[64] "Effects of Environmental Tobacco Smoke Exposure *in Utero* and/or Postnatally on Brain Development," S.M. Gospe, S.S. Zhou, and K.E. Pinkerton, *Pediatric Research* 39: 494-498, 1996 [See Appendix A]

Based on data from experiments in which pregnant female rats and their offspring were exposed to sidestream smoke, the authors conclude that exposed rats had decreased numbers of cells in the hindbrain region. They speculated that this change could result in neurologic dysfunction.

[65] "In Utero Exposure to Tobacco Smoke," E. Hossny, A. Hosni, and R. Mabrouk, *Journal of Allergy and Clinical Immunology* 97: 377, 1996 [See Appendix A]

In this abstract, Egyptian researchers report lower birth weights for infants of smokers and infants whose mothers were exposed to ETS. Infants of ETS-exposed mothers also reportedly had lower Apgar scores.

[66] "Carbon Monoxide -- Does Fetal Exposure Cause Sudden Infant Death Syndrome?" C.D.D. Hutter and M.E. Blair, *Medical Hypotheses* 46: 1-4, 1996 [See Appendix A]

The authors of this paper speculate that carbon monoxide from tobacco smoke and home appliances has a "noxious effect" on the development of respiratory control in the brain, thus leading to infants increased susceptibility to "insults" such as infection or overheating, and death from respiratory dysfunction.

OTHER HEALTH ISSUES

[67] "Cigarette Smoking and Health," American Thoracic Society, *American Journal of Respiratory and Critical Care Medicine* 153: 861-865, 1996 [See Appendix A]

In this official statement, adopted by the American Thoracic Society (ATS) Board of Directors in March 1995, the society espouses positions on both active smoking and ETS. With respect to ETS, the organization claims that ETS causes lung cancer and is a particular hazard for children.

[68] "Air Pollution and Daily Mortality in London: 1987-92," H.R. Anderson, A. Ponce de Leon, J.M. Bland, J.S. Bower, and D.P. Strachan, *British Medical Journal* 312: 665-669, 1996 [See Appendix A]

Current daily air pollution fluctuations in London are reportedly associated with adverse effects on daily mortality by the authors of this study.

[69] "Morbidity and Mortality in Children Associated With the Use of Tobacco Products by Other People," J.R. DiFranza and R.A. Lew, *Pediatrics* 97: 560-568, 1996 [See Appendix A]

Based on meta-analyses of published literature, the authors conclude that childhood ETS exposure is associated with otitis media, tympanotomy, tonsillectomy, adenoidectomy, asthma, coughs, lower respiratory tract illness, and fires initiated by smoking materials. Using a population-attributable risk approach, they present numbers of illnesses, hospital admissions, and deaths purportedly due to ETS exposure in children.

This paper has received extensive press coverage, as did a paper by the same authors one year ago, which discussed the purported effects of maternal smoking on pregnancy complications and SIDS. *See* issue 95 of this Report. Press reports cited the article's claim that millions of childhood illnesses are due to ETS exposure. Coauthor DiFranza is quoted as saying, "'If a soft drink or breakfast cereal caused four million children to get sick it would be taken off the market within minutes.'" DiFranza also reportedly recommended a smoking ban "wherever children are present." *See* Reuters, Limited, April 8, 1996; *The Boston Herald*, April 9, 1996, AP Online, April 9, 1996.

[70] "Do People Living Near Inner City Main Roads Have More Asthma Needing Treatment? Case-Control Study," A.E. Livingstone, G. Shaddick, C. Grundy, and P. Elliott, *British Medical Journal* 312: 676-677, 1996 [See Appendix A]

By analysing computer records of asthma-related prescriptions, the authors maintain that living close to a busy road does not increase the risk of asthma in children and adults.

[71] "Health Effects of Passive Smoking in Adolescent Children," G.A. Richards, A.P.S. Terblanche, A.J. Theron, L. Opperman, G. Crowther, M.S. Myer, K.J. Steenkamp, F.C.A. Smith, R. Dowdeswell, C.A. van der Merwe, F.K. Stevens, and R. Anderson, *South African Medical Journal* 86: 143-147, 1996 [See Appendix A]

Having assessed more than 700 16-year-olds, the authors of this study report that children exposed to ETS in the home, and especially those exposed to maternal smoking, are more likely to exhibit respiratory illness before and after two years, earache during the past year, as well as decreased birthweight and learning difficulties. ETS exposure was not reported, however, to affect either spirometric or laboratory parameters.

[72] "Diet and Overall Survival in Elderly People," A. Trichopoulou, A. Kouris-Blazos, M.L. Wahlqvist, C. Gnardellis, P. Lagiou, E. Polychronopoulos, T. Vassilakou, L. Lipworth, and D. Trichopoulos, *British Medical Journal* 311: 1457-1460, 1995 [See Appendix A]

In a study of elderly Greek men and women, the authors report that individual components of diet were not associated with survival, but that a compound measurement of diet based on the traditional Mediterranean diet (considered to be healthful), was associated with a decrease in mortality. Although ETS was not mentioned, the assessment of diet has relevance to epidemiologic studies of ETS and chronic disease.

ETS EXPOSURE AND MONITORING

[73] "Exposure Assessment Needs in Studies of Acute Health Effects," M.D. Lebowitz, *The Science of the Total Environment* 168: 109-117, 1995 [See Appendix A]

Although ETS is mentioned only briefly, this article is of interest because it discusses the necessity of good exposure data in epidemiologic studies and the difficulty of obtaining such data.

GENOTOXICITY AND MUTAGENICITY

[74] "Evaluation of Micronuclei in Exfoliated Urothelial Cells and Urinary Thioether Excretion of Smokers," S. Burgaz, A. Iscan, Z.K. Buyukbingol, A. Bozkurt, and A.E. Karakaya, *Mutation Research* 335: 163-169, 1995 [See Appendix A]

Based on two endpoints measured from urine, the authors conclude that chromosome damage in bladder tissue is associated with tobacco use. The authors also examined one of the indices in ETS-exposed nonsmokers; although reportedly increased, it was not statistically significant.

INDOOR AIR QUALITY

[75] "Assessment of Particulate Concentrations from Domestic Biomass Combustion in Rural Mexico," M. Brauer, K. Bartlett, J. Regalado-Pineda, and R. Perez-Padilla, *Environmental Science & Technology* 30: 104-109, 1996 [See Appendix A]

According to this study, very high levels of fine particulate matter are found in Mexican homes, which is associated with cooking over unvented stoves that burn wood and other natural substances.

[76] "A Review of the Nature of Odour Perception and Human Response," A.H. Frey, *Indoor Environment* 4: 302-305, 1995 [See Appendix A]

The author of this article discusses the perception of odors as it relates to IAQ complaints.

[77] "Chemical Mass Balance Source Apportionment of Indoor PM_{15} in Brazilian Corporate Offices and Restaurants," A.H. Miguel, W. dos Reis Pedreira Filho, A.G. Allen, *Indoor Environment* 4: 355-361, 1995 [See Appendix A]

Particulate matter samples from a number of sites in urban and rural areas of Brazil were examined for the contribution of different sources in this study, which reports significant contributions from diesel exhaust, wood burning, and charbroiled meat.

[78] "Risk Perception and Indoor Air Quality," A. Stratico and P. Dingle, In: *Indoor Air: An Integrated Approach*, L. Morawska, N. Bofinger, and M. Maroni, Eds., Oxford, Elsevier, pp. 467-470, 1995 [See Appendix A]

Based on a survey of 1,500 individuals in Australia, the authors of this study report that many participants perceived the risk of indoor air pollutants as "acceptable."

SMOKING POLICIES AND RELATED ISSUES

[79] "Double-Barreled Assault: Tobacco's Two-Pronged Attack on Smoking Regulations Narrowly Fails," K. Ortolon, *Texas Medicine* 91: 12-15, 1995 [See Appendix A]

This article describes an alleged "two-pronged attack" waged by the tobacco industry in the 74th Texas Legislature in an attempt to prevent local communities from regulating public smoking.

STATISTICS AND RISK ASSESSMENT

[80] "Cancer Risk of Low-Level Exposure," M. Goldman, *Science* 271: 1821-1822, 1996 [See Appendix A]

This commentary suggests that the "no-threshold" concept in addressing cancer risk should be reconsidered, and that new paradigms for considering risk should be examined.

IN EUROPE & AROUND THE WORLD

REGION 1–WESTERN EUROPE

REGULATORY AND LEGISLATIVE MATTERS

[81] Voluntary Smoking Measures Mostly Ineffective in England

According to a recent press report, Department of Environment officials are expected to announce soon that efforts to encourage public places to voluntarily prohibit smoking have largely been ignored. The department is reportedly not expected to endorse smoking ban legislation, however, because of current government attempts to project itself as a "champion of deregulation."

"Even if the Department of Environment were to favor legislation, it would be difficult to get other departments on board," a Department of Environment official is quoted as saying.

A government deadline of January 1, 1995, encouraging establishment of smoking policies in 80 percent of public places has reportedly been extended indefinitely. Such policies have apparently been initiated in 14 percent of pubs and 36 percent of restaurants. *See The Financial Times*, April 8, 1996.

[82] Smoking Ban Broadened in Italian Public Offices

An agreement extending the scope of an existing smoking ban to all areas of public administration offices has reportedly been signed by Italian Health Minister Elio Guzzanti and the chair of the Italian regions' association, Pietro Badaloni. The ban will apparently apply to autonomous provinces and regions and will require all public offices to display "no smoking" signs. Legislation that would ban smoking in restaurants, discos, pubs and bars is apparently pending. *See La Repubblica*, March 31, 1996.

[83] Norway Proposes Smoking Restrictions on Ferries; Hospitals, Prisons Encounter Problems with Law

Norway has reportedly submitted a proposal to the Nordic Council of Ministers that would severely restrict smoking on ferries serving the Nordic countries. Under the proposal, smoking would be banned in corridors and other public areas, in restaurants and cafeterias facing public areas, in one-half of the cabins available, and in at least one-third of the restaurants, bars and disco seating areas. Smoking on ferries is already regulated, but a survey conducted by the Statens Tobakkskaderaad (the National Council on Smoking and Health) apparently indicates that the regulations are not enforced.

Meanwhile, a Nordic Council survey of hospitals also indicates that eight out of 10 hospitals in Norway that prohibit smoking are experiencing problems with employees who ignore the ban. The survey reportedly shows that 85 percent of the country's hospitals prohibit smoking among employees.

In a related development, a press report indicates that it has been difficult to enforce the new tobacco act in Norwegian prisons, where it is estimated that up to 95 percent of inmates smoke. Complaints by nonsmokers have apparently resulted in several prisoners being moved to nonsmoking units. The report suggests it may be necessary to reconstruct prisons to comply with the provision of the Act. *See Aftenposten*, March 20 and 30, 1996; *Arbeiderbladet*, April 3, 1996.

Other Developments

[84] German Scientists Claim ETS Exposure Is Third Leading Cause of Lung Cancer

Scientists at the German Cancer Research Center in Heidelberg reportedly claim that ETS exposure is the third leading cause of lung cancer deaths, following active smoking and breathing radon gas. Their assertion is apparently based on an epidemiological study in which they concluded that 400 Germans die each year from lung cancer caused by ETS exposure. The number of deaths attributable to ETS exposure was reportedly determined by utilizing a new method for calculating the relationship between dose and impact. The researchers also reported that children in families where the parents smoke have a higher incidence of respiratory illnesses. *See Die Welt, Frankfurter Allgemeine*, April 3, 1996.

[85] Tobacco Friends Club Established in Switzerland

The Club der Tabakfreunde (Club of Friends of Tobacco) has reportedly been established in Bern in reaction to the increasing restrictions smokers face. The club will purportedly defend the rights of smokers and ask for tolerance from extremist groups. Founders of the club reportedly plan to launch a magazine during the club's first year. They will also communicate with club members through an Internet site (http://www.swiss-smoker.ch/). *See Club der Tabakfreunde Press Release*, April 1996.

[86] British Study Concludes That Designing Smoker-Friendly Offices Increases Costs

Designing a building friendly to smokers could add 7 percent to construction costs and lead to higher maintenance bills, according to a study commissioned by the Organization for Economic Cooperation and Development (OECD). The organization commissioned the study in conjunction with its move to a new headquarters building in Paris, France.

The study reportedly found that designing a building where staff were allowed to smoke in all areas increased the cost of mechanical and electrical systems by 15 to 20 percent. In addition, cleaning offices occupied by smokers was anticipated to add UK$10 per square meter to the OECD's annual maintenance costs. *See The Financial Times* and *Reuters*, March 29, 1996.

[87] Compensation Board Employees in Scotland Threaten Industrial Action; House of Commons Confronts *Legionella* Bacteria

Owners of the building that houses the Criminal Injuries Compensation Board in Glasgow, Scotland, reportedly face industrial action if they fail to respond to complaints of illness by board employees. According to a recent press report, the threat was issued by a spokesperson for the Civil and Public Servants' Association, who stated that illness rates at the board's headquarters have purportedly tripled since the board's 300 workers moved into Tay House, which overlooks

the congested M8, in February 1995. She added that unions were hopeful that managers could persuade the owners of the building to at least overhaul the heating system. "If management do not act, we shall have to consider bringing in the Health and Safety Executive (HSE) to look at the problem," she said.

Apparently, the union first threatened to call in HSE inspectors in April 1995 after workers complained of a mystery "illness," which allegedly caused headaches, nausea and cold sores. An independent study of the building conducted last year by Strathclyde University reportedly highlighted a number of problems, including noise, inadequate fresh air, and poorly controlled ventilation.

Meanwhile, unacceptable levels of the bacteria that cause Legionnaires' disease were reportedly found at the House of Commons in late December 1995. Although engineers tried to clean out the hot water system, tests conducted at the time indicated that there were still traces of the bacteria near the offices of the speaker, Betty Boothroyd. Further tests were to be conducted before MPs, journalists and thousands of support staff were to return in early January. *See The Times*, December 29, 1995; *The (Glasgow) Herald*, March 26, 1996.

REGION 2 -- AUSTRALIA

OTHER DEVELOPMENTS

[88] Survey Reveals Strong Opposition to Smoking Bans

A national survey of more than 1,000 Australians has reportedly found that a majority of Australians oppose public smoking bans and that one in five would vote against a political party that introduced such bans. The survey was commissioned by WD & HO Wills (Australia) Ltd.

Of those surveyed, 66 percent purportedly opposed a smoking ban in pubs and bars. That figure was even higher when respondents were asked if they would support a ban if adequate ventilation were installed, with 81 percent then opposed to smoking bans in pubs and bars, and 80 percent in clubs. Even in restaurants, where the majority of people preferred to have a choice between smoking and nonsmoking areas, 68 percent of those surveyed apparently opposed a ban, provided there were adequate ventilation. Seventy-one percent of smokers said they would change their patronage of pubs and bars if bans were implemented, either by going to another establishment, going out less often or not staying as long. Similarly, 67 percent of the club patrons and 48 percent of the restaurant patrons said they would change their patronage.

Wills officials reportedly said that the survey results indicate a growing preference for adoption of a conciliatory self-regulatory approach, whereby hospitality owners and managers make such decisions rather than the government. The company recently launched a public education and communication program that emphasizes the role of adequate ventilation in removing ETS in hospitality venues. *See RWE Australian Business News*, April 2, 1996.

REGION 3– JAPAN

ETS-RELATED LITIGATION NOT INVOLVING CIGARETTE MANUFACTURERS

[89] *In re: Japan Tobacco Inc.* (Nagoya District Court) (filed April 4, 1996)

Four smokers and one nonsmoker have reportedly filed a complaint against Japan Tobacco Inc., in what their attorney claims is the first suit brought by smokers against the government-controlled cigarette manufacturer. Nonsmokers with ETS claims have apparently been unsuccessful, to date, in three lawsuits reportedly filed during the last 10 years against the company.

The smokers claim that nicotine addiction and nonsmoking regulations have harmed their careers and daily lives, while the nonsmoker alleges his health is at risk from ETS exposure. Although none of the plaintiffs alleges illness from smoking, each is apparently demanding one million yen (US$9,350) in compensation and a halt to the production and sales of cigarettes, or warnings on cigarette packages similar to warnings required in the United States.

According to a press report, one of the smokers, a 49-year-old graphic designer, claims that smoking affects his productivity on the job because he must leave his nonsmoking office to smoke. He also reportedly claims that it is difficult for him to travel on business or for pleasure because of airline smoking bans. *See The Daily Yomiuri*, April 5, 1996; *Associated Press Worldstream* and *Agence France Presse*, April 4, 1996.

REGION 6– LATIN AND SOUTH AMERICA

REGULATORY AND LEGISLATIVE MATTERS

[90] Nicaraguan Assembly Approves Smoking Ban in Public Places

The Nicaraguan National Assembly reportedly approved a measure at the end of March 1996 that prohibits smoking in public places and in all indoor areas in which more than three people are located nearby. The provision is part of the General Law on the Environment and Natural Resources, intended to protect the environmental and natural resources of Central America's largest country. *See Xinhua News Agency*, March 28, 1996.

REGION 7–ASIA

REGULATORY AND LEGISLATIVE MATTERS

[91] Smoking Banned in China's Great Hall

As of April 1, 1996, smoking was prohibited in China's Great Hall of the People, the seat of government of the world's largest producer and consumer of tobacco, according to a news report. The new regulation apparently applies to the entire Great Hall, where all state functions are held and the national legislature meets. Cigarette sales are also banned in the hall, and large signs at the entries will remind visitors that, "Smoking is banned in the Great Hall of the People."

According to numerous press reports, Premier Li Peng severely criticized smoking delegates during the annual legislative session in March, stating they should set an example in observing a ban on smoking in public places that takes effect in Beijing May 15. *See Xinhua News Agency*, March 14, 1996; *Reuters*, March 16 and 29, 1996; *South China Morning Post International Weekly*, March 23, 1996; *Associated Press*, March 28, 1996.

[92] Smoke-Free Policy Takes Effect in Hong Kong Government Premises

As of April 1, 1996, a new smoke-free workplace policy took effect in all Hong Kong government premises, according to a press account. Under the new policy, smoking will apparently be banned in both office and non-office environments, which include all enclosed or open working areas, corridors, foyers, conference rooms, reception and counter areas, waiting rooms, and public areas. Designated smoking areas will reportedly be established for employees who smoke. A government spokesman was quoted as stating, "As a responsible employer, government needs to balance between the interests of both smoking and nonsmoking employees, while taking into account government's overall antismoking objective." *See Comtex Scientific Corporation*, March 25, 1996.

[93] India to Introduce Nonsmokers' Protection Bill

A recent press report indicates that the Delhi Prohibition of Smoking and Nonsmokers' Health Protection Bill, 1995, is likely to be introduced in the budget session of the Delhi Assembly, which convened in mid-March 1996. *See The [Chandigarh] Tribune*, March 18, 1996.

APPENDIX A

The numbers assigned to the following article summaries correspond with the numbers assigned to the synopses of the articles in the text of this Report.

LUNG CANCER

[49] **"Lung Cancer and Air Pollution," A.J. Cohen and C.A. Pope, *Environmental Health Perspectives* 103(Suppl. 8): 219-224, 1995**

"Epidemiologic studies over the last 40 years suggest rather consistently that general ambient air pollution, chiefly due to the incomplete combustion of fossil fuels, may be responsible for increased rates of lung cancer. This evidence derives from studies of lung cancer trends, studies of occupational groups, comparisons of urban and rural populations, and case-control and cohort studies using diverse exposure metrics."

"We will review this evidence, focusing on studies of occupational groups, comparisons of urban and rural populations, between-community studies, and case-control and cohort studies, including three recent prospective cohort studies. In addition, we will discuss the plausibility of [an] ambient air pollution-lung cancer effect by summarizing epidemiologic evidence of relative risks of various types of exposure to combustion-source pollutants. Finally, we will identify additional epidemiology research needs."

"[B]reathing fine or respirable particles from a wide variety of combustion sources increases the risk of lung cancer. . . . Cigarette smoking represents the high end of combustion-source particle exposure, and involuntary exposures to ambient air pollution and environmental tobacco smoke represent the low end of exposure."

"The similar lung cancer risk estimates for environmental tobacco smoke and ambient air pollution may reflect similar differences in exposure. . . . Estimated effects of ambient air pollution and environmental tobacco smoke can be viewed as at least partially complementary, which suggests that there are small lung cancer effects at relatively low levels of exposure to combustion-source air pollution."

"Direct epidemiologic observation of exposed populations can provide the best information for evaluating the magnitude of air pollution-related excess lung cancer if we can make more valid and precise estimates of the increases in lung cancer associated with air pollution and of the numbers of people exposed. Clearly, better data to support these estimates are needed."

"Better estimates of the magnitude of effect will require large-scale epidemiologic studies. Large numbers of cases will be necessary to measure the effects of air pollution and to measure joint effects of air pollution and factors such as occupation and smoking."

"The air pollution mixtures in various U.S. population centers should be characterized both in terms of physical and chemical constituents and in terms of sources of major constituents."

"The epidemiologic evidence suggests that combustion-source air pollution contributes to the occurrence of lung cancer among the general population. These results are consistent with studies of other types of exposure to combustion-source pollution such as occupational exposures and exposures to environmental tobacco smoke. The excess lung cancer risk associated with ambient air pollution is small compared with that from cigarette smoking. However, given the ubiquity of combustion-source ambient air pollution exposure, the contribution of this exposure across a population may be of public health importance. Errors in the measurement of other risk factors including cigarette smoking continue to limit our ability to quantify the magnitude of the excess lung cancer risks associated with air pollution. It is important to conduct additional research that addresses these concerns."

CARDIOVASCULAR ISSUES

[50] **"Atherosclerosis: Risk Factors and the Vascular Endothelium," S.P. Glasser, A.P. Selwyn, and P. Ganz, *American Heart Journal* 131: 379-384, 1996**

"[The endothelium's] effects (which include endocrine, paracrine, and autocrine components) regulate vascular smooth muscle tone, platelet adhesion and aggregation, local clotting, and vascular growth. . . . It

secretes relaxing and constricting factors. The interaction between these dilators and constrictors provides a local control mechanism that regulates vascular tone."

"[T]he endothelium also exerts a dual effect on vascular growth. Endothelial cells can initiate both angiogenesis and abnormal growth of smooth muscle in disease. . . . [T]he loss of EDRF [endothelium-derived relaxing factor] effect at the site of endothelial damage (such as the endothelium overlying an atherosclerotic plaque) could result in increased thrombogenesis, adhesion of inflammatory cells, and other cell dysfunctions that favor atherogenesis."

"Normal endothelium functions in an inhibitory mode; it inhibits smooth muscle contraction, platelet aggregation, vascular smooth muscle growth, thrombosis, and white cell (e.g. monocyte) adhesion, which is an early abnormality in the generation of an atherosclerotic plaque. Indeed, atherosclerosis is likely a consequence of endothelial dysfunction. Understanding the role of the endothelium in vascular tone has provided new insights into the evaluation of atherosclerosis and its consequences in patients. . . . Our knowledge of the role of endothelial dysfunction in disease, therefore, is expanding, and the interaction of endothelial dysfunction with risk factors for atherosclerotic coronary artery disease is reviewed here."

"Cigarette smoking is a major risk factor for the development of atherosclerosis and coronary events. One theory is that components of cigarette smoke may be toxic, in part by inducing oxidative stress and thereby causing endothelial damage. This may be the initiating mechanism for the development of an atherosclerotic plaque. In addition, endothelial dysfunction may be worsened by cigarette smoke, which could explain why smokers who give up cigarettes after myocardial infarction have a lower risk of recurrent myocardial infarction than those who do not. Other studies have demonstrated a direct toxic effect of tobacco smoke on human endothelium associated with an increase in the number of endothelial cells with nuclear damage in the circulating blood. Celermajer et al. have shown that there is a dose-dependent impairment of endothelial dysfunction in asymptomatic young smokers and that the abnormal vasomotion was reversible with smoking cessation. Kiowski et al. studied the effects of short- and long-term smoking on vascular tone. They also found that long-term smoking is associated with vasodilation and further that short-term smoking is associated with enhanced endothelin-1 induced vasoconstriction. These observations are particularly interesting given the present concern regarding passive or second-hand smoke because changes in platelet sensitivity have been demonstrated with passive smoking."

"The endothelium can respond to a local environment by releasing a variety of substances that regulate the level of vascular tone. One of the most important of these vasoregulatory substances is EDRF. The function of the endothelium is altered in a variety of pathologic and physiologic conditions. This review focused on the role of risk factors for atherosclerosis as it relates to EDRF. Atherosclerotic blood vessels respond abnormally on exposure to stimuli that release EDRF. It is now also apparent that this abnormal vascular response may precede the development of significant atherosclerosis and that normalization of the EDRF response with treatment is possible. Thus abnormal endothelium-dependent relaxation has been demonstrated in hypercholesterolemic patients with little or no evidence of coronary angiographic disease and in patients with hypertension before the development of atherosclerosis. The interaction between risk factors and the function of the vascular endothelium with development of atherosclerosis may become a useful focus for therapies that benefit patient outcomes."

[51] **"Passive and Active Smoking Are Related to Progression of Atherosclerosis," G. Howard, L.E. Wagenknecht, F.J. Nieto, D. Arnett, and G. Burke for the ARIC Investigators, *Circulation* 93: 624, 1996**

"Progression of atherosclerosis (as indexed by increases in the common carotid intimal-medial thickness (IMT) over a 3-year period), smoking history, lifestyle and cardiovascular risk factors were assessed in 8,415 ARIC participants aged 45-65 at baseline. The mean IMT progression rate was calculated for each of 5 levels of exposure to cigarette smoke after adjustment for age, race, gender, hypertension, diabetes, alcohol intake, education, leisure time activity level, body mass index, and baseline IMT. There was a dose-response relationship with increasing smoking exposure with 43% greater progression rates from 39 um/3 yr for never smokers not exposed to environmen-

tal tobacco smoke (ETS) to 56 um/3 yrs for current smokers. Exposure to ETS was associated with IMT progression rates 5 um/3 yrs greater than those not exposed to ETS. Increasing pack-years of exposure was positively associated with increased IMT progression in current and past smokers. These are the first data suggesting that exposure to both active and passive tobacco smoke are related to an increased rate of progression of atherosclerosis."

[52] **"1,3 Butadiene, A Vapor Phase Component of Environmental Tobacco Smoke, Accelerates Arteriosclerotic Plaque Development,"** A. Penn and C.A. Snyder, *Circulation* 93: 552-557, 1996

"Recent in vivo studies from this laboratory have demonstrated that inhalation exposure to ETS is sufficient to promote arteriosclerotic plaque development. . . . This suggested strongly that plaque-promoting levels of ETS can be encountered routinely by people in smoke-filled environments."

"In the experiments reported here, we asked whether the in vivo plaque-promoting effects of ETS can be attributed to components other than PAH carcinogens. Cockerels were exposed to one of two prominent ETS components: NNK, a tar fraction component of ETS, or 1,3 butadiene, a vapor phase component of ETS."

"To the best of our knowledge, there are no data that implicate NNK in the development of arteriosclerotic heart disease."

"There are no animal studies that implicate butadiene in arteriosclerotic plaque development."

"Studies of the effects of cigarette smoke or its components on morbidity and mortality have emphasized the roles of these agents in carcinogenesis, especially lung cancer. There has been considerably less attention paid to the effects of these agents on cardiovascular disease even though (1) the correlation between cigarette smoking and heart disease is nearly as strong as that between cigarette smoking and lung cancer and (2) each year the number of deaths from heart disease far exceeds the number of deaths from lung cancer. Largely in response to the suggestion that arteriosclerotic plaques can be viewed as benign smooth muscle cell tumors of the artery wall, a number of laboratories, including our own, investigated the role of known PAH carcinogens in the initiation/development of arteriosclerotic plaques. The striking effectiveness of these agents on plaque development, albeit at relatively high doses, combined with the presence of PAH carcinogens in cigarette smoke (especially in the tar fraction of sidestream smoke) and the strong epidemiological correlation between smoking and heart disease, led us to investigate first whether exposure to sidestream tobacco smoke would accelerate plaque development. Our studies showed that it does. . . . In the experiments described here we asked whether individual, non-PAH cigarette smoke carcinogens play a role in plaque development."

"Two sets of results are presented. First, we demonstrate that a prominent particulate fraction ETS component, NNK, has no effect on plaque development. . . . 20 NNK-treated and 10 control cockerels were examined. Thus, NNK, tested in a proven protocol for the promotion of arteriosclerosis, does not accelerate plaque development."

"Second, in contrast to the results from the NNK study, those from the butadiene study demonstrate that this vapor phase component of ETS accelerates arteriosclerotic plaque development. Here, butadiene effectively promoted plaque development in concentration only twice the TLV. This represents the first time that a single cigarette smoke component has been shown to directly affect the development of heart disease at doses that are within an order of magnitude of those found in cigarette smoke. Butadiene is far more concentrated in sidestream smoke than either benzo(a)pyrene or NNK."

"Since butadiene is found in such high concentration in ETS relative to NNK and benzo(a)pyrene, it is probably one of the compounds most responsible for the arteriosclerotic plaque-promoting potential of ETS. However, literally thousands of compounds have been identified in the gas and particulate fractions of cigarette smoke, both sidestream and mainstream. Thus, other compounds besides butadiene must contribute to the plaque-promoting qualities of ETS."

"In the experiments reported here, butadiene exposure levels, while higher than those present in sidestream smoke from one cigarette, were still only twice the occupational TLV. This, combined with the elevated standardized mortality ratio for death from arteriosclerotic heart disease among black production

and maintenance workers in the butadiene rubber industry, strongly suggests that the TLV for butadiene may have to be lowered."

Respiratory Diseases and Conditions -- Adults

[53] **"Thunderstorm Associated Asthma: A Detailed Analysis of Environmental Factors," A. Celenza, J. Fothergill, E. Kupek, and R.J. Shaw, *British Medical Journal* 312: 604-607, 1996**

"*Objectives* -- To seek associations between meteorological factors, concentrations of air pollutants or pollen, and an asthma epidemic which occurred in London on 24 and 25 June 1994 after a thunderstorm."

"*Design* -- Retrospective study of patients' accident and emergency department records, with bivariate and multivariate analysis of environmental factors and data collection for the two months surrounding the epidemic."

"Our findings in west central London suggest that a fall in air temperature and a high pollen count were the best predictors of the asthma epidemic, though all the individual environmental variables were closely related."

"The sudden thunderstorm caused the greatest and most sudden fall in temperature and air pressure as well as the most pronounced increased in humidity, rainfall, and lightning strikes observed during the two month study period. . . . [L]ightning strikes, rainfall, air temperature, air pressure, and humidity seemed to be related to the onset of the asthma epidemic. We could not identify from the data which of the environmental conditions occurred on other days during the study period without increases in asthma presentations."

"The meteorological change which showed the best association with a rise in new asthma cases was a fall in air temperature six hours previously."

"The changes in meteorological conditions were accompanied by a sharp rise in grass pollen concentration shortly after the thunderstorm."

"It seems unlikely that high concentrations of vehicle exhaust pollutants were the precipitating factor for the asthma epidemic."

"In conclusion, the thunderstorm associated sudden fall in air temperature and sudden rise in grass pollen concentration were independently associated with a rise in epidemic asthma presentations to our accident and emergency department. Several environmental changes which occurred immediately before and during the thunderstorm were also significantly temporally associated with the epidemic. This supports previous findings that under certain conditions thunderstorms may precipitate an asthma epidemic. Our study also suggests that the factors associated with non-epidemic asthma differed from those associated with the epidemic. This indicates that the many patients attending the accident and emergency department with reversible airways obstruction related to the thunderstorm may have been a different population, sensitive to different environmental stimuli."

[54] **"Asthma Programme in Finland 1994-2004," Ministry of Social Affairs and Health, *Clinical & Experimental Allergy* 26(Suppl. 1): i-iii, 1-24, 1996**

"The prevalence rate of asthma in Finland may be up to 5%, or 250000 individuals, and it has been on a clear increase since the 1960s. Asthma is the third most common chronic disorder, after hypertension and coronary heart disease, requiring medication in Finland. The number of new cases, calculated from the number of patients entitled to special reimbursement for prescriptions of anti-asthmatic drugs, increased between 1986-1995 most quickly in the population below 15 years of age. In 1995, approximately 150000 persons received special drug reimbursement. Most of the patients (60%) suffer from mild disease, and 20% from severe or very severe asthma."

"The overall annual cost of asthma was estimated at FIM 2.5 billion (0.6 billion US dollars) at the start of the 1990s. This included direct costs resulting from medical care, and indirect costs relating to disabilities and loss of production. The costs of severe asthma account for approximately 60% of the total costs."

"The Finnish society, like many other Western countries, have [sic] experienced profound structural changes during recent decades: urbanization, increasing education, smaller family size, etc. Many of these factors have been connected with asthma or other allergic diseases. People suffering from asthma are a

sensitive indicator group of changes in the environment and lifestyles. Development of the disease and exacerbation of symptoms are affected by many environmental factors."

"In Finland, mortality from asthma has been exceptionally low for 25 years, compared with many Western countries, and the mortality rate has even lowered during the last decade. Only 60 people died from asthma in 1992, and 66 in 1993. The low mortality is one reason why asthma, as a major health issue, has received much less attention compared, for example, with coronary heart disease. However, the importance of asthma in terms of health care and social welfare expenditure has increased dramatically and continues to do so. Changes in the population-age structure alone will increase the number of asthma patients by 7000 by the year 2000. If the trend observed between 1986-1995 continues, the number of individuals suffering from asthma will be 60% higher in 2000 than it is now."

"The Ministry of Social Affairs and Health realized the situation and appointed a working group to design a national programme for the prevention and alleviation of problems caused by asthma and for reduction of the relevant costs paid by the society. It is important to note that the aim was to create a action programme not a consensus report. The goals of prevention and treatment were: (1) as many patients as possible with early asthma recover; (2) asthma patients feel well, and their ability for work and functional capacity correspond to their age; (3) the percentage of patients with severe and moderate asthma falls from the current 40% to 20%; (4) the number of bed-days of asthma patients decreases by 50% by the year 2000, that is to 50000 a year; and (5) the annual costs per patient fall by 50% as a result of more effective prevention and treatment. These are hard, but not unrealistic, goals to achieve."

"The measures towards achieving the goals were: (1) early diagnosis and active treatment; (2) guided self-care is the primary form of treatment; (3) irritants such as smoking and tobacco smoke are decreased; (4) rehabilitation is implemented on an out-patient basis in connection with normal treatment, planned individually and timed appropriately; (5) knowledge about asthma is increased in key groups; and (6) scientific research is promoted."

"The dogma has been: 'Once asthma always asthma, it cannot be cured but only controlled'. The working group had more optimistic a view: (1) most patients have, in fact, a mild type of disease; (2) inflammation of the bronchial mucosa can be detected early; and (3) early intervention often leads to complete recovery, although the disposition to asthmatic inflammation remains. With improved early detection the asthmatic inflammation is traced when the functional disturbance is mild or just developing. Consequently, treatment to control the inflammation is initiated, which should influence the outcome, and may even prevent overt asthma in the patient. It may be argued that when clinical asthma with increased bronchial responsiveness is detected, the diagnosis is always late."

"The working group also pointed out that those subjects who show disturbed lung function (real asthmatics), are only part of the population with the problem of recurring eosinophilic inflammation. It was estimated that, while 5% of the Finnish population have asthma, another 10% experience occasional asthma-like symptoms. The latter patients are treated with antibiotics, antitussives and with everything else but adequate anti-inflammatory treatment. Stopping the disease at this stage may decrease morbidity to real asthma."

"Inflammation is a response, and the cause should always be searched for in the individual patient. Allergological tests should be carried out on every patient at an early state of symptoms. Allergenic factors at home, in the working environment and exacerbations of symptoms associated with food and consumer habits should be investigated. This is especially important in children, who show an atopic disposition in 90% of cases. However, preventive measures should be individualized and based on careful deliberation. The aim is to impose as few restrictions as possible on the life of asthma patients and their families."

"The programme also advocated the idea that joint allergological laboratories are established in central hospitals, and co-operation between different specialties is increased. Some hospital districts have already gained good experience from such units."

"Data about the natural course of the disease, the incidence, risk factors, changes in the severity of the disease and effects of long-term treatment are insuffi-

cient. Studies on preventive measures should be an integral part of asthma research, and multidisciplinary projects should be promoted. These were some of the important thesis [sic] among the needs for research and follow-up related to the Asthma Programme."

"The working group was convinced that a widened view of asthma would improve early detection of symptoms and lead to the correct type of interventions. The severity of asthma can be lessened. In Finland, the need for days in hospital because of asthma has already started to decline: from 186000 days in 1985 to 99000 in the early [sic] 1992. The whole concept of asthma may face a new era which is good news for those who are at risk of this disease."

Respiratory Diseases and Conditions -- Children

[55] **"Evaporative Cooling and Other Home Factors and Lower Respiratory Tract Illness During the First Year of Life," M.B. Aldous, C.J. Holberg, A.L. Wright, F.D. Martinez, L.M. Taussig, and Group Health Medical Associates,** *American Journal of Epidemiology* **143: 423-430, 1996**

"The Tucson Children's Respiratory Study is a prospective study of respiratory disease in children followed from birth. A previous report showed a relation between LRI in these infants and environmental tobacco smoke. The present paper examines the effects of other common home environmental factors on the risk of LRI during the first year of life. Exposures studied included perceived neighborhood dustiness, type of home cooling, type of home heating, cooking fuel, and indoor pets."

"Healthy infants from a health maintenance organization were recruited at birth (1980-1984). Analysis was restricted to one infant per family, and to those followed through the first year (n = 936). Environmental data were collected at enrollment, and clinicians diagnosed LRI according to predetermined criteria. During the first year of life, 196 infants (21%) had wheezing LRI, and 60 (6%) had nonwheezing LRI."

"These data from the Tucson Children's Respiratory Study demonstrate associations between two factors in the home environment and LRI in infants in the first year of life: first, between evaporative cooling in the home at birth and wheezing LRI, and second, between neighborhood dustiness rating and nonwheezing LRI. Neither association could be explained by confounding factors. No relation was found between LRI and gas heating, gas cooking, or indoor dogs or cats."

"The increase in wheezing LRI associated with evaporative cooling occurred during the winter viral respiratory season, when coolers are not in use, and the association was stronger among infants who live with other children. These observations suggest that evaporative cooling may render infants more susceptible to viral LRI, perhaps as a result of increased exposure to indoor fungi, dust mites, or pollen."

"The observed association between neighborhood dustiness rating and nonwheezing LRI is difficult to interpret and may be the result of chance, because multiple variables were considered. The dustiness rating was subjective, so dust composition was unknown, and quantitation might have been biased by parental perceptions. However, two likely sources of bias, parental histories of asthma and hay fever, were minimally associated with dustiness ratings and did not confound the findings."

"Because evaporative cooling and dustiness are common in arid regions, these findings merit further investigation for confirmation and to elucidate mechanisms involved and other associated respiratory effects."

[56] **"Association Between Air Pollution and Acute Childhood Wheezy Episodes: Prospective Observational Study," R. Buchdahl, A. Parker, T. Stebbings, and A. Babiker,** *British Medical Journal* **312: 661-665, 1996**

"[S]tudies show a pattern that suggests that fluctuations in concentrations of air pollutants may trigger asthma attacks in susceptible individuals or may interact in a more complex way to increase airway hyperresponsiveness to virus or allergy triggers. We investigated the association between sulphur dioxide, nitrogen dioxide, and ozone and rates of attendance for wheezy episodes at a local accident and emergency department."

"The incidence of childhood acute wheezy episodes is greatest in autumn and winter."

"This study shows that after seasonal adjustment the incidence was found to be high on days when ozone concentrations were very low or very high."

"The log incidence increased in a linear manner with increasing concentrations of sulphur dioxide."

"Nitrogen dioxide was not found to have a significant effect on the incidence of wheezy episodes."

"The non-linear U shaped relation between ozone and incidence suggests that at low ozone concentrations either other factors are more important in determining wheezy episodes or an optimum protective concentration of ozone exists in the atmosphere."

"Previous studies relating ozone concentrations to attendances for asthma at accident and emergency departments have shown conflicting results."

"Our study has not sought to explain the pathophysiological mechanisms behind the interaction of pollutant and meteorological variables. For ozone these have been well reviewed. Clearly pollutants may interact with each other and with allergic or infective factors. We have observed unexpectedly that concentrations of ozone above and below a critical level are associated with an increased incidence. Whether a physiological, chemical, or biometeorological explanation exists for this phenomenon is open to speculation."

[57] **"Socioeconomic Status and Lung Function Among Primary School Children in Canada," K. Demissie, P. Ernst, J.A. Hanley, U. Locher, D. Menzies, and M.R. Becklake,** ***American Journal of Respiratory and Critical Care Medicine*** **153: 719-723, 1996**

"There is limited information on which environmental characteristics might determine an association between SES and lung function. Several factors that might be expected to vary with SES have been reported to modify lung function. These include the presence of pets in the home, daycare attendance, area of residence, outdoor air pollution, type of heating or cooking fuel used, crowding, being raised by a single parent, maternal smoking during pregnancy, and postnatal exposure to tobacco smoke. Finally, differential access to medical care by the rich and poor has been proposed as a partial explanation for the differences in lung function levels observed."

"We set out to investigate the relationship of SES to lung function in primary school children in a country where there is universal access to health care. We also examined whether differences in lung function according to SES could be explained by differences in the home environment."

"Among primary school children mostly 6 to 12 yr of age, lower SES, as determined from parental occupation, was associated with a smaller FEV_1 and FVC among boys, suggesting a negative effect of social disadvantage on lung size. FEV_1 and FVC among girls, and FEV_1/FVC, a measure of airway caliber, in both boys and girls, did not vary significantly with SES."

"Various methods have been used to estimate SES or social class. The disadvantage of income as a single indicator of SES are [sic] its poor correlation with education and social status, its relation to age, and its instability over time. As well, income is a sensitive issue and reporting is likely inaccurate. Educational level is stable over one's lifetime; therefore, changes in SES after leaving school are not taken into account. The specificity of educational attainment is further reduced because of variability of school years completed between various birth cohorts."

"In the present study the relationship of SES to lung function was the primary study hypothesis, and particular care was taken to assess the independent contribution of SES. Parents were interviewed directly to obtain detailed employment histories, including type of industry, department with a company, job title, and job description."

"In Canada, there is universal access to health care, and the cost of medical services per capita has not been found to vary significantly with income. Therefore, differences in medical care should not account for our findings. It should be noted, however, that universal access to medical care does not necessarily guarantee equal utilization. In our study population, the observed associations between SES and lung function could not be explained on the basis of family history, early life experiences, or various environmental exposures that have been linked to SES."

"There were significant sex differences in several factors associated with adverse effects on lung size or airway caliber, including SES. Such sex differences have been reported previously for various environmen-

tal exposures, especially second-hand smoke to which boys appear more sensitive than girls. This may be due to differences in the maturation rate of the lungs in boys and girls, resulting in differing susceptibilities at various stages of childhood. We cannot rule out the possibility that sex may in some way determine the quality or quantity of various indoor exposures, however."

"Children with mothers who smoke and fathers who report asthma may have been overrepresented in our study sample as suggested by a comparison of parental responses to a questionnaire for those who did and did not allow their children to participate. There were, however, no differences between participants and nonparticipants as judged by SES indicators based on information from the neighborhoods where children lived. The refusal rate of 10% is sufficiently small to require large differences among the nonparticipants in order to alter our results."

"In conclusion, this study adds further evidence that social disadvantage, even in modern relatively affluent societies, is associated with reduced lung function. Further research is needed into the factors responsible for the adverse effect of low SES since these may be amendable to specific corrective measures."

[58] **"Passive Smoking and Respiratory Function in Very Low Birthweight Children," L.W. Doyle, G.W. Ford, A. Olinsky, A.M.L. Knoches, and C. Callanan, *The Medical Journal of Australia* 164: 266-269, 1996**

"To survive the neonatal period, many very low birthweight (VLBW) children (less than 1500 g at birth) require prolonged periods of assisted ventilation, and some may develop bronchopulmonary dysplasia (BPD) and suffer from ongoing respiratory problems as a consequence. We have previously reported the respiratory health to eight years of age of cohorts of children of birthweight 500-999 g, 1000-1500 g and > 2500 g. Passive smoking was significantly related to the duration of hospitalization for respiratory problems up to two years of age for all children in that study, but was not associated with changes in respiratory function at eight years of age."

"Because the effects of passive smoking could increase with increasing duration of exposure, the aim of this study was to determine if an adverse relationship exists between passive smoking and respiratory function at 11 years of age in VLBW children."

"Passive smoking was associated with reduced airflow and air- trapping in VLBW children at 11 years of age, which is consistent with observations in non-preterm children free of lung disease. However, this finding was different from our observations of these children at eight years of age, when passive smoking was unassociated with any lung function variable."

"The association between passive smoking and adverse respiratory function in our VLBW children at 11, but not at eight years of age suggests that the harmful effects of passive smoking take time to become obvious in VLBW children. Moreover, the adverse response seems to accelerate with increasing dose of passive smoking. We are concerned that continued exposure to passive smoking, or, even worse, active smoking, beyond 11 years will lead to not only further, but also to an accelerating rate of, deterioration in respiratory function."

"Our results should not be overinterpreted. They were not substantially altered by adjusting for potentially confounding perinatal or other variables, but we did not have data on a wide range of confounding variables. Moreover, they were heavily influenced by one child who lived in a household whose members consumed 115 cigarettes per day. Excluding this child from the analysis, the only remaining statistically significant associations indicated air-trapping with increasing exposure to passive smoking. However, we consider that this child's data should not be excluded just on the basis of heavier-than-average exposure to passive smoking. To remove any doubt about the association between passive smoking and adverse lung function in VLBW children, lung function could be measured in another cohort of VLBW children, or the same cohort when they are older."

"Parents of VLBW children, particularly those of children who have received assisted ventilation, frequently ask about long-term lung problems. Many variables, such as family history or duration of assisted ventilation and oxygen therapy, may be related to long-term lung problems, but most cannot be altered by the parents. Exposure to passive smoking is one variable associated with poorer respiratory function in VLBW children they can influence. Until there is

evidence to the contrary, families of VLBW children should be encouraged to stop exposing their children to cigarette smoke in the household. As there appears to be a dose-response relationship, those who cannot stop smoking should at least reduce their children's exposure to passive smoking."

[59] "Is Daycare a Risk Factor for Exacerbation of Bronchial Asthma (BA)," D.F. German and R. Watson, *Journal of Allergy and Clinical Immunology* 97: 375, 1996

"BA morbidity is on the rise in the U.S., and is the major reason for pediatric hospitalizations at Kaiser Northern California. Respiratory infection (RI) has been demonstrated as a major risk factor for BA in children (C) less than 5 years. The respiratory tract is the most common site of infection for C in day care (DC). C less than 6 years attending DC are at increased risk of RI. It was hypothesized that DC would be a risk factor for exacerbations of BA in this population."

"Method: C less than 6 years with a likely diagnosis of BA were identified from the Kaiser Pharmacy Information System using an algorithm of medications prescribed for treatment from 12/1/93 to 5/31/94. Utilizing a standardized telephone script, trained interviewers from a private contractor interviewed the parents."

"Results: Of the 471 respondents (70.8% of identified BA subjects) there was no statistically significant difference (NSSD) in the number of attacks of BA per week, or in the number of school, preschool days or other activities missed whether or not the child attended DC or attended DC with more or less than 5 peers (183 vs. 66 C). There was NSSD in the severity of BA determined by the parent whether or not the child attended DC; however, the severity of BA was increased in the [sic] those C who attended DC with 5 or less peers."

"Conclusion: With the exception of increased severity of BA as assessed by a parent for those C attending DC with 5 or fewer peers, DC was not demonstrated to be significant risk factor for BA exacerbation or severity, or days missed from normal activities."

[60] "Pre- and Perinatal Risk Factors for Asthma in Inner City African-American Children," J.F. Oliveti, C.M. Kercsmar, and S. Redline, *American Journal of Epidemiology* 143: 570-577, 1996

"Increased asthma prevalence in African-Americans as compared with Caucasians is apparent for children between the ages of 1 and 3 years. Thus, exposures that occur early in life may be particularly important in influencing susceptibility to asthma."

"Previous studies have related pre- and perinatal factors, such as low birth weight, maternal age, and maternal smoking, to the later development of wheezing illnesses, asthma, and reduced lung function. However, previous relations between prenatal factors and respiratory disease may have been partly confounded by socioeconomic status or race. To minimize the effects of confounding, we assessed the relations between pre- and perinatal exposures and asthma in a study population restricted to African-Americans living in impoverished inner city census tracts. In this high risk population, we performed a case-control study to test the hypothesis that pre- and perinatal stressors are associated with an increased risk of developing asthma which is independent of race per se."

"Susceptibility to asthma is determined by genetic risk factors that influence atopy, as well as by environmental exposures that cause sensitization or airway irritation and/or inflammation. In this study, the strong association between maternal history of asthma and asthma susceptibility confirms the results of previous studies that have suggested the importance of familial factors in predisposing people to asthma. This study also suggests the importance of environmental factors including those that occur in utero and during early childhood, in increasing asthma risk. Specifically, in analyses restricted to African-American children from the inner city, asthma was significantly increased in children born to mothers who did not receive prenatal care and who had poor weight gain and smoked during pregnancy. Thus, risk factors that predict adverse pregnancy outcomes are also significant independent predictors for the development of asthma during childhood."

"Mothers of asthmatic children were three times more likely to have weight gains under 20 pounds, and they had lower mean weights at the time of delivery than

the mothers of controls; the mean birth weight of the asthmatic children also was significantly lower than that of the nonasthmatic children. . . . Whether low maternal weight gain and/or low birth weight are markers for nutritional deprivation, and whether this predisposes to airway hyperreactivity and asthma, are not known."

"The mechanisms by which lack of prenatal care predisposes to the birth of an asthmatic child also are unclear. Absence of prenatal care, a problem that disproportionately affects poor African-Americans, is a well established risk factor for low birth weight and prematurity. However, even after adjustment for maternal weight gain, birth weight, and prematurity, absence of prenatal care remained a significant independent risk factor for asthma. . . . Thus, there are probably aspects of prenatal care apart from those that directly influence maternal nutrition and prematurity that also favorably influence asthma risk."

"Children with asthma were significantly more likely to have been born to mothers who smoked than were the nonasthmatic children. In-utero exposure to tobacco smoke increases the risk of intrauterine growth retardation and prematurity. In-utero tobacco smoke exposure also may influence lung development . . . [I]t is possible that passive smoking during early childhood also contributed to the increased asthma risk observed among children of smoking mothers."

"The occurrence of respiratory illnesses during early infancy and childhood may predispose people to respiratory illness later in life. . . . In our study, the need for positive pressure ventilation at delivery and the occurrence of bronchiolitis prior to 2 years of age were both significant independent predictors of asthma. In this cross-sectional study, it is difficult to assess whether these risk factors directly predisposed children to asthma or rather were markers for children with compromised lung function who were predisposed to problems both in early infancy and in later childhood."

"Similarly to what has been reported in other populations, maternal history of asthma and atopy (history of allergies and eczema) were more common in asthmatic children than in the nonasthmatic children. We had postulated that subjects with these 'intrinsic host' risk factors may have had different susceptibilities to the influences of adverse pre- and perinatal exposures. However, stratified analyses did not demonstrate significant differences in the influences of pre- and perinatal factors on asthma risk among subsets of children with and without a family history of asthma. Similarly, a history of bronchiolitis or prematurity did not cause significant effect modification."

"The study subjects were all born at a single hospital located within their community and received their primary health care from this hospital's continuity care clinic. The extent to which the observations made in these subjects are generalizable to children with more varied health care (i.e., children born at a different facility than the one providing their primary pediatric care) is not clear."

"[T]hese data provide further support for programs aimed at wider provision of prenatal care, including maternal nutritional support and strategies for smoking cessation, to favorably influence pregnancy outcome as well as to reduce asthma risk during childhood."

[61] **"Housing Factors and Respiratory Health Symptoms: Kanawha Valley, West Virginia," J. Spengler, S. Nakai, H. Ozkaynak, and M. Schwab, In: *Indoor Air: An Integrated Approach*, L. Morawska, N. Bofinger, and M. Maroni, Eds., Oxford, Elsevier, pp. 189-195, 1995**

"Harvard University, School of Public Health researchers, along with colleagues from Marshall Medical School and the University of New Mexico Medical School, conducted an air pollution respiratory health study across the Kanawha County, West Virginia, USA. Nine-thousand children, grades 3 through 5, participated in a school-administered health survey. Reported here are the results of analyzing the school-wide health questionnaire to ascertain the associations for three composite variables of respiratory health and housing factors. Logistic regression for the three composite symptoms controlled for gender, parental asthma, parental education and geographic location. The logistic regression analyses examined respiratory symptom association with combustion sources (cigarettes, wood stoves, unvented heaters, gas cooking), appliances (humidifiers, air cleaners, vaporizers), housing type (mobile home vs. other types), dampness conditions (mold, mildew, water damage) and the reporting of unusual odors. Results show consistent association between all symptom variables

and home dampness indicators (odds ratios between 1.2 and 1.6)."

"Only about 10% of the children living near industry, within and outside of the valley, lived in mobile homes. However, 14% of those living far from industry within the valley and 21% living far from industry outside of the valley lived in mobile homes. Half of the participants reported that someone smoked in their homes. . . . Combining a positive response to any of two moisture/mold-related questions, 21% to 25% of the homes near industry reported these dampness-related conditions without an apparent relationship to geographic location."

"Home dampness was not associated with the presence of a gas-cooking stove, fireplace, humidifier, and air cleaner. Conditions of dampness occurred more frequently in the homes with gas-cooking stoves, unvented heater, and vaporizer. Parental education, and parental occupation were associated with housing factors. The higher the socioeconomic index, the more likely the parents were to report dampness and having humidifiers, air cleaners, and/or vaporizers. The frequency of living in a mobile home, having a gas stove, and using an unvented space heater increased with lower socioeconomic characteristics."

"Three composite variables (asthmatic symptoms, bronchitic symptoms, and lower respiratory symptoms) were reported more often for children living in the valley than outside of the valley."

"Adjusted odd ratios for asthmatic symptoms were high among the children living in the homes with air cleaners (OR=1.72), vaporizers (OR=1.54), any dampness (OR=1.29), and unusual odors (OR=1.50). Air cleaners (OR=1.75), vaporizers (OR=1.51), any dampness (OR=1.59), and unusual odors (OR=1.91) were associated with bronchitic symptoms after adjustment. For the reporting of lower respiratory symptoms, adjusted odds ratios for air cleaners (OR=1.75), vaporizers (OR=1.58), any dampness in homes (OR=1.48), and unusual odors (OR=1.74) was significant. In addition, smoking in the home (OR=1.13) and use of unvented heaters (OR=1.13) also showed slight but significant increases of symptoms. Gas cooking and wood stoves were not associated with any of the three composite variables."

"The associations between home dampness and respiratory symptoms are consistent with other cross-sectional studies. . . . We . . . conclude that housing conditions that result in excessive moisture will contribute to causing and/or exacerbating respiratory symptoms for children living in Kanawha County, West Virginia and most likely elsewhere as well."

OTHER CANCER

[62] "Molecular Epidemiology and Prevention of Cancer," F.P. Perera, *Environmental Health Perspectives* 103(Suppl. 8): 233-236, 1996

"Preventable environmental causes of cancer, including tobacco smoke and other carcinogens in the diet, workplace, and ambient environment are responsible for the vast majority of human cancers. This paper reviews recent molecular epidemiologic studies that have focused on environmental carcinogenesis and environment-host interactions."

"Molecular epidemiology fuses advances in the molecular biology and molecular genetics of cancer with epidemiology to understand the molecular dose of specific agents, their preclinical biological effects, and the biologic factors that modulate susceptibility to these exposures. Biomarkers can thereby mitigate the two problems that have plagued epidemiology -- the long latency of cancer and fragmentary information on exposure."

"Tobacco smoke is a classic carcinogen and has provided a valuable model for validation or biomarkers, one with direct relevant to cancer prevention."

"Passive smoking in the home affects as many as 9 million American children under the age of 5 years. Passive smoking is associated with respiratory illness and lung cancer in nonsmokers. Moreover, children may be at heightened risk of cancer later in life as a result of exposure to such carcinogens during their early development. Biomarkers can be useful in understanding potential risks of environmental tobacco smoke (ETS) to certain groups of people (including minorities, young children, and women of reproductive age) by providing direct measurements of the

internal and biologically effective dose of ETS, its molecular effects, and susceptibility factors that modulate it."

"We have recently studied biomarkers among Hispanic and African American preschool children and their mothers with varying exposures to ETS. Serum cotinine and PAH-albumin adducts were both significantly higher in the children whose mothers smoked than in the children of nonsmoking mothers. Cotinine levels were also significantly higher in the children whose mothers did not smoke but who had ETS exposure from other household members than in the unexposed children of nonsmokers."

"A second important environmental exposure is ambient air pollution containing PAH and other products of fossil fuel combustion."

"In a pilot study of biomarkers in breast cancer, DNA adducts were detected in breast tissue from breast cancer cases and controls . . . Aromatic-DNA adduct levels were lower among the noncancer patients than in the cancer patients, although the numbers are too small to draw conclusions. . . . DNA samples from five of the seven smokers displayed the characteristic pattern of smoking-related adducts that has been reported in previous studies of lung cancer patients."

"These findings are interesting in light of the mixed results from epidemiologic studies of smoking and breast cancer risk. . . . The data from this pilot study demonstrate that carcinogens found in cigarette smoke, diet, and other environmental media reach the breast and damage DNA."

"An investigation of mothers and newborns in Eastern Europe has shown higher levels of both cotinine and PAH-DNA adducts in the cord blood of newborns than in their mothers, which is quite surprising given that *in utero* exposure to both compounds is likely to be 10-fold lower for the fetus than for the mother. This finding suggests developmentally related susceptibility to tobacco smoke and environmental PAH. The fetus appears to be less protected against DNA damage than the mother, which is inconsistent with experimental data."

"Although more research is needed to fully validate this approach, the results to date are encouraging and suggest that molecular epidemiology ultimately may prove to be a useful tool in prevention of environmentally related cancer."

Reproductive and Developmental Issues

[63] "Sleeping Position and Sudden Infant Death," C. Faure, *La Presse Medicale* 24: 1879-1881, 1995

"In western countries, the sudden infant death syndrome (SIDS) is the leading cause of mortality in infants under one year of age. In an official statement on prevention from the French Ministry of Health, sleeping in the supine position or on the side is recommended for all infants unaffected by a particular medical condition. This clear restrictive recommendation is based on valid epidemiological data but raises questions in the minds of paediatricians and general practitioners since the most recent recommendations for treatment of gastro-oesophageal reflux indicate that the prone position at a 30_ angle is the first preventive measure to be taken. We present here an objective view point on this complex problem which others may find helpful in developing a sound approach to each individual case."

"First it must be emphasized that multiple factors are involved in SIDS. While the confirmed correlation between the supine sleeping position and reduced incidence of SIDS is a valid rationale for population-based preventive measures, it does not indicate any causal relationship. Secondly, epidemiological data is [sic] valid for a given geographical area but cannot be extrapolated to other areas without taking into account intercurrent factors such as soft bedding, use of feather-bed quilts, excessive bedroom temperature and passive smoking. The public campaign for the prevention of SIDS should be encouraged as an effective low-cost measure, but both physicians and parents should be aware of its multifactorial nature in order to avoid psychologically catastrophic consequences of the guilt syndrome."

"For infants with uncomplicated simple gastro-oesophageal reflux, a formerly well-known condition but currently less well tolerated by modern parents, it is essential to explain the physiological nature of the reflux to parents then to propose formula

thickeners, antacids or prokinetic agents in particularly symptomatic cases. Sleeping in the 30_ prone position should not, in this particular case, be introduced as a preventive measure since the risk induced would probably be greater than the beneficial effect. For complicated reflux, after careful exploration and elimination of other causes of vomiting, treating should be optimized first, followed by discussion on placing the infant in the 30_ prone position which should be considered as a therapeutic tool with the same risk of secondary effects as expected with drugs."

[64] "Effects of Environmental Tobacco Smoke Exposure *in Utero* and/or Postnatally on Brain Development," S.M. Gospe, S.S. Zhou, and K.E. Pinkerton, *Pediatric Research* 39: 494-498, 1996

"We evaluated whether environmental tobacco smoke exposure *in utero* and/or postnatally affects the biochemical composition of the brain. Pregnant Sprague-Dawley rats were exposed to filtered air (FA) or to sidestream smoke (SS) for 4 h/d, 7 d/wk from d 3 of pregnancy until delivery, then their female pups were exposed to either FA or SS for 9 wk postnatally. This resulted in four exposure conditions: *in utero* FA followed by postnatal FA (FA/FA), *in utero* FA followed by postnatal SS (FA/SS), *in utero* SS followed by postnatal FA (SS/FA), and *in utero* SS followed by postnatal SS (SS/SS). After completion of the exposures, the brains were removed and divided at the pontomesencephalic junction into forebrain and hindbrain; each specimen was then analyzed for DNA, protein, and cholesterol concentration."

"This study demonstrates that perinatal exposure to SS significantly affects the biochemical composition of the brain. Although *in utero* exposure to SS did not affect the biochemical indicators of brain development, postnatal SS exposure did cause a reduction in DNA concentration. This change was more significant in the hindbrain, which contains the cerebellum, a brain region which undergoes significant postnatal development in the rat. The decrease in hindbrain DNA concentration suggests that cellular density in this brain region was reduced. In addition to this reduction in hindbrain cellular density, the total DNA content (an indicator of cell number) of the hindbrain was also decreased by postnatal SS exposure. The reduction in hindbrain cellular density was accompanied by a significant increase in the protein/DNA ratio, which is an indicator of cell size. These two changes may explain why hindbrain weight was not affected by SS exposure (brain sparing), with cellular hypertrophy helping to counteract the reduction in cell number. . . . Although cellular hypertrophy may have prevented a postnatal SS-induced reduction in brain weight, the reduction in cell number may still result in abnormal neurologic function. Therefore, it is likely erroneous to conclude that physiologic brain sparing occurred in this study."

"Although the majority of clinical studies of the effects of prenatal maternal exposure to ETS on fetal growth have focused on birth weight, one study did examine the effects of maternal passive smoking on neonatal head circumference. . . . With only this small amount of clinical data regarding the effects of ETS on fetal head growth, it is difficult to correlate the results of our animal study with the observations made in newborn humans."

"The absence of an effect of *in utero* SS exposure is difficult to explain directly from this study. It is possible that prenatal SS exposure did affect certain aspects of brain development which, in the SS/FA animals, normalized after 9 wk of post-natal FA exposure. Given the design of this study, where all of the pups were evaluated at 9 wk of age, any effects of *in utero* SS exposure, which would be present only at birth, could not be assessed. Previous work on the effects of maternal nicotine exposure on fetal brain development suggests that this is a possible explanation."

"The mechanism by which tobacco smoke produces teratogenic effects has not been established. . . . [N]icotine likely has direct teratogenic effects on developing CNS and peripheral nervous system tissues, as well. . . . The low does of nicotine used in these experiments did not adversely affect maternal weight, pup body weight, or pup brain weight. Therefore, nicotine likely has a direct teratogenic effect on developing neurotransmitter systems apart from its effect on systemic growth."

"The present study provides biologic evidence of an alteration of brain development due to SS exposure. Although the changes in the biochemical composition of the hindbrain suggest both a reduction in cell number and an increase in cell size due to SS, morphologic studies will be necessary both to further quantify

and to fully characterize these developmental effects. Although only postnatal SS exposure resulted in statistically significant changes in brain development, the observations from this study have important clinical implications. Brain development in the rat during the first 2 wk of postnatal life is substantial (brain growth spurt) and corresponds to human fetal brain growth during the third trimester. Therefore, maternal passive smoking during the latter months of pregnancy may adversely affect certain aspects of neuronal development."

[65] "In Utero Exposure to Tobacco Smoke," E. Hossny, A. Hosni, and R. Mabrouk, *Journal of Allergy and Clinical Immunology* 97: 377, 1996

"To document the fetal exposure to maternal active and passive smoking, 181 consecutive term deliveries were enrolled in this study. According to maternal self report, the sample comprised 12 active smokers, 97 passive smokers (paternal smoking) and 72 non-smokers. Cotinine -- the major nicotine metabolite -- was measured . . . in 102 cord blood samples to objectively verify the fetal exposure."

"The mean cord blood cotinine level of the 12 infants of smoking mothers was significantly higher than that of 50 infants of the group of passive smokers and of 40 infants of non-smoking mothers. The latters [sic] still had detectable amounts of cotinine denoting significant exposure to nicotine despite the negative self reporting. Maternal active smoking was associated with significantly lower birth weight, length and skull circumference in the newly born babies while passive smoking was associated with lower birth weights only and apgar scores as compared to neonates of non-smoking parents."

"Thus, Egyptian fetuses are at risk of exposure to tobacco smoke and its hazards not only from parental sources but also from exposure to environmental tobacco smoke. These data emphasize the need for nation-wide systematic persistent efforts to stop the exposure of pregnant women to tobacco smoke."

[66] "Carbon Monoxide -- Does Fetal Exposure Cause Sudden Infant Death Syndrome?" C.D.D. Hutter and M.E. Blair, *Medical Hypotheses* 46: 1-4, 1996

"No single mechanism [for SIDS] has been found but there are strong statistical associations with maternal smoking, age of the mother, parity, low social class, infant sleeping position and hyperthermia. We suggest that hypoxia, as a result of carbon monoxide exposure in early pregnancy both from tobacco smoke and other internal environmental sources in the home, results in significant pathological changes to developing fetal central respiratory control mechanisms resulting in death from central respiratory dysfunction."

"It is now accepted that cigarette smoking is a significant aetiological factor in SIDS, as this relationship satisfies the criteria for causation as described by Bradford-Hill. Carbon monoxide (CO) is the major biologically active constituent of cigarette smoke, at 40000 parts per million (ppm), it is present in concentrations much larger than that of any other potentially hazardous ingredient, for example, nicotine which is present at a tenth of this concentration. For this reason any analysis of the mechanisms underlying the relationship between maternal smoking during early pregnancy and cot death must include an examination of the possible role of carbon monoxide. Pregnant women who smoke may have mean carboxyhaemoglobin (COHb) levels in their blood up to 14% compared with values of 2.6% in non-smoking pregnant women which is produced from endogenous sources. CO causes tissue hypoxia, is readily transferred from mother to fetus and hence will put the fetus at a greater risk from the effects of hypoxia. . . . A clear dose response relationship in both animals and humans has been demonstrated between CO exposure during pregnancy and low birthweight which is another SIDS related factor and the characteristics of this growth retardation in the cot death infant are strongly suggestive of aetiological influences acting during early gestation. The dose response relationship therefore is consistent with the possibility that CO induced fetal hypoxia during early pregnancy underlies the dose-related association between tobacco consumption by the mother during pregnancy and the incidence of cot death."

"Morphological changes in the appearance of the brain stem, particularly reactive gliosis in the medulla oblongata, are found more frequently in SIDS infants, and these lesions have been shown to have a hypoxic basis which is consistent with other diagnostic markers of chronic hypoxia during early pregnancy. Parental exposure to CO levels even as low as 65 ppm alters the righting reflex in neonates indicating neurotoxicity, which indicates that parental exposure to very small amounts of ambient CO may be neurotoxic."

"If CO is to be considered as the main or sole aetiological factor in SIDS, it is necessary for there to be evidence of exposure to toxic levels of CO in the non-smoking mothers of cot death infants."

"SIDS deaths are more common in the winter months and so is the time of conception in SIDS-related pregnancies. . . . We postulate that the critical seasonal factor in both smoking and non-smoking mothers is the exposure to neurotoxic concentrations of CO at a sensitive time in fetal brain development during early pregnancy and that the damage caused may lead to subsequent cot death."

"Exposure of the infant to tobacco smoke postnatally, which includes paternal smoking, is also considered a risk factor in SIDS. As mothers who smoke postnatally have usually smoked throughout pregnancy as well, this association may only reflect the fact that these infants have already sustained damage to their brainstem as a consequence of exposure to CO in tobacco smoke during early gestation. In addition, however, exposure of the infant to smoke after delivery may in itself be a risk factor in SIDS by leading to a greater risk of apnoeic episodes when central respiratory control mechanisms have already been compromised. Amongst non-smokers, low socioeconomic status was found to be a major factor in the likelihood of significantly increased exposure to CO, and was attributed primarily to indoor sources."

"Our hypothesis is that a prime mechanism for SIDS is antenatal hypoxic damage to the fetal central respiratory control mechanism by exposure to CO from cigarette smoke and emissions from household appliances, with subsequent central respiratory dysfunction, either spontaneously or on exposure to provoking factors such as hyperthermia."

OTHER HEALTH ISSUES

[67] **"Cigarette Smoking and Health," American Thoracic Society, *American Journal of Respiratory and Critical Care Medicine* 153: 861-865, 1996**

"In 1985, the American Thoracic Society (ATS) first issued a position statement titled 'Cigarette Smoking and Health,' which reviewed the adverse health consequences of smoking known at that time. During the ten years since this initial statement, considerable scientific evidence has emerged confirming the findings of the initial report, expanding the number of conditions known to be caused or worsened by smoking, and describing the biological mechanisms by which smoking causes adverse health effects. Furthermore, passive inhalation of environmental tobacco smoke (ETS) by nonsmokers has been associated with many of the same health consequences as active smoking, albeit with much smaller degrees of increased risk, and has recently been classified by the Environmental Protection Agency as a Class A (known human) carcinogen."

"As in the 1985 ATS statement on smoking, the conclusions reached here are based on the total weight of scientific data and consensus opinion. This evidence derives both from laboratory studies and from epidemiologic studies of human populations, with causal inferences based on the consistency, reproducibility, and strength of associations, as well as the presence of an exposure-response relationship."

"Since the previous ATS statement on smoking and health in 1985, knowledge about the harmful effects of exposure to ETS indoors has greatly expanded. Many of the deleterious health effects known to be caused by active smoking have now been associated with passive smoking."

"Environmental tobacco smoke is composed of sidestream and mainstream smoke. Sidestream smoke (SS), which is emitted from the burning end of a lit cigarette, contains the same compounds found in mainstream smoke (MS), which is inhaled into the smoker's lungs and exhaled. In fact, many of the 4000 known compounds and more than 40 known carcinogens found in MS are present in greater concentrations in SS. This fact supports the potential for adverse health outcomes also to be associated with intensive and/or protracted exposure to ETS. Furthermore,

increased levels of some of the known constituents of ETS have been measured in exposed nonsmokers and vary, in part, with room size, ventilation, number of smokers, and rate of smoking."

"Early in the 1980s, several controversial epidemiologic studies found that nonsmoking women living with husbands who smoked cigarettes had a significantly higher risk of developing lung cancer than nonsmoking women whose husbands were also nonsmokers. More than 30 additional studies have since provided compelling evidence that nonsmoking women living with smoking spouses have a 1.2 to 2 times the risk [sic] of developing lung cancer during their lives than nonsmoking women in smoke-free homes. The causal nature of this association can be inferred from the consistency of investigational results from many different geographic areas and/or cultures, the presence of a dose-response relationship, and the persistence of the association in studies where other potential confounding factors were controlled. In addition, passive smoking has been causally related to the development of lung cancer among occupational cohorts, independent of exposure to carcinogenic occupational toxins."

"In 1992, the U.S. Environmental Protection Agency issued a report in which environmental tobacco smoke was classified as a Class A (known human) carcinogen. The report estimated that annually in the U.S., 3,000 new cases of lung cancer in nonsmokers or former smokers can be attributed to ETS exposure. The risk of lung cancer posed by shorter periods of passive smoke exposure, as might occur in occupational settings or public environments such as restaurants, or to children exposed to ETS by household smokers remains to be determined."

"Most studies that have evaluated the association of involuntary smoking in CHD have reported an excess risk of 20 to 50% among nonsmokers living with smokers. Further, an exposure-response relation has been documented in several of these investigations. The American Heart Association estimates that even with risk ratios as low as 1.2, ETS exposure would account for 30,000 to 40,000 excess heart disease deaths per year in the U.S., which is a significantly larger number than suggested for lung cancer."

"In adults, few studies have examined the impact of household involuntary smoking on respiratory symptom frequency. Most of the available investigations, however, do support a modest increase in symptoms for exposed nonsmoking spouses. Involuntary smoking has also been associated with modest declines in levels of forced expiratory flow measures (1 to 3%) such as FEV_1, which are unlikely to be of clinical significance."

"Results from more than 50 epidemiologic studies support a substantial increase in respiratory morbidity for children exposed to household ETS. Infants exposed to maternal smoking have a greater incidence of acute lower respiratory illnesses such as pneumonia, bronchiolitis, and bronchitis in the first 2 yr of life. This increased risk may also be influenced by paternal smoking and the total number of smokers in the household. The EPA report estimates that ETS causes 150,000 to 300,000 excess cases of lower respiratory illnesses per year in the U.S. in infants 18 mo or younger. Chronic respiratory symptoms such as cough, phlegm, and wheeze are all more common in children whose parents smoke. The association of passive smoking with childhood asthma is less certain."

"Involuntary smoking reduces the growth rate of lung function in children. Fewer studies of the effects of ETS on airway responsiveness have been reported, but most describe increased bronchial responsiveness in children from homes of smokers."

"Cigarette smoking remains the primary cause of preventable death and morbidity in the United States. Smoking causes lung cancer, COPD, and CHD and contributes significantly to mortality from other conditions such as stroke. Maternal smoking during pregnancy causes low birthweight and perinatal mortality, and it may have lasting impact on the child's physical and cognitive growth. Passive exposure to ETS causes lung cancer and poses particular danger to the respiratory health of young children. Smoking cessation strategies are important, but they should be supplemented by community and policy-level interventions. Workplace or community smoking bans, statewide taxes on tobacco, and antismoking media campaigns may be effective adjuncts to individual cessation strategies. These strategies may be an even more important disincentive to smoking initiation. The expanding horizon of health consequences of smoking and its costs to American society should again

challenge public health agencies to develop and implement effective strategies to prevent smoking acquisition by young people. These health effects should also motivate health professionals in other countries where smoking prevalence is increasing, rather than decreasing, to initiate more effective efforts to reverse this trend and minimize the excess morbidity and death that accompany this dangerous habit."

[68] **"Air Pollution and Daily Mortality in London: 1987-92," H.R. Anderson, A. Ponce de Leon, J.M. Bland, J.S. Bower, and D.P. Strachan, *British Medical Journal* 312: 665-669, 1996**

"Various recent studies, mainly from the United States, have reported associations between daily mortality and levels of air pollution within the range experienced by London in recent years. Currently no such evidence exists for any city in Britain. We report the results of an analysis of air pollution and daily mortality for London during 1987-92. The work forms part of a collaborative European project (Air Pollution and Health, a European Approach (APHEA))."

"We found associations between daily mortality in Greater London and various indicators of air pollution. The strongest association was with ozone, followed by black smoke, and these associations were independent of the effects of other pollutants. Several associations were also observed with nitrogen dioxide and sulphur dioxide, but these were partly explained by their correlation with ozone or black smoke. More associations were observed in the warm than in the cool season."

"While it is accepted that major smog episodes such as in London in 1952 have adverse health effects, it is more difficult to believe that the current historically low pollution levels could have even a small effect. Nevertheless, plausible mechanisms have been postulated that might explain a toxic effect on the lung of low concentrations of inhaled particles, and such effects might be sufficient to precipitate the death of persons rendered vulnerable by pre-existing conditions such as advanced cardiorespiratory disease. The relation with all cause mortality (1.1% increase for 10 ug/m increase in black smoke) was similar to that observed in a number of North American studies in cities where the sources of particles are somewhat different from sources in London. However, contrary to most other studies we did not observe relatively greater effects of particles on respiratory and cardiovascular mortality than on all cause mortality."

"The few studies that have looked at ozone and mortality are less consistent than those for particles. Significant effects have been reported for Los Angeles and New York but not for several other cities in the United States. Considerable evidence exists, however, that ozone is associated with daily admissions and emergency room attendances for respiratory disease and with reductions in lung function. Our own studies of London during the same period show a significant effect of ozone on hospital admissions. Good evidence exists that ozone may be toxic to the lung at concentrations encountered in London, and, as for black smoke, it is plausible that exposure could advance the time of death in an already ill person."

"These results, if indicative of a causal relation, suggest that air pollution has a measurable effect on mortality. The extent to which this is mainly due to deaths of individuals who would have died in the very near future is unclear and cannot be addressed by this type of analysis. Perhaps the main public health implication of these results lies in the possibility that much of the population is currently experiencing levels of pollution that are capable of adversely affecting the lung. Recent evidence suggests that such exposure may be associated with long term as well as short term effects on mortality. It would be prudent to assume that current levels of air pollution do have adverse health effects, and this should be taken into account in determining policies for reducing emissions of pollutants, standards for ambient concentrations, and advice to vulnerable groups."

[69] **"Morbidity and Mortality in Children Associated with the Use of Tobacco Products by Other People," J.R. DiFranza and R.A. Lew, *Pediatrics* 97: 560-568, 1996**

"This study estimates the number of children who are adversely affected by involuntary smoking. . . . This report focuses on the association of smoking with otitis media, tympanotomy, tonsillectomy, adenoidectomy, asthma, coughs, lower respiratory tract illness, and fires initiated by smoking materials."

"A literature review identified relevant research reports. Meta-analysis was used to compute a pooled

risk ratio for each condition studied. The risk ratios were combined with data on exposure rates to produce estimates of the population-attributable risk."

"Thirty-two studies concerning environmental tobacco smoke (ETS) and middle-ear disease were located."

"Only 4 of 17 cohort studies provided usable data. Of the 13 with insufficient data, 5 had positive findings and 8 did not. The meta-analysis produced a pooled RR of 1.19 (CI, 1.05-1.35)."

"Among the 11 case-control studies, 4 did not supply sufficient data, and 3 of these had negative findings. Meta-analysis produced a pooled OR of 1.58 (CI, 1.11-2.24)."

"Because the overwhelming majority of episodes of otitis media occur among preschool children, the prevalence of exposure to household smokers for children younger than 6 years of age (42.4%) was used in the population-attributable risk calculation. A best-case calculation based on the lower limit of the 95% CI around the pooled RR (1.05) indicates that 2% of cases of otitis media, or 354,000 cases annually, are attributable to ETS. A worst-case calculation using the upper limit of the 95% CI for the pooled RR (1.35) indicates that 13% of cases of otitis media, or 2.2 million cases annually, are attributable to ETS."

"Four case-control studies concerning tympanostomy tube insertion have documented an increased risk associated with parental smoking, but only in two were the results statistically significant."

"Meta-analysis produced a pooled OR of 1.38 (CI, 1.02-1.85)."

"Using an exposure rate of 42.4% and the lower range of the 95% CI around the pooled OR (1.02) in a best-case calculation, we found that 0.84% of tympanotomy operations, or approximately 5200 procedures annually, would be attributable to household smoking. The worst-case calculation, using the upper range of the 95% CI (1.85), produces an estimate that 26% of these operations, or 165,000 procedures annually, are attributable to household smoking."

"Six studies concerning the association of ETS exposure with the performance of tonsillectomy or adenoidectomy have been published."

"Meta-analysis of the two case-control studies produced a pooled OR of 2.06 (CI, 1.42-2.99) . . . A best-case calculation using the lower limit of the 95% CI results in an estimate that 16% of these procedures, some 14,000 per year, are attributable to parental smoking. A worst-case calculation, using the upper limit of the 95% CI, puts these values at 24% and 21,000 procedures."

"Thirty-three studies concerning ETS and asthma, persistent wheeze, wheeze most days or nights, or wheezy bronchitis in children were identified. Eight of these were excluded, because they did not meet our study design criteria, or because other reports on the same populations were already included. Seven studies concerning the exacerbation of asthma by ETS are considered below. Twenty studies concerned the incidence or prevalence of asthma, but three of these did not provide sufficient data. Two of the studies with insufficient data reported statistically significant elevations in the RR (1.6 and 5.0), whereas one did not."

"The remaining 17 studies were included in the meta-analysis. Sixteen reported elevated risks, and in 11 the risks were statistically significant. The meta-analysis produced a pooled OR of 1.46 (CI, 1.14-1.85) and a pooled RR of 1.43 (CI, 1.31-1.56)."

"Using the lower limit of the 95% CI around the pooled RR (1.31) in a best-case calculation, about 8% of cases of asthma, equivalent to 307,000 cases, among children younger than 15 years of age are attributable to household smoking. Using the upper limit of the CI (1.56) in a worst-case calculation, about 13% of cases of asthma, equivalent to 522,000 cases, among children younger than 15 years of age are attributable to household smoking."

"The seven studies concerning exacerbation of existing asthma by ETS all showed statistically significant risks."

"With an RR of 1.63, 21% of asthma exacerbations would be attributable to household smoking. To determine the number of office visits that are attributable to this cause, it must be taken into account that household smoking increases the overall prevalence of asthma by about 12% (based on the pooled RR). If the prevalence of household smoking exposure is assumed to be 42.4% for children up to the age of 14 years,

529,000 office visits for asthma each year in this age group are attributable to household smoking."

"The availability of national incidence data made computations for four additional categories of respiratory tract illness possible: lower respiratory tract infections (LRIs) in children younger than 5 years of age, LRIs in children 5 years of age and older, hospitalizations for any respiratory tract illness in children up to 5 years of age, and coughs in children younger than 15 years of age. LRIs include pneumonia, bronchitis, and bronchiolitis but not asthma."

"Six cohort studies were identified concerning household smoking and coughs among children. . . . All six studies reported significant elevations in the risk of coughs associated with ETS exposure."

"Meta-analysis produced a pooled RR of 1.36 (CI, 1.26-1.46). Despite the small P value, it would take only one additional neutral study to render the pooled estimate nonsignificant."

"Using the lower range of the 95% CI around the pooled RR (1.26) in a best-case calculation produces an estimate of 10% of children's coughs attributable to household ETS exposure, resulting in 1.3 million visits to physicians annually. Using the upper range of the CI in a worst-case calculation indicates that 16% of children's coughs are attributable to household ETS exposure, resulting in 2 million visits to physicians annually."

"Fourteen studies concerning LRIs in children younger than 5 years of age met the criteria for inclusion in the meta-analysis. All but two very small studies reported statistically significant elevations in the risk of LRIs associated with ETS exposure. The meta-analysis reveals a pooled OR of 2.50 (CI, 1.86-3.36) and a pooled RR of 1.46 (CI, 1.33-1.60). This large discrepancy between the OR and the RR is likely attributable to the fact that all of the case-control studies were limited to children younger than 3 years of age, who are more adversely affected by ETS than are slightly older children."

"Using a prevalence of household smoking of 42.4% and the lower range of the 95% CI around the pooled RR (1.33) for a best-case calculation, 12% of LRIs, equivalent to 260,000 cases of bronchitis and 115,000 cases of pneumonia annually, among children younger than 5 would be attributable to household smoking. Using the upper limit of the CI (1.60) for a worst-case calculation, 20% of LRIs, or 436,000 cases of bronchitis and 190,000 cases of pneumonia annually, in this age group would be associated with parental smoking."

"Only two studies addressed bronchitis in children older than 5 years of age. . . . These RRs bracket the pooled RR for LRIs among children younger than 5 years of age, suggesting that the risk persists throughout childhood."

"Eleven studies concerned hospitalizations for respiratory tract illnesses among children 5 years of age and younger. All but two very small studies demonstrated significantly increased risks of hospitalization associated with ETS exposure. One study was excluded because of insufficient data."

"The pooled OR of 2.41 (CI, 1.75-3.30) was much larger than the pooled RR of 1.55 (CI, 1.41-1.71), which included two studies of children up to 5 years of age."

"Assuming an exposed population of 42.4% and using the lower range of the 95% CI around the pooled RR (1.41) in a best-case calculation, 15% of hospitalizations for LRIs among children younger than 5 years of age are associated with household ETS exposure. Using the upper range of the 95% CI (1.71) produces a worst-case estimate that 23% of these hospitalizations are associated with household ETS exposure."

"The RR for hospitalization for LRI is slightly greater than the risk for LRI overall, suggesting that LRIs among children of smokers are at least as severe as those among children of nonsmokers. If the case-specific mortality rates because of LRI are the same for the children of smokers and nonsmokers, between 136 and 212 children under 5 years of age die each year of LRIs attributable to household smoking."

"In 1990, 148 children younger than 18 years of age died and 359 had injuries as a result of fires initiated by smoking materials."

"Children are commonly classified as exposed to ETS or not based on the mothers' smoking habits. . . . Misclassification of exposure status, inherent to all studies concerning ETS reviewed here, tends to reduce the disparity in disease rates between the exposed and

unexposed groups, resulting in an underestimate of the true magnitude of the risk. Therefore, the true risk is probably closer to our worst-case than our best-case estimates."

"Because the individual studies that were combined by meta-analysis used a variety of methods, it was not possible to make adjustments for confounding. In the individual studies, adjustment for other factors was as likely to increase the magnitude of the risk as to decrease it."

"More than 20 states have enacted laws granting smokers the right to smoke when they are not working. Yet, not a single state has enacted a law recognizing the right of children to remain free from bodily harm as a result of the smokers' use of tobacco products. Smoking should be banned wherever children are present. Children should be excluded from designated smoking areas. Organizations that cater to children should guarantee them smoke-free environments at all facilities and events."

"Potential exposure to ETS should be one of many factors considered in custody cases and situations in which children are placed in homes. Continued household exposure to ETS for asthmatic children despite physicians' advice to the contrary may constitute neglect or abuse."

"The propensity of cigarettes to initiate fires is largely the result of a failure on the part of cigarette manufacturers to use proven fire-safe cigarette designs. The fire-related deaths and injuries of hundreds of children each year could be prevented by the adoption of federal fire-safe cigarette standards or by the responsible action of manufacturers."

[70] "Do People Living Near Inner City Main Roads Have More Asthma Needing Treatment? Case-Control Study," A.E. Livingstone, G. Shaddick, C. Grundy, and P. Elliott, *British Medical Journal* 312: 676-677, 1996

"Hospital admissions for asthma in east London are 80% above the national rates. This may reflect the high incidence of acute asthma. Recent reports of a higher prevalence of wheeze or hospital admissions in children in association with traffic flow or proximity of residence to roads have highlighted concerns about the possible health effects of road traffic in the London Borough of Tower Hamlets."

"In each of two computerised general practices in Tower Hamlets around 20% of the population have received computer prescriptions for bronchodilators, inhaled steroids, or inhaled anti-inflammatory drugs since 1990. The diagnostic computer coding for asthma showed a prevalence of treated asthma of 9% in one practice and 17% in the other. We examined whether the proximity of residence to main roads was associated with these high prescribing rates for asthma in the two inner city practices."

"This study shows no increase in risk of asthma with living close to busy roads. . . . These negative findings are consistent with an ecological study of the prevalence of wheeze near the M25 motorway, but they contradict other reports. The use of routine data from general practice computers allowed basic covariates to be adjusted in a way that is impossible when using many routine data sources. The definition of cases and controls made misclassification between them unlikely. Possibly, some true cases were missed because of the requirement for computer recording of both treatment and asthma diagnosis. There is no reason to suspect that this was a source of bias. On the other hand, distance of residence from a busy road is a crude proxy for exposure to traffic related pollution, especially among adults for whom work and commuting patterns may be more relevant. Misclassification of exposure is therefore inevitable."

[71] "Health Effects of Passive Smoking in Adolescent Children," G.A. Richards, A.P.S. Terblanche, A.J. Theron, L. Opperman, G. Crowther, M.S. Myer, K.J. Steenkamp, F.C.A. Smith, R. Dowdeswell, C.A. van der Merwe, F.K. Stevens, and R. Anderson, *South African Medical Journal* 86: 143-147, 1996

"[W]ell-described adverse effects of passive smoking may be related to sensitisation of the migratory and oxidant-generating activities of circulating neutrophils."

"In this study we investigated the effects of passive exposure to cigarette smoke in the home on the levels of two plasma anti-oxidative nutrients, vitamins C and E, and the development of smoke-mediated, pulmonary immunological or haematological abnormalities.

In addition, we utilised data derived from a questionnaire and related this to domestic smoke exposure."

"In this study we investigated certain health parameters in a group of schoolchildren resident in the Vaal Triangle, an area known to have relatively high levels of atmospheric pollutants, particularly suspended particulate matter. Pulmonary functions and selected immunological investigations, including measurement of reactive oxidant generation, circulating leucocyte counts, plasma IgE and salivary IgA levels, as well as serum vitamin C concentrations were all found to be within the ranges considered normal for subjects not exposed to significant atmospheric pollution. These observations demonstrate that pulmonary and immune functions are not affected by the levels of industrial atmospheric pollution prevalent in the Vaal Triangle."

"Pulmonary functions, leucocyte counts, oxidant generation by circulating neutrophils, plasma vitamin C levels and immunological parameters were also within normal limits in the subgroup of children passively exposed to cigarette smoke in the home. We have previously reported that acute experimental exposure to high levels of sidestream tobacco smoke is accompanied by increases in both the number and pro-oxidative activity of circulating leukocytes, while plasma vitamin C levels are significantly reduced in passively smoking adults. The absence of detectable effects on these systemic parameters of smoking-related pro-inflammatory activity indicates a relatively low intensity and/or duration of exposure to sidestream smoke in our study group. However, we did observe that current maternal smoking strongly and negatively influenced most of the historical evidence of respiratory illness and symptoms. In addition, we confirmed previous findings showing that maternal smoking during pregnancy is associated with low birth weight and learning difficulties (low socio-economic status was also associated with low birth weight and cough). These effects of maternal smoking may be due to the fact that children are exposed for longer periods to their mothers, but may also relate to the fact that respiratory damage is initiated *in utero*. On a cautionary note, however, there was a greater frequency of single parents in the current maternal smoking group and the possible influence of emotional stress cannot be excluded."

"Finally, this study has highlighted the detrimental effects of parental smoking, especially maternal smoking. Our previous data have shown that although the Vaal Triangle has heavy atmospheric pollution, the present levels have only a trivial impact on the health of that population. At present, the most important preventive strategy with regard to atmospheric pollution is to dissuade parents from smoking within the vicinity of their children."

[72] "Diet and Overall Survival in Elderly People," A. Trichopoulou, A. Kouris-Blazos, M.L. Wahlqvist, C. Gnardellis, P. Lagiou, E. Polychronopoulos, T. Vassilakou, L. Lipworth, and D. Trichopoulos, *British Medical Journal* 311: 1457-1460, 1995

"The prospective component of the present study was initiated by the Greek investigators to evaluate the hypothesis that the traditional Mediterranean diet, which is still widely followed in the rural parts of the country, has beneficial effects on health and survival."

"The Greek variant of the traditional Mediterranean diet is low in saturated fat, high in monounsaturated fat (mainly from olive oil), high in complex carbohydrates (from grains and legumes), and high in fibre (mostly from vegetables and fruits). Total fat may be high (around 40% of total energy intake), but the monounsaturated:saturated fat ratio is high (around 2 or more). Actual foods and dishes include large quantities of whole grain bread, and cooked meals, soups, and salads rich in olive oil in which legumes and vegetables are consumed in large amounts. Intake of milk is rather low, but consumption of cheese and, to a lesser extent, yogurt is high; feta cheese is regularly added to most salads and vegetable stews. Until recently meat was expensive whereas fish consumption was a function of proximity to the sea. The high content in the diet of vegetables, fresh fruits, and cereals and the liberal use of olive oil guarantee a high intake of beta carotene, vitamin C, tocopherols, various important minerals, and several possibly beneficial non-nutrient substances like polyphenols and anthocyanines. Wine is consumed in moderation and almost always during meals."

"The results of this study provide evidence that an a priori defined nutritional pattern which closely reflects the Greek version of the Mediterranean diet favourably affects life expectancy among elderly people. . . . The

individual components of the diet score, however, had weak and generally non-significant associations with survival, whereas the overall score had a substantial and significant effect. A complex statistical model with appropriate interaction terms could perhaps harvest the same information, but the approach we have used has the advantages of being simple and derived from collective clinical and epidemiological evidence rather than from a best fitting process based on an individual dataset."

"As the focus of our study was survival beyond age 70 it may be argued that our results are strictly applicable to this 'surviving cohort' of elderly people. All studies in humans, however, are studies of 'survivors' beyond the age of enrolment, and there is no evidence in the epidemiological literature for interactive effects of diet and age with respect to survival. . . . Residual confounding by smoking or age is unlikely as neither of these variables was strongly related to diet score and age was controlled for in sufficiently narrow intervals."

ETS Exposure and Monitoring

[73] "Exposure Assessment Needs in Studies of Acute Health Effects," M.D. Lebowitz, *The Science of the Total Environment* 168: 109-117, 1995

"[A]ssessment of exposure is a crucial element of every study of health effects related to various environmental factors. Further, evidence on such relationships is necessary for proper environmental health policy. . . . [E]nvironmental epidemiology (and other environmental health studies as well) should use the best methods to study exposure-response relationships. The objective of this paper is to examine the validity of exposure measurements relevant to acute health effects. It evaluates some of the more pressing needs in exposure assessment for such purposes and discusses further utilization of exposure assessment results."

"The need for valid, appropriate assessment is to relate exposure to dose, and dose to acute response; this is critical in epidemiological studies and health hazard assessments of such acute responses. Thus, the objective is to insure that knowledge of the exposure to pollutants is sufficient and accurate, and that the correct pollutants of concern are being monitored and modelled. One can certainly say that without adequate exposure data, epidemiological studies may be of little use in studying such effects."

"Changes in insulation and ventilation, and the use of other heating sources (e.g., wood-burning), have appeared to affect concentrations of many combustion products and of pollutants."

"It has been obvious in evaluating ambient standards that total exposure to the pollutants needed evaluation."

"It also appears that some of these other pollutants may interact in producing disease and may be of major public health concern."

"The exposure analyst knows that many factors related to outdoor and indoor characteristics affect the temporal-spatial strengths (concentrations) of the pollutants. Indoors, they include: (1) the source strength (e.g., the number of smokers in the home or office), (2) the building structure and types of ventilation, (3) the types of fuel used, (4) the usage of pollutant sources (e.g., cooking, pesticides, paint, other consumer products), and (5) the nature and volume of local sources (including traffic and hazardous waste sites)."

"Unvented combustion of gas, wood and kerosene appliances may produce large indoor concentrations of carbon monoxide and oxides of nitrogen; concentrations may be in excess of acceptable ambient and even occupational air quality standards."

"Monitoring the air in the locations in which individuals spend time provides information on exposures during the time periods that are monitored and can be used to help calibrate models to estimate exposures in these locations for other time-periods. These measurements or estimates can be coupled with individual time-location-activity patterns to make 'indirect' estimates of total personal exposures. The most comprehensive or 'direct' approach is personal exposure monitoring."

"There are several key issues in examining the acute health effects associated with pollutant exposures:"

"The most significant factor in these exposure-response relationships is the susceptibility or sensitivity of the host, as this will determine the nature

of the reaction (if any), the degree of reaction, and the degree of exposure necessary for it. It will also be a specific function of time, which is in any case the second most important factor."

"*Primary requirements.* For studies of acute effects, one requires both precise time-activity and source usage diaries and state-of-the-art monitoring. One also requires questionnaire input (explanatory variables) related to the environment and exposures therefrom (including occupational and personal activity exposures)."

"*Key needs for exposure assessment.* The most obvious need is for personal monitors of pollutants, personal monitors/sensors of location, and better models."

"For establishment of good dose-response relationships, we need good measures of dose. . . . Although dosage at the tissue level is very important, it is usually beyond the scope of health studies; then exposure estimates become even more critical. We hope to see that the advent of biological markers change this."

"Even for those pollutants that are well-known risks to health, and certainly for others with insufficient health information, we do not know enough about the population distribution of exposure and the determinants of exposure to perform risk management and protect public health. . . . [T]here is a major scientific need to provide exposure data that are directly relevant to answering these important questions."

GENOTOXICITY AND MUTAGENICITY

[74] **"Evaluation of Micronuclei in Exfoliated Urothelial Cells and Urinary Thioether Excretion of Smokers," S. Burgaz, A. Iscan, Z.K. Buyukbingol, A. Bozkurt, and A.E. Karakaya,** *Mutation Research* 335: 163-169, 1995

"Mutagens are present in large quantities in the urine of cigarette smokers, thus, their urothelial cells may represent a possible target for absorbed and excreted mutagens. Our aim is to validate the micronucleus (MN) test in exfoliated urothelial cells obtained from urine samples of cigarette smokers. The urinary thioether (UT) test is also carried out on the same individuals in order to find out whether there is any correlation between these two end-points."

"MN frequencies were significantly higher in the smoking group than among nonsmoking subjects. The difference between the control group and each of the two subgroups of smokers was significant."

"There was no significant effect of age, coffee and alcohol consumption on both parameters analyzed, MN frequencies and UTs for smokers and for nonsmokers."

"Passive smoke exposure by nonsmokers was evaluated although this study was not designed to address the passive smoking issue. . . . A comparison of MN frequencies in nonsmokers passively exposed to smoke at home and/or at work and nonsmokers having no passive exposure to smoke revealed only a marginal increase, not significant, between the two groups."

"The frequency of MN provides a simple, reliable indicator for genotoxic damage in human tissues which are exposed to carcinogens and from which carcinomas will develop. . . . We found significantly elevated MN frequencies for 23 smokers compared to 20 nonsmokers."

"Because active smoking is a risk factor for bladder cancer, it may be possible that heavy exposure to sidestream smoke increases the risk of bladder cancer in nonsmokers. The possibility of a relationship between passive inhalation and bladder cancer receives some support from studies in which elevated levels of nicotine or cotinine or mutagens have been measured in the urine of nonsmokers passively exposed to smoke. In this study, the MN frequencies showed an increasing trend after passive smoking in relation to nonsmoking values. The results of this study are inconsistent. As the difference is not statistically significant it might be possible that it is due only to chance. On the other hand, our data on passive smoking are based on self-reported estimates of exposure. So we are aware that questions from questionnaires provide only a rough estimate of current sidestream smoke exposure rather than of lifetime exposure. However, we feel that validation of passive smoking status with the MN assay deserves attention and needs more research."

"In conclusion, our findings provide evidence of chromosomal damage in bladder tissues consistent with an increased risk of cancer at this site among smokers."

INDOOR AIR QUALITY

[75] "Assessment of Particulate Concentrations from Domestic Biomass Combustion in Rural Mexico," M. Brauer, K. Bartlett, J. Regalado-Pineda, and R. Perez-Padilla, *Environmental Science & Technology* 30: 104-109, 1996

"Recent evidence has suggested that woodsmoke exposure in developed countries is associated with acute and chronic health impacts. Accordingly, it is increasingly important to investigate the much higher woodsmoke exposures associated with the use of wood and other biomass for cooking and heating in developing countries."

"Here we report fine particle measurements in the kitchens of homes in rural Mexico in which biomass combustion was used for cooking."

"We sought to investigate particle exposures in rural Mexican kitchens and to investigate the differences in indoor particle concentrations between kitchens using different cooking fuels and stove types. An additional goal of these measurements was to use a portable nephelometer in conjunction with traditional filter sampling to improve the assessment of fine particle exposure."

"Of the 22 homes in which samples were collected, eight used biomass only for cooking during the sampling period and six homes used a combination of biomass and LPG. Biomass used for cooking usually consisted of dried corn stalks and husks. Cactus leaves, wood, and cow dung were also used in some instances."

"Our results indicate that very high particulate levels were associated with cooking on unvented biomass stoves. . . . [L]evels recorded in this study were somewhat lower than those reported elsewhere. . . . The mean PM_{10} level measured during the day in our study was 768 ug m^{-3}. . . . In the Mexican homes, we estimated that peak (5-min) $PM_{2.5}$ concentrations reached 2000 ug m^{-3} or higher in most of the homes cooking with biomass."

"Although the concentrations measured in Mexican homes may be somewhat lower than those reported in other developing countries, they are still much greater than PM_{10} concentrations reported for urban settings in developed countries and well above both the 24-h National Ambient Air Quality Standard of 150 ug m^{-3} or the California Air Resources Board Standard of 50 ug m^{-3}."

"Assuming that 24-h exposures are approximately 40% of the daytime exposure level, and using the mortality relationship described by Dockery and Pope, individuals living in kitchens with only biomass cooking would have mortality risks that were elevated by 40-50% over individuals cooking only with LPG."

[76] "A Review of the Nature of Odour Perception and Human Response," A.H. Frey, *Indoor Environment* 4: 302-305, 1995

"This paper is a distillation and integration of much of the recent biological research as it bears on IAQ. In it, I will first provide an update on the nature of odour perception relevant to IAQ and, second, I will provide an explanation for why there can be such a strong occupant response to what often seems to be trivial levels of contaminants. With this information, you may be better able to deal with present problems and avoid future IAQ problems."

"[R]ecent advances in the physiology and biochemistry of olfactory receptor cells show that odorant receptors are members of a large family of proteins that transmit signals to the inside of the cell by interacting with G proteins. These newly discovered receptor proteins can be grouped into at least 7 subfamilies."

"The odour molecule is called the first messenger of information to the brain. After it binds to the receptor protein, as described above, it triggers second, or intracellular, messengers."

"We are now almost at the point of being able to precisely specify what measures will work for odour control in a planned building at the minimal cost."

"I will turn now to the other side of the coin and, out of the results of recent biological research, provide an explanation for why there can be such a strong occu-

pant response to what often seems to be trivial levels of contaminants."

"[K]indling is a special type of time-dependent sensitisation in which repeated, intermittent, sub-threshold stimuli (electrical or chemical) induce an amplification of nerve responses to a convulsive endpoint. The various parts of the brain associated with odour perception, emotion and memory are the most susceptible to this kind of sensitisation."

"Once kindling has occurred, the same low-intensity stimulus that originally evoked little electrophysiological response, now triggers a full seizure. . . . One would expect a wide variety of symptoms, i.e. emotional, sensory, motor, hormonal, immune, and/or cognitive, depending, in part, on the limbic areas of the brain that have been kindled and the functions they regulate."

"There is also a phenomenon in biology called response facilitation. If unpleasant stimuli are repeated, two competing processes occur. One is habituation and the other is facilitation: the latter is a type of sensitisation in which the threshold for response to a stimulus is lowered. If a person perceives the stimuli as mild, then there is habituation, e.g. we quickly get used to a clock ticking and cease to perceive it. If, on the other hand, a person perceives the stimuli as strong, then there is facilitation. And whether the stimuli are perceived as 'strong' depends upon the person. There are wide individual differences and what might be mild stimuli for most people can be strong for some."

"Once response facilitation has occurred, such as by a variant of the kindling route, a person can be super-sensitised to a stimulus odour or cross-sensitised to other stimuli such as wall colour. Thus, there can be bizarre emotional response to what most of us would perceive as trivial levels of contaminant."

"In the IAQ context, fixing the source of an odorant and acting to bring the concentration down to a trivial level or even to zero may not solve the problem for some of the occupants. They may be both super-sensitive and cross-sensitised."

[77] **"Chemical Mass Balance Source Apportionment of Indoor PM_{15} in Brazilian Corporate Offices and Restaurants,"** A.H. Miguel, W. dos Reis Pedreira Filho, A.G. Allen, *Indoor Environment* 4: 355-361, 1995

"In the present study, we report the results of the application of the chemical mass balance receptor model (CMB) to speciated particulate matter samples collected for [approximately] 6 h during regular working hours at six locations which included three corporate offices, a hotel and two restaurants located in the cities of Sao Paulo (ca. 10 million inhabitants), Campinas (ca. 900,000 inhabitants), and a rural area [approximately] 20 km from the latter."

"At all sites, diesels contributed a significant fraction of the PM_{15} mass, with a maximum indoor contribution of 44% observed in office 1, a site located in the area with the heaviest traffic (14,090 veh.h^{-1})."

"In the only two sites where soft wood was apportioned, the steak house and the pizzeria, soft wood burning contributed, respectively, 23 and 26% of the mass."

"During sampling at the hotel, it was possible to smell charbroiled meat smoke. For this reason, the high charbroiled meat contribution (29%) at this site was expected to be among the highest of all. Meat cooking contribution in the steak house was smaller (11%)."

"Natural gas contribution was also high at the hotel (31%), resulting from food preparation at other restaurants located in the ground and first floor."

"Road dust contributions at the hotel, the pizzeria, and office sites 1 and 2 were very uniform (11-13%)."

"The cigarette smoke profile we used did not give satisfactory results. For this reason, in the PM_{15} apportionment . . . we used UV-RSP levels . . . to calculate the ETS contribution. The highest levels (8 and 10%) were found, respectively, at the steak house and office 1 sites, consistent with the larger number of smokers in the restaurant and the office site category."

"In the rural site and the pizzeria, respectively 37 and 22% of the PM_{15} mass could not be allocated using either [of] the profiles."

"Finally, in future source apportionment studies at indoor sites, a combination of CMB model results with air exchange and interior volume measurements would allow the calculation of average source strengths impacting the sites."

[78] **"Risk Perception and Indoor Air Quality," A. Stratico and P. Dingle, In: *Indoor Air: An Integrated Approach*, L. Morawska, N. Bofinger, and M. Maroni, Eds., Oxford, Elsevier, pp. 467-470, 1995**

"The aim of this study was to complete a preliminary investigation of the risk perceptions and attitudes of the people of Perth, the capital of West Australia, in relation to indoor air pollution. Topics related to indoor air quality are typically poorly understood in West Australia outside professional circles and well defined, researched and promoted aetiological agents (asbestos, pesticides and environmental tobacco smoke). These pollutants have featured in Government health information, legal discussion and subsequently, the general media. It was, therefore, hypothesised before the survey, that the risk perceived to be posed by indoor air pollutants would be low and the public would not demonstrate a high level of concern about the issue."

"Risk ladders are diagrammatic representations of various risks, arranged on a ladder type table. Participants were asked to rate the risk of indoor air pollutants to their health by aligning their response with a risk descriptor on a step, the health risk of which they felt was most similar to that of indoor air pollutants."

"82.9% of participants rated the risk of indoor air pollution on the risk ladder as being between steps 2 to 6 of the ladder. Most people rated tobacco smoke as being of the same risk to health as indoor air pollution. Given current knowledge of the health effects of tobacco smoke, this would suggest the risk was rated as a concern. This apparent concern was not evident in further findings. The fact that only 4.3% of people rated indoor air pollutants as posing the same risk as step 1 (Pure, Clean Air) indicates that the population generally acknowledged that there was some risk involved."

"The majority of participants described the risk of indoor air pollutants to health as acceptable. Only 9.4% rated the risk as unacceptable, though only 4.2% felt that there was no risk at all. 85.7% found the risk to be of an acceptable or negligible level. . . . Some 74% of participants indicated they were prepared to spend no money to reduce the risk they perceived. This figure rose to 86.4% when combined with those prepared to spend up to $500. Only one person was prepared to spend a sum greater than $5000."

"It is not clear whether the lack of concern demonstrated here about the risks of IAQ is based on informed or ignorant decisions. Some 76% of the population surveyed claimed to have seen some information on indoor air pollutants, suggesting that awareness of the problem is quite high."

"The results presented here have important ramifications for risk managers. Given the concerns most IAQ professionals have regarding the potential impacts of indoor air pollutants on human health, it would appear that communication programs are necessary to educate the public to the risks involved and remediation processes. Such programs will need to focus on the apathetic attitudes of the public towards the risk being communicated, highlighting that such risks are considerable and need to be acknowledged as being so. There is an obvious role for the media in such programs."

Smoking Policies and Related Issues

[79] **"Double-Barreled Assault: Tobacco's Two-Pronged Attack on Smoking Regulations Narrowly Fails," K. Ortolon, *Texas Medicine* 91: 12-15, 1995**

"In the 7th Texas Legislature, the tobacco industry launched a two-pronged attack it hoped would deal a devastating blow to local communities' attempts to regulate public smoking."

"[T]he tobacco industry pushed two major pieces of legislation. The first, Senate Bill 1237 by Sen Ken Armbrister (D-Victoria) and Rep Curtis Seidlits (D-Sherman), would have established statewide standards for smoking in all public places, such as restaurants and work sites."

"Antitobacco forces say the bill was directly targeted at cities such as Arlington, Austin, and Wichita Falls that have stringent antismoking ordinances already on the books."

"The second bill, House Bill 2460, by the same sponsors, euphemistically was labeled a children's smoking prevention measure. Representative Hirschi says the bill, again, was nothing more than an attempt to circumvent meaningful regulation of the tobacco industry."

"Both tobacco bills drew vocal opposition from health-related groups and antismoking organizations. In addition, they were condemned unanimously by the membership of the House Public Health Committee, both Republican and Democrat."

"Unfortunately, neither bill was sent to House Public Health. Instead, they went to the House State Affairs Committee, where they got a warmer reception."

"HB 2460 moved easily through both the House and Senate and was sent to Gov George W. Bush to be signed into law. SB 1237 also won Senate approval and was voted out of State Affairs. In early May, it was sitting in the House Calendars Committee waiting to be scheduled for House floor debate. That's when the tobacco industry launched the second prong of its attack."

"The Wichita Falls City Council had enacted its antismoking ordinance in the fall of 1994 by a narrow margin of 4-3. The ordinance was stringent, prohibiting smoking in workplaces, restaurants, bowling alleys, and other public places that did not have separately ventilated areas for smokers."

"Local protests prompted the council to put the matter up for a vote of the people. Even supporters of the measure feared that without a referendum, the city council might be pressured to repeal the ordinances."

"For the tobacco companies, the Wichita Falls election seemed made to order. Coming as it did in early May, possibly just days before the House would debate SB 1237, it could have given the tobacco industry lobbyists the perfect ammunition to show lawmakers that local voters did not want antismoking ordinances."

"But opponents of public smoking in both Wichita Falls and Austin were not prepared to let the Wichita Falls ordinance go down without a fight. The local coalition that had fought and won enactment of the ordinance organized again to defeat the rollback."

"The issue supporters of the ordinance attempted to drive home was the public health aspect of second-hand smoke."

"A week before the election, the tobacco industry ran a major mail campaign to support the rollback. They also employed newspaper and radio ads, but their efforts came up short."

"On election day, an overwhelming turnout of Wichita Falls voters buried the rollback attempt by a 60-40 margin."

"SB 1237 . . . never was scheduled for a floor vote and died a quiet death when lawmakers adjourned at the end of May."

STATISTICS AND RISK ASSESSMENT

[80] "Cancer Risk of Low-Level Exposure," M. Goldman, *Science* 271: 1821-1822, 1996

"It is time to scientifically challenge the old tenet stating that cancer risk is always proportional to dose, no matter how small. This seemingly blasphemous statement is based on new approaches that allow testing of the hypothesis that cancer risk is linearly proportional to dose with no threshold, the basis of much regulatory and assessment documentation. We hear much these days about the need for all assessments and regulations for risk to be based on sound and solid science. This has not been the case for physical and chemical cancer risks to humans."

"For both physical and chemical exposure to agents that are thought to increase cancer risk, it has been traditional to state that responsible evaluations and recommendations should assume that all exposures, no matter what the amount, carry an associated cancer risk. This assumption allows estimation, for example, of the lifetime cancer risk of a single ionization or the risk from intake of a single molecule of a putative carcinogen. It further leads to the concept of a collective dose, where all the ionizations are added up in all