve other metals were examined with emission spectroscopy. Arsenic levels were obtained with wet chemical methods. Curphey and Perkins (Los Angeles and Berkeley) reported on the carboxyhemoglobin levels in individuals examined by the Los Angeles County Coroner's Office. A smoking history was obtained from the next-of-kin, and the distribution of carboxyhemoglobin levels in individuals dead from cardiac disease resembled very closely the comparable distribution obtained by expired air analysis in the studies of living populations.

Pernis (Milano, Italy) described the role of lymphocytes in infiltrative lung disease. Experimental studies with guinea pigs, immunized against ovalbumin, involved inhalation of aerosols of extremely minute amounts. Despite the absence of immediate anaphylactic reaction, induration, which was largely lymphocytic, was observed. Pernis then considered whether haptens might be capable of producing similar reactions in occupational exposure. The implication of these mechanisms for effects of complete antigens thought to be involved in the farmer's lung syndrome were discussed. Similar effects were thought to possibly play a role in silicosis or coal worker's pneumoconiosis. Rankin *et al.* (Madison) reported on agricultural dusts as an agent producing infiltrative lung disease. They outlined the experimental, immunologic, and epidemiologic evidence relating thermophilic actinomyces as an agent causing farmer's lung. Rankin also reported that certain industrial exposures to polymers could lead to changes similar to those predicted by Pernis.

Epidemiologic methods suitable for air pollution studies were reported by Blackburn *et al.* (Minneapolis) who compared ventilatory function and respiratory conditions in active and sedentary railway employees. When corrections were made for age and smoking, clinical chest findings were used to test the hypothesis that regular exercise of the ventilatory apparatus may enhance its efficiency and protect against the development of chronic bronchopulmonary disease. Only small and inconsistent differences in ventilatory function and respiratory complaints existed between sedentary and active workers. Stone (New York) studied the frequency of respiratory complaints among volunteers in a telephone company. The volunteers had significantly less frequent evidence of disease than did a population in which all of the subjects were available for study. Gocke *et al.* (Jersey City) reported on a respiratory survey in an industrial population of men 40 to 64 years of age and compared the results with the absence of respiratory disease absenteeism. Cough, exacerbations of cough and sputum, shortness of breath, and the forced expiratory volume in one second, were best predictors of the absence of respiratory disease lasting one week or more. Ury (Berkeley) presented a rank order test for evaluating interviewer agreement.

Two major new directions of research were highlighted by the conference. One concerned the immunologic mechanisms involved in air pollution exposure. This includes the relationship of air pollution with epidemic asthma on the one hand, and infiltrative lung disease on the other. A second was the use of reactions of biochemical, tissue, or organ culture, and protozoa to pollutants, especially to potential carcinogens, as biological pollution monitors.

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Cross-Linkages in Collagen

Collagen is the major structural protein of vertebrates and comprises approximately one-third of the total body protein. It undergoes conspicuous changes with age and plays an important role in the healing of wounds and other pathologic processes. It is also the basis of the gelatin, glue, and leather industries. Important questions in the chemistry of collagen deal with the type of bonds which hold three polypeptide chains together in the collagen molecule and the nature of intermolecular cross-links responsible for fibril and fiber formation. Ten researchers in this field discussed these problems at a workshop on cross-linkages in collagen, held at Western Reserve University School of Medicine, 28–29 February 1964.

K. A. Piez (NIH) reported that when skin from a human infant was extracted with guanidine, two-chain components (β-components) were obtained, some of which arose from intermolecular links. Isotope incorporation