EPIDEMIOLOGY

Ozone, Team Sports Participation, and Childhood Asthma

Source: McConnell R, Berhane K, Gilliland F, et al. Asthma in exercising children exposed to ozone: a cohort study. Lancet. 2002;359:386-391.

Between 1993 and 1998, 3,535 children between the ages of 9 and 16 with no history of asthma were recruited from schools in 12 communities in southern California and were followed for 2-5 years with annual interviews. The investigators, from the University of Southern California, the National Institute of Environmental Health Science, and the California Air Resources Board, established a network of community monitors to measure air pollutants, including ozone, PM_{10} (particulate matter less than 10 μm in aerodynamic diameter), $PM_{2.5}$, NO_2, and acid vapor. They calculated 4-year mean concentrations of each pollutant (1994-1997) for each community. On the basis of mean pollutant concentrations, 6 communities were categorized as high pollution communities and 6 as low pollution communities.

Of the 3,535 children, 265 developed asthma during the course of the study. The risk of developing asthma was no greater for children living in the 6 high pollution communities than for children living in the 6 low pollution communities, regardless of which pollutant was used to classify communities as high or low. In all 12 communities, there was a small increase in asthma among children playing team sports. This increased risk was largest among children who had played 3 or more team sports in the previous year (RR 1.8; 95% CI, 1.2-2.8). In communities with high ozone levels between the hours of 10 AM and 6 PM, children who played 3 or more team sports had a 3.3-fold increased risk of developing asthma (95% CI, 1.9-5.8). Children living in communities with low ozone levels who played 3 or more team sports did not experience an increased risk of a new asthma diagnosis (RR .8; 95% CI, .4-1.6). The amount of time children spent outdoors was also associated with asthma in communities with high ozone (RR 1.4; 95% CI, 1.0-2.1), but not in communities with low ozone.

Commentary by Ruth A. Etzel, MD, PhD, FAAP
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Playing team sports appears to increase a child's risk of developing asthma if s/he lives in a community with high ozone levels. This is a new observation that expands on previous findings that summer ambient ozone levels are a risk factor for respiratory problems in infants and toddlers.[1]

It is now fairly well accepted that the increases in new-onset asthma in the United States and other industrially-developed countries are more closely linked to exposures to indoor air pollutants than to outdoor air pollutants.[2] How does this fit with the findings of the above study? One possible explanation is the following: ozone, the primary component of urban smog, is known to increase bronchial hyper-reactivity of children to house dust mite allergen. Children who participate in 3 or more team sports inhale more ozone deeper into the lungs, which could result in increased airway hyper-reactivity to indoor allergens. Studies to test this hypothesis would be of interest.

Meanwhile, what advice can clinicians provide to concerned parents? One suggestion would be to schedule team sports activities during times of day when ozone is lower (ie, mornings rather than afternoons). In 1999, the South Coast Air Quality Management District started a pilot project to distribute pagers to coaches and parents of children with asthma. When air pollution alerts occur, a message is sent by email to pager companies.[3] This study suggests that it is not only the parents of children with asthma who should be notified, but the parents of all children participating in team sports. During periods of heavy ozone pollution, coaches may choose not to take their students outside or to reschedule practices for the morning hours.

References

1. Burnett RT, et al. *Am J Epidemiol.* 2001;153:444-452.
2. Strachan DP. *Br Med Bull.* 2000;56:865-882.
3. Etzel RA. *Environmental Health Perspectives.* 1999;107:691.

GASTROENTEROLOGY AND NUTRITION

Complementary Medicine in Inflammatory Bowel Disease

Source: Heuschkel R, Afzal N, Wuerth A, et al. Complementary medicine use in children and young adults with inflammatory bowel disease. Am J Gastroenterol. 2002;97:382-388.

The authors from the United States and the United Kingdom reviewed complementary and alternative medicine (CAM) use in children and young adults (208 patients; median age 15 years; range 3.8 to 23) with a diagnosis of Crohn's Disease (57%), ulcerative colitis (35%) or unstated or indeterminate colitis (8%). They evaluated prevalence and predictors of usage of CAM in patients with inflammatory bowel disease (IBD). Patients who modified their diets and/or consumed standard "One-a-Day" multivitamins were excluded from being considered "CAM" users. Only those patients using CAM therapy by historical questionnaires in the preceding 12 months were included as positives for statistical purposes.

CAM usage was 41% overall, excluding diet and multivitamin use. The prevalence of CAM use was similar in the United States and the United Kingdom centers in the study. The most common CAM use was megavitamin therapy (19%). Dietary supplements (17%), herbal supplements (14%), and environmental changes (eg, allergen reduction, music and aroma therapy, bioresonance, exercise, and prayer) at 10% were the next most common. Only 24% of the respondents in this survey had admitted to their physicians that they

NEUROLOGY

Early Prediction of Intractable Childhood Epilepsy

Source: Berg AT, Shinnar S, Levy SR, et al. Early development of intractable epilepsy in children: a prospective study. Neurology. 2001;56:1445-1452.

The early identification of children at risk for intractable epilepsy (IE) would facilitate a more aggressive and, perhaps, more effective medical or surgical management. Children with newly diagnosed epilepsy were prospectively identified by participating pediatric neurologists in Connecticut from January 1993 through December 1997. Parental interviews and follow-up medical record reviews and analyses were conducted by researchers at Montefiore Medical Center in Bronx, NY, Yale, and Northern Illinois Universities. Median follow-up was 4.8 years, and 98% were followed for more than 18 months. Intractability was defined as at least 1 seizure per month over 18 months despite treatment with 2 or more drugs. Only patients with intractable seizures occurring within 2 years of diagnosis were included. Drugs were titrated to maximum tolerable doses and noncompliance was ruled out. Of a total of 613 newly diagnosed cases (median age 5.3 years), 60 (10%) met criteria for intractability. Thirty-five percent (18/52) were classified (according to International League Against Epilepsy guidelines)[1] as cryptogenic/symptomatic generalized epilepsies, 2.7% (5/184) as idiopathic, 10.7% (31/290) as other localization-related, and 8.2% (6/73) were unclassified. Risk of intractability was highly correlated with etiology and syndrome ($P<.001$). The highest risk of IE was in the symptomatic (eg, secondary with CNS pathology such as anoxic brain damage) group and the lowest in the idiopathic (eg, primary or genetic and without CNS pathology) cases. IE was also correlated with a high initial seizure frequency (an interval of .5 months vs 4.7 months between 2 seizures) ($P<.0001$); focal EEG slowing ($P=.02$); and acute symptomatic or neonatal status epilepticus ($P=.001$). Age at onset between 5 and 9 years was associated with a lowered risk of IE ($P=.03$). Factors not significantly correlated with early intractability included age of onset less than 1 year, absolute number of seizures and duration of epilepsy, and unprovoked (by fever or other known stimulus) or febrile status epilepticus.

Commentary by J. Gordon Millichap, MD, FAAP

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The prognosis of intractable epilepsy (IE) may be improved by a more timely selection of cases for trials of newer antiepileptic drugs, and surgical or dietary methods of management. The authors have provided some valuable data on the risk factors for IE. Epilepsies are grouped as localization-related (focal, local, partial) or generalized.[1] *Localization-related epilepsies* are idiopathic/genetic (eg, benign childhood epilepsy with centrotemporal spikes [BECTS]), or symptomatic/cryptogenic (of known or unknown etiology). *Generalized epilepsies* are grouped as idiopathic with age-related onset (eg, benign neonatal, benign myoclonic in infancy, childhood and juvenile absence), symptomatic, and idiopathic and/or symptomatic (eg, West's and Lennox-Gastaut syndromes). Idiopathic or primary forms of epilepsy usually carry a better prognosis. As might be expected, symptomatic generalized epilepsies, a high initial seizure frequency, and focal EEG findings correlate with an intractable course.

The validity of predicting intractability based on these criteria is questioned by some authorities.[2] Is failure to respond after a trial of only 2 drugs sufficient for inclusion as IE, when 14% eventually were controlled within 1.5-3 years? A rush to surgical intervention based on these criteria may be inappropriate. May some patients who are initially responsive develop intractability later? Children with mesial temporal lobe epilepsy, a condition not addressed in this study and most commonly treated surgically, are particularly susceptible to late onset intractability.[3] Despite these criticisms and cautionary comments, the criteria for IE identified above will be a valuable tool in counseling parents on the increased need for adequate treatment and careful, frequent monitoring of seizures in these at-risk children.

References

1. Commission on Epidemiology and Prognosis, et al. *Epilepsy.* 1993;34:592-596.
2. Holmes GL, et al. *Neurology.* 2001;56:1430-1431.
3. Engel J Jr, et al, eds. *Epilepsy: A Comprehensive Textbook.* Philadelphia, PA: Lippincott-Raven. 1997.

EPIDEMIOLOGY

Ozone Pollution Linked to Increased Hospitalizations for Respiratory Diseases

Source: Burnett RT, Smith-Doiron M, Raizenne ME, et al. Association between ozone and hospitalization for acute respiratory diseases in children less than 2 years of age. Am J Epidemiol. 2001;153:444-452.

This study evaluated the association between air pollution and hospital admissions for acute respiratory illnesses (croup, pneumonia, asthma, and acute bronchitis/bronchiolitis) in children less than 2 years of age at hospitals in the greater Toronto area during the 15-year period between 1980 and 1994. Daily variation in hospital admissions was adjusted to account for the effects of day of the week, season, and weather. They found that ozone (the principal component of urban smog) was positively associated with increased hospital admissions for each of the 4 days prior to admission and on the day of admission. A 45 parts per billion increase in ozone during summer (May-

August) was associated with a 35% increase in the daily number of acute hospitalizations for respiratory diseases among children less than 2 years old (95% CI, 19%-52%). Ozone levels were not associated with acute hospital admissions due to respiratory illnesses from September to April.

Commentary by Ruth A. Etzel, MD, FAAP

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Concentrations of ground level ozone (not to be confused with the thinning ozone layer in the stratosphere) are typically highest in the mid to late afternoon on hot summer days. This is because ozone is formed by a chemical reaction between oxides of nitrogen and volatile organic compounds (primarily from vehicular exhaust) which requires the presence of sunlight. Earlier epidemiologic studies have shown that children with asthma are more likely to visit an emergency room on days following a "high ozone" day.[1] The present study documents that what was known to be true for asthma attacks among children is also true for croup, pneumonia, and acute bronchiolitis among children under 2 years. Summer ambient ozone levels are a risk factor for respiratory problems in infants and toddlers.

Epidemiologists from the Georgia Division of Public Health demonstrated that efforts to reduce downtown traffic congestion during the Atlanta Olympics were associated with reductions in ozone and lower rates of childhood asthma events.[2] Although a cause-and-effect relationship has not been established by Burnett et al, it supports the notion that children with asthma might breathe easier during the hot summer months if we increased our efforts to encourage use of mass transportation, carpooling, and bicycles.

References

1. White MC, et al. *Environ Res.* 1994;65:56-68.
2. Friedman MS, et al. *JAMA.* 2001;285:897-905.

HEMATOLOGY-ONCOLOGY

My Child Was Diagnosed with Cancer: Am I Satisfied?

Source: Dixon-Woods M, Findlay M, Young B, et al. Parents' accounts of obtaining a diagnosis of childhood cancer. The Lancet. 2001;357:670-674.

The United Kingdom's government is committed to increasing public awareness of cancer and to rapid referral to treatment centers of patients suspected of having cancer. To investigate the process of arriving at a diagnosis and possible reason(s) for diagnostic delay, the authors undertook semi-structured interviews with parents of 20 children (ages 4-18 years) with cancer who had been diagnosed 1-36 months before interview (median 11 months). Nine had leukemia, 2 had brain tumors, and the remainder had other solid tumors. The interviews were done in the home with 1 or both parents and were conducted by 1 of the investigators who was not involved in the treatment of the children. The interview consisted of a prompt-guided, but open-ended, questionnaire, and was performed only when the medical conditions of the children were judged to be stable. The interview was designed to develop insight into how parents felt about the process, how the process affected them, the signs and symptoms that parents reported as "serious," how they and the health service providers acted on these, and whether the information collected had implications for an earlier diagnosis of children with cancer.

Most parents could recall detailed information about the events leading up to their child's diagnosis. The majority of reported signs and symptoms were complaints commonly associated with viral infections, excessive tiredness, etc. Others included alarming events such as convulsion, loss of coordination, and hematuria, all of which either persisted or worsened until a diagnosis was made. Parents expressed satisfaction with the arrangement when appropriate investigation and referral were made, and accepted a few weeks delay as inevitable. On the other hand, some parents rejected seemingly reasonable diagnoses offered by MDs and insisted that additional evaluation(s) be done because they felt something was wrong. In 7 families the diagnosis of cancer was made between 2-1/2 and 8 months after symptoms were first noticed. These parents complained about the perceived inadequacy of medical response, incompetence or delay in investigation, and doctors' failure to realize that their child's symptoms were serious. The authors conclude that arriving at a diagnosis of cancer is a complex process which might be aided by paying more attention to the worries expressed by the parents when unusual or serious signs and/or symptoms are reported. They note that the current rapid referral system is activated only when a GP suspects cancer.

Commentary by Abbas Emami, MD, FAAP

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This is only one of a number of studies exploring the reasons for the delay in the diagnosis of cancer and other serious illnesses.[1-3] The diagnosis of cancer in a child is a tragic and shocking event for the family. Delay magnifies this trauma since, in most cases, later treatment results in a worse prognosis. On the other hand, the presentations of childhood cancers are so diverse that it would be extremely difficult to define useful educational interventions aimed at parents and primary care physicians. Primary care physicians need to include cancer in the differential diagnosis of patients who present with signs and/or symptoms that can not be explained by common and benign conditions. At the end of this article, the authors include the following advice from Dr John Halliday, whose own child died of cancer:[4]

- Always be prepared to see a child.
- If you are unable to find any abnormality after examination always tell the parents you cannot find anything, but are prepared to examine the child again if symptoms persist.
- Always take seriously the mother who comes and tells you that although she does not know what is wrong, she knows her child is not right.
- Beware of telling a family categorically that there is nothing wrong with their child.