

WHAT CAUSES ASTHMA? Using the Primary Scientific Literature in Introductory Biology

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Abstract: Peer-reviewed literature is the single most important forum in which research findings are presented for critical review. College biology students can benefit a great deal from early exposure to this resource, but insufficient background information, technical jargon, and complex statistical analyses often present considerable obstacles to entry-level students. This paper describes an instructional module on asthma that seeks to overcome some of the barriers to use of the primary scientific literature with introductory college biology classes. Twenty-four papers have been selected from major international biomedical journals reporting on clinical and epidemiological studies of asthma, each of which explores one or a few possible causes of the disorder in everyday life. A different paper is assigned to each student or group of students. Background material on asthma and alternative research designs is presented to prepare students for their assigned reading. At the conclusion of the module, each student or group presents a paper, its methods and findings, along with insights into the study's strengths and weaknesses.

Keywords: Allergy, asthma, respiratory disorders, peer-reviewed scientific literature

Introduction

Peer-reviewed literature represents the cutting edge of science, the single most important forum in which recent research findings are presented for critical review by one's peers. The benefits of introducing undergraduate biology students to that resource are many. Students will be exposed to the latest thinking of practitioners in the field. They will come to appreciate the breadth of skills related to the scientific enterprise such as research design, data analysis and presentation, and, of course, clear, concise writing. They can also be encouraged to look critically at a paper and identify its strengths and weaknesses.

For all the obvious benefits to a biology student of an early encounter with the primary scientific literature, significant obstacles exist. Entry-level students often lack sufficient grounding in the field to understand the concepts involved, the experimental treatments employed, and the results described. They may also find the technical jargon and statistical analyses daunting.

Presented here is a module that seeks to overcome these barriers to using the primary scientific literature in introductory college biology classes. The topic is asthma, a subject that is all too familiar to many



Normal



Asthma

Figure 1. Asthma and breathing difficulties. Source: "What You and Your Family Can Do About Asthma" by the Global Initiative for Asthma. Funded by NIH/NHLBI.

students today. Twenty-four papers have been selected from major international biomedical journals reporting on clinical and epidemiological studies of asthma. The papers have been selected for accessibility. Each explores one or a few possible causes of asthma in everyday life. Most include from 6 to 8 pages of text along with tables and figures summarizing the study's findings. While all include some statistical analysis, it is not necessary to understand the details of those analyses in order to interpret the results.

Most of the fundamentals of human biology required to understand the papers may be found in introductory college biology texts. Some additional material specific to the physiology of asthma and to research design that may not appear in most introductory texts is presented below. A format is

BACKGROUND

One of the most alarming epidemics of our times is the rapid rise in incidence of asthma and associated respiratory disorders. The epidemiological data are striking: from 1982 to 1996, the prevalence of asthma in the United States increased 59 %; mortality due to asthma went up 50 % during the same period (National Center for Health Statistics, www.cdc.gov/nchs). Fortunately, the death rate from asthma has begun to decline since 1996, probably due to both improved therapies for treating attacks and greater awareness of environmental factors in development of the disease (Figure 2).

Despite progress in combating the epidemic of asthma, we still lack a full understanding of the disease and its correlates. One thing is clear: the etiology of this disorder is complex, and its causes are many and varied. Environmental contaminants, toxins in the workplace, inherited tendencies toward allergic sensitivity, exposure to mites, dust, or cold air, vigorous outdoor exercise, use of over-the-counter pain relievers, and diet are just a few of the causal factors that have been associated with asthma.

Naturally, such a common disease of the developed world has been the subject of much research. The extensive clinical literature on asthma and the growing prevalence of this disease make it an ideal topic for college-level biology courses.

then proposed for assigning papers, assisting students in reading and understanding their paper, and in preparing a presentation before their peers. In addition to annotated citations for the 24 articles, a bibliography of additional print, video, and web-based resources for teachers and students is also provided.

While the module strives to give students an understanding of the causes of asthma, the larger pedagogical objective is to introduce students to the style, structure, and content of the primary scientific literature. Each student should also be encouraged to think critically about the strengths and weaknesses of the paper and the experimental design employed. In the concluding forum students encounter a sampling of papers that can provide insights into broader trends in current-day asthma research.

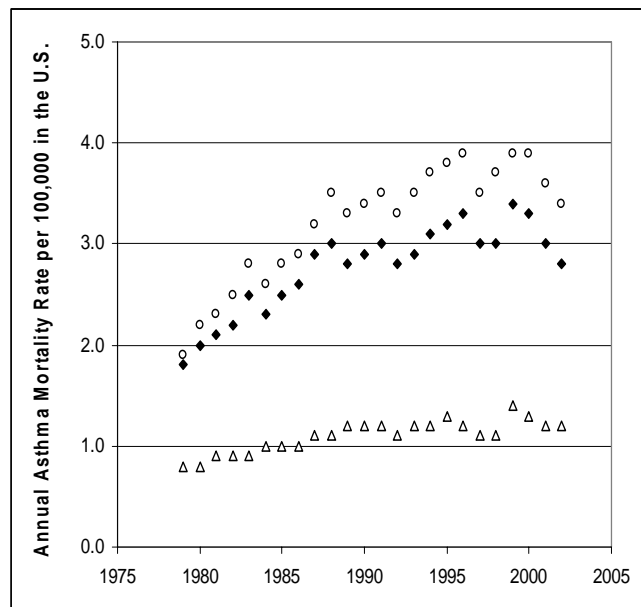


Figure 2. Annual age-adjusted mortality rate per 100,000 for blacks (circles), whites (triangles), and all others (diamonds) in the United States, 1979-2002.)Centers for Disease Control, National Center for Health Statistics (www.cdc.gov/nchs).

Anatomy and Physiology Fundamentals

Before wading into the primary literature of asthma research, your students will need an introduction to the anatomy and physiology of the human respiratory system, the human immune system, and a few basic terms related to asthma. Human respiration and immunity are well covered by most introductory college biology texts and will not be repeated here. Following is material pertinent to the subject of asthma that may not be part of an introductory biology text. Additional details on the causes of asthma are better addressed in a text on human physiology, several of which are listed under print resources below.

The lungs are a frequent point of entry for disease into the human body. With every breath, we inhale pathogens such as bacteria and viruses as well as potential irritants such as dust and pollen. While minor respiratory infections such as colds and flu are quite common, most of us enjoy generally good respiratory health. This is due to the natural defenses of the human body. Cilia line our respiratory tract, trapping dust and other particles before they can do harm. The mucous lining of the airways also aids in excluding foreign microorganisms from the lungs.

Eventually, of course, everyone suffers from some sort of respiratory infection. But when we do, the body's local inflammatory response is activated. Blood and other fluids move to the lungs carrying lymphocytes and antibodies capable of destroying most pathogens and repairing damaged tissues. For serious infections the body's immune response is a more effective weapon. Exposure to potential irritants or infections in a healthy child early in life results in development of lymphocytes that recognize each pathogen and destroy it promptly upon subsequent exposure. Once that happens, the child has developed an immunity to that pathogen.

What are allergies? Sometimes the human body seems to overreact to the presence of foreign matter in the lungs or elsewhere. Otherwise harmless substances such as dust and pollen can trigger the local inflammatory response or an all-out attack by the immune system. Such overreactions are known as allergies or allergic responses; the substances that trigger them are known as allergens.

Some allergic reactions are relatively minor, causing inflammation, congestion, or headache, much like a cold. Such mild reactions often go away in a matter of hours or days. Rarer allergic reactions may be

more serious; for example, a patient with a severe reaction to a bee sting can go into anaphylactic shock and die if not treated promptly.

Some allergies seem to be inherited, and these conditions are referred to as atopy. One common test for atopy involves injections of a number of common allergens; a patient who exhibits a reaction to a certain number is classified as atopic. Hay fever is an allergic condition affecting the mucous membranes of the upper respiratory tract and the eyes, most often characterized by nasal discharge, sneezing, and itchy, watery eyes and usually caused by abnormal sensitivity to airborne pollen. Wheeze is an obstruction of the air passages that sometimes occurs with allergies. Often a person breathes with difficulty and makes a whistling sound with each breath.

What is asthma? Asthma is an inflammatory disorder of the respiratory system, particularly of the bronchioles, the major passages for air into the lungs. During an attack, the bronchioles become constricted and the volume of oxygen reaching the alveoli is greatly reduced. The patient feels short of breath and anxious.

An asthmatic patient often suffers from hay fever, allergic dermatitis, and wheezing, but attacks of asthma are more severe. Asthma symptoms include coughing, wheezing, and shortness of breath that can interfere with sleep, exercise, and other normal activity. Severe and prolonged attacks that are untreated may be fatal.

Asthma is treated with bronchodilator drugs that open up the airways or with steroids that suppress the immune response. Medications can be taken routinely to reduce the occurrence of attacks. Avoiding the triggers of asthma attacks is also important, but identifying those triggers is not always easy.

Asthma is one of the most common disorders in the U.S. and worldwide, although it seems to be more prevalent in industrialized nations than in developing nations. Rates of occurrence of asthma seem to be rising steadily in the U.S. and it has been described as an epidemic in this country. Although asthma-related deaths in the U. S. increased 50 percent between 1982 and 1996, some data suggest that there has been a decline in deaths due to asthma in recent years (Figure 1).

What causes asthma? Few human diseases exhibit such a complex etiology as asthma. It is a disorder

that correlates very closely with a number of variables from weather and air quality to presence of allergens to heavy exercise, smoking, stress, and certain environmental pollutants. Heredity is clearly an influence as well; patients with a family history of asthma and atopy are at significantly higher risk of developing asthma than those from families without such a history.

Research Design

Each paper includes a detailed description of the research design. Since this topic is not always addressed in introductory college texts, a few words about the major types of studies may be helpful.

In a **prospective study** researchers follow several groups of subjects, often called cohorts, observing the outcomes of one or more experimental treatments and a control group over time. In a prospective study of asthma, for example, researchers might follow two groups of children, one growing up on a farm, the other in a city, and compare the prevalence of asthma and other allergic disorders in the two groups over a period of ten years.

In a **retrospective study** researchers identify a group of subjects with a disorder, then look back to determine what past exposures may have affected the occurrence of the disorder. In a retrospective study of asthma, researchers might interview a group of adult asthmatics regarding past occupational exposures to potential allergens.

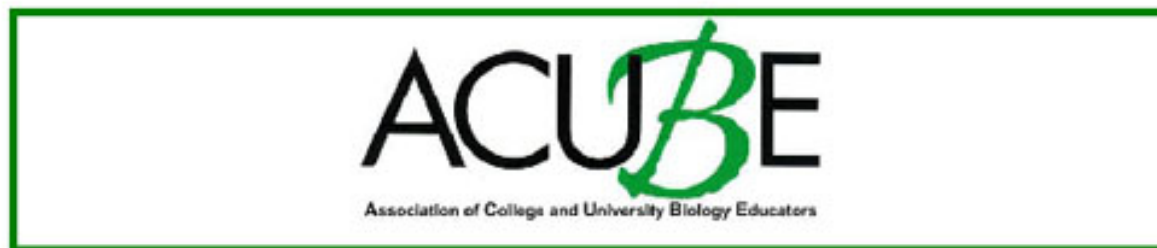
In a **cross-sectional study** researchers sample a large population such as an entire community for the presence or absence of a disorder and attempt to associate its occurrence with one or more causal factors. An example of a cross-sectional study of asthma would be the random distribution of a questionnaire to several thousand residents of a community asking if they have ever been diagnosed with asthma and whether they have had any past exposures to potential allergens or other causal factors.

In a **randomized clinical trial** researchers begin with a large population of subjects selected at random. Each subject is then assigned arbitrarily to one of several groups, then followed for years. A randomized clinical trial for asthma might involve assigning an experimental medication to one group and a placebo to another group, then evaluating the development of asthma in each group. Most clinical trials are double-blind experiments; that is, neither the subjects nor the researchers know until the study is complete which group received the experimental treatment and which group received the placebo. Human clinical trials of experimental medications proceed through a number of stages. Only a few hundred carefully-selected volunteers may be involved initially to test the safety of a medication. In subsequent stages more diverse groups of thousands of subjects are tested to assess the therapeutic efficacy of the product.

Each design has its strengths and weaknesses. Large samples are always preferable to small samples. But studies involving large numbers of participants are invariably more expensive and time-consuming, and identifying a large pool of participants who meet the necessary selection criteria may also be difficult. On the other hand, time and financial constraints may require that studies with very large samples utilize impersonal data collection methods such as mailed questionnaires or telephone surveys that may introduce subjectivity or confounding factors.

Long-term studies are often complicated by the loss of subjects. Much time spent gathering initial data may be wasted if an individual or family leaves the area or discontinues their participation midway through the study.

Authors frequently address potential weaknesses of experimental design in published papers. This can help students appreciate the many challenges and trade-offs of doing research.



ASTHMA RESEARCH: A SAMPLING OF THE PRIMARY LITERATURE

While much progress has been made in the diagnosis and treatment of asthma, the challenge of sorting out the many possible causes of the disease is truly a work in progress. Thousands of scientific papers describing research on asthma have been published in the last twenty years alone.

The 24 papers cited have been tested with introductory biology students and proved accessible. Each describes a study of one or a few putative causes of asthma; a variety of research designs is represented. Most papers are 6 to 8 pages long; publication dates range from 1997 to 2005. While all papers follow a common format (abstract, introduction, methods, results, discussion), considerable variation can be observed from journal to journal in details such as headings, subheadings, text citations, and illustrations.

All journals included are indexed and abstracted by PubMed (www.pubmed.gov). The search engine scholar.google.com will in most cases yield a link to a full-text source, although in some cases a fee is charged to non-subscribers. URLs are provided for 11 of the 24 papers that were available for free in PDF format at the time this manuscript was prepared. Other papers can probably be obtained at no cost either in the library's print collection or via interlibrary loan.

Instructors should consult library personnel regarding copyright restrictions before distributing either hard copies or electronic files to students. Requiring students to locate their own copies is an excellent educational experience in itself, but ample lead time should be provided for this process, especially for students who utilize interlibrary loan.

Following each citation is a brief summary of the study including factors investigated, target population, methodology, and major results followed by the URL where free access is available.

Akpinar-Elci, M., A. H. Cimrin, & O. C. Elci. (2002). Prevalence and risk factors of occupational asthma among hairdressers in Turkey. *Journal of Occupational and Environmental Medicine*, 44, 585-590.

A population of 206 hairdressers working in hair salons in Turkey was the subject of this study. Methods employed included a questionnaire, pulmonary function tests in the worksite, and allergen

skin tests. The authors conclude that intensity of exposure to allergens found in hair salons such as dyes, shampoos, and cosmetics are significant risk factors for asthma among hairdressers.

Ball, T. M., J. A. Castro-Rodriguez, K. A. Griffith, C. J. Holberg, F. O. Martinez, & A. L. Wright. (2000). Siblings, day-care attendance, and the risk of asthma and wheezing during childhood. *The New England Journal of Medicine*, 343, 538-543.

Over 1000 children from the Tucson, AZ, area were followed from birth until age 13 in this study of the effects of older siblings and day-care attendance on risk of asthma and wheeze. Methods employed included family questionnaires at birth and at ages 6, 8, 11, and 13, and allergen tests at ages 6 and 11. The authors conclude that exposure of a child to older children either at home or in a day care setting provides significant protection against development of asthma and wheeze later in life.

Barr, R. G., C. C. Wentowski, G. C. Curhan, S. C. Somers, M. J. Stampfer, J. Schwartz, F. E. Speizer, and C. A. Camargo, Jr. (2004). Prospective study of acetaminophen use and newly diagnosed asthma among women. *American Journal of Respiratory and Critical Care Medicine* 169, 836-841. (<http://ajrccm.atsjournals.org/cgi/content/full/169/7/836>)

Over 120000 participants in a long-term study of nurses were subjects of this study of the effect of use of the pain-killer acetaminophen on asthma. Methods employed included questionnaires regarding acetaminophen use and asthma diagnoses. The authors conclude that there is a relationship between acetaminophen use and adult-onset asthma but that further research is required on the relationship.

Gilliland, F. D., Y. Li, & J. M. Peters. (2001). Effects of maternal smoking during pregnancy and environmental tobacco smoke on asthma and wheezing in children. *American Journal of Respiratory and Critical Care Medicine* 163, 429-436. (<http://ajrccm.atsjournals.org/cgi/content/full/163/2/429>)

Over 5000 fourth, seventh, and tenth grade children in southern California were included in this study of the effects of maternal smoking on development of asthma and wheeze. A parental questionnaire was

employed to assess both maternal smoking and incidence of wheezing and asthma. Maternal smoking before birth almost doubled the incidence of asthma compared to no exposure; maternal smoking before and after birth were both significantly related to occurrence of wheezing.

Illi, S., E. von Mutius, S. Lau, R. Bergmann, B. Niggemann, C. Sommerfeld, U. Wahn, and the MAS Group. (2001). Early childhood infectious diseases and the development of asthma up to school age: a birth cohort study. *British Medical Journal* 322, 390-395.
(<http://bmj.bmjournals.com/cgi/reprint/322/7283/390.pdf>)

Over 1300 children born in five German cities were followed from birth to age 7 in this study of the relationship of early childhood infections to later development of asthma. Parental interviews conducted by a physician were used to gather data on infectious disease exposure and respiratory symptoms. The authors conclude that repeated viral infections other than lower respiratory tract infections early in life may reduce the risk of developing asthma up to school age.

Jamason, P. F., L. S. Kalstein, & P. J. Gergen. (1997). A synoptic evaluation of asthma hospital admissions in New York City. *American Journal of Respiratory and Critical Care Medicine* 156, 1781-1788.
(ajrcm.atsjournals.org/cgi/content/full/156/6/1781)

Overnight hospital admissions for asthma were compared to meteorological data collected over an eleven year period in New York City. During spring and summer, highest asthma admissions occurred during periods of increased atmospheric pollutants and pollen; during fall and winter, highest asthma admissions occurred with the arrival of cold air masses. The first or second influx of cold air in autumn triggered the most dramatic spike in asthma admissions each year. The authors conclude that cold air masses in early autumn have a two-fold effect on asthmatics, the direct effect of cold air on the lungs and the indirect effect of dust particles accumulated in heating systems and emitted the first time the system is activated for the new heating season.
Johnson, A. R., H. D. Dimich-Ward, J. Manfreda, M. R. Becklake, P. Ernst, M. R. Sears, D. M. Bowie, L. Sweet, & M. Chan-Yeung. (2000). Occupational asthma in adults in six Canadian communities. *American Journal of Respiratory and Critical Care Medicine* 162, 2058-2062.

(<http://ajrcm.atsjournals.org/cgi/content/full/162/6/2058>)

Over 18000 persons in six communities in Canada were surveyed in an effort to measure the risk of occupational exposures on incidence of adult-onset asthma. Methods employed included a questionnaire about occupational history and symptoms and risk factors for asthma followed by laboratory lung function and allergy skin tests for 25 % of the participants. The authors observed a much higher than expected occurrence of asthma among patients who worked in jobs related to nursing, baking, hairdressing, and manufacture of chemicals, plastics, or rubber. They conclude that about 1/3 of adult-onset asthma in the study population may be caused by occupational exposure.

Kogevinas, M., J. M. Anto, J. Sunyer, A. Tobias, H. Kromhout, P. Burney, & the European Community Respiratory Health Survey Study Group. (1999). Occupational asthma in Europe and other industrialised areas: a population-based study. *The Lancet* 353, 1750-1754.

Over 15000 adults living in nine European countries, Australia, New Zealand, and the United States, were subjects of this study of the relationship of occupation to asthma. Methods employed included a questionnaire on asthma symptoms and occupational history. A random sample of 20 % of those surveyed were given a spirometric test of lung function and a challenge test with a known bronchial irritant. Highest rates of asthma were observed among farmers, painters, cleaners, and farm workers.

Kraft, M., G. H. Cassell, J. Pak, & R. J. Martin. (2002). *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* in asthma: Effect of Clarithromycin. *Chest* 121, 1782-1788.
(<http://www.chestjournal.org/cgi/content/full/121/6/1782>)

Several bacterial pathogens have been identified as possible causes of asthma. Fifty-five asthma patients from the Denver area were studied for the possible effects of the antibiotic Clarithromycin. More than half the patients tested positive for the presence of one of four bacterial pathogens associated with asthma. Approximately half the patients received a course of the antibiotic, the other half received a placebo in a double-blind test. Patients receiving the antibiotic and who tested positive for at least one of the pathogens showed significant improvement in asthma symptoms. If these bacteria prove to be related to asthma, the authors conclude, antibiotics

may become an important therapy for some asthmatics.

Kramer, U., J. Heinrich, M. Wjst, & H-E. Wichmann. (1999). Age of entry to day nursery and allergy in later childhood. *The Lancet* 353, 450-454.

The authors studied the effects of early exposure to infection on development of allergies in 2500 children from three towns in eastern Germany. Methods employed included a questionnaire and tests of skin sensitivity to allergens. Risk of asthma was lowest among children who first attended day care between ages 6 and 11 months, about double for those who first attended day care between ages 12 and 23 months, and nearly triple for those who first attended day care at age 24 months or older. The authors conclude that early infection may protect children from development of allergies later in life.

Lau, S., S. Illi, C. Sommerfeld, B. Niggemann, R. Bergmann, E. von Mutius, U. Wahn, & the Multicentre Allergy Study Group. (2000). Early exposure to house-dust mite and cat allergens and development of childhood asthma: a cohort study. *The Lancet* 356, 1392-1397.

About 900 new-born infants in five German cities were followed from birth to age seven. Repeated assessments were made by parental questionnaire and by a pediatrician of sensitivity to a number of allergens; carpet dust samples were also collected from homes and analyzed for presence of mite and cat allergens. At age seven pulmonary function and bronchial sensitivity were measured in about 2/3 of the children. The authors reported no relationship between development of wheeze or asthma and early exposure to mite and cat allergens.

Litonjua, A. A., V. J. Carey, H. A. Burge, S.T. Weiss, & D. R. Gold. (1998). Parental history and the risk for childhood asthma: does mother confer more risk than father? *American Journal of Respiratory and Critical Care Medicine* 158, 176-181. (<http://ajrccm.atsjournals.org/cgi/content/full/158/1/176>)

About 200 families in the greater Boston, Massachusetts area were subjects of this study of hereditary factors in asthma. Methods employed included an initial questionnaire on parental history of smoking and respiratory disorders followed by a home visit 2 to 3 months after the birth of a child during which more detailed information was gathered. The authors conclude that the risk of having a child with asthma was three times greater in families with one asthmatic parent, six times greater

in families with two asthmatic parents. The maternal contribution to risk of asthma in children under 5 years of age was more than triple the paternal contribution, but the parental contributions were approximately equal for children older than 5 years. Liu, L. Y., C. L. Coe, C. A. Swenson, E. A. Kelly, H. Kita, & W. W. Busse. (2002). School examinations enhance airway inflammation to antigen challenge. *American Journal of Respiratory Critical Care Medicine* 165, 1062-1067. (<http://ajrccm.atsjournals.org/cgi/content/full/165/8/1062>)

Twenty Wisconsin college students suffering from mild asthma were the subjects of this study of the relationship between asthma and stress. Methods employed included a questionnaire to assess psychological state, a test of lung response to irritants, and a number of measures of immune response during periods of low stress and periods of high stress related to examinations. The authors conclude that stress contributes to increased airway inflammation and may enhance the severity of asthma attacks.

Mattes, J., W. Karmaus, M. Moseler, T. Frischer, & J. Kuehr. (1998). Accumulation of atopic disorders within families: a sibling effect only in the offspring of atopic fathers. *Clinical and Experimental Allergy* 28, 1480-1486.

About 1400 families from three urban areas of Germany participated in this study of sibling effects on atopic disorders. Method employed was a standardized questionnaire on symptoms and diagnoses of asthma, hay fever, and eczema. The authors found an inverse relationship between atopic disorders and the number of older siblings. They conclude that children with older siblings gain some increased protection from atopic disease.

McConnell, R., K. Berhane, F. Gilliland, S. J. London, T. Islam, W. J. Gauderman, E. Avol, H. G. Margolis, & J. M. Peters. (2002). Asthma in exercising children exposed to ozone: a cohort study. *The Lancet* 359, 386-391.

About 3500 children with no history of asthma were followed for five years in this study of the effects of atmospheric ozone and outdoor exercise on development of asthma. Participants were selected from 12 communities in southern California with a range of concentrations of ozone. Methods employed included questionnaires and interviews of children and parents. The authors conclude that development of asthma in the study population was associated with

heavy exercise in communities with high ozone concentrations.

McKeever, T. M., S. A. Lewis, H. A. Smit, P. Burney, J. R. Britton, and P. A. Cassano. (2005). The association of acetaminophen, aspirin, and ibuprofen with respiratory disease and lung function. *American Journal of Respiratory Critical Care Medicine* 171, 966-971.

Adult Americans participating in the Third National Health and Nutrition Examination Survey were included in this study of relationships between use of common pain relievers and development of asthma and other lung disorders. Methods employed included questionnaires administered by trained interviewers on medical history, smoking, and medication use. Laboratory lung function and skin prick tests were also administered to all participants. The authors conclude that a relationship does exist between use of over-the-counter pain relievers and incidence of asthma.

Ownby, D. R., C. C. Johnson, & E. L. Peterson. (2002). Exposure to dogs and cats in the first year of life and risk of allergic sensitization at 6 to 7 years of age. *Journal of the American Medical Association* 288, 963-972. (<http://www.rci.rutgers.edu/~donas/g-epi/Reading16.pdf>)

A cohort of 474 children in suburban Detroit was followed from birth to age 6 or 7 years in this study of the relationship of exposure to dogs and cats on allergic sensitivity. Methods employed included interviews administered by health care professionals for history of allergies, hay fever, asthma, and smoking by parents, and presence of pets in the home, antibody assays from cord blood collected at birth, as well as periodic home visits and telephone interviews. The authors conclude that exposure of a child to two or more dogs or cats in the first year of life may reduce risk of allergies later in life.

Riedler, J., C. Braun-Fahrlander, W. Eder, M. Screuer, M. Waser, S. Maisch, D. Carr, R. Scieri, D. Nowak, E. von Mutius, & the ALEX Study Team. (2001). Exposure to farming in early life and development of asthma and allergy: a cross-sectional survey. *The Lancet* 358, 1129-1133.

Over 2500 parents of children ages 6 - 13 in rural areas of Austria, Germany, and Switzerland were included in this study of exposure to a farm early in life on later development of asthma and allergy. Methods employed included standardized

questionnaires and blood samples tested for antibodies to common allergens. The authors conclude that childhood exposure to stables and farm milk provide strong protection against asthma, hay fever, and allergy.

Somerville, M., I. Mackenzie, P. Owen, & D. Miles. (2000). Housing and health: does installing heating in their homes improve the health of children with asthma? *Public Health* 114, 434-439.

The subjects of this study were 72 children living in 59 homes lacking central heating systems in a community in Cornwall, UK, where public funds were available for the installation of central heating. Methods employed included a site visit to each home to assess the condition of the heating system and completion of a parental questionnaire regarding each child's respiratory symptoms and school absenteeism due to asthma both before and after the heating system upgrade. The authors reported a significant reduction in respiratory symptoms and in school absenteeism due to asthma following the installation of central heating.

Thunqvist, P., G. Lilja, M. Wickman, & G. Pershagen. (2002). Asthma in children exposed to nitrogen dioxide in ice arenas. *European Respiratory Journal* 20, 646-650. (<http://www.erj.ersjournals.com/cgi/content/full/20/3/646>)

Over 2000 Swedish children ages 10 to 16 were the subjects of this study of the effect of nitrogen dioxide and other combustion products present in ice arenas on development of asthma. Methods employed included a parental questionnaire on allergic disease, risk factors, and years of activity in an ice arena. Measurements of nitrogen dioxide and other combustion products were also made in each ice rink on three consecutive days. The authors conclude that there is no relationship between exposure to nitrogen dioxide and other combustion products in arenas and risk of asthma.

Thurston, G. D., M. Lippmann, M. B. Scott, & J. M. Fine. (1997). Summertime haze air pollution and children with asthma. *American Journal of Respiratory and Critical Care Medicine* 155, 654-660.

About 150 children attending a New England summer camp for asthmatics were the subjects of this study of the relationship of air pollution to asthma attacks. Methods employed included daily monitoring of atmospheric ozone and fine particulate matter as well as medication use, lung function, and

other common asthma symptoms in the subjects. The authors conclude that air pollution, particularly ozone, is a major contributor to respiratory problems of asthmatic children in summer.

Von Ehrenstein, O.S., E. von Mutius, S. Illi, L. Baumann, O. Bohm, and R. von Kries. (2000). Reduced risk of hay fever and asthma among children of farmers. *Clinical and Experimental Allergy* 30, 187-193.

Over 10000 children ages 5 - 7 years living in two rural areas of Germany were the subjects of this study of the relationship of living on a farm to risk of hay fever and asthma. Methods employed included a parental questionnaire and an examination by a school physician. The authors conclude that exposure to bacterial agents on farms helps reduce the risk of development of asthma and related respiratory disorders.

Von Mutius, E., S.K. Weiland, C. Fritsch, H. Duhme, and U. Keil. (1998). Increasing prevalence of hay fever and atopy among children in Leipzig, East Germany. *The Lancet* 351, 862-866.

Over 2300 children ages 9 - 11 years living in the former East Germany were subjects of this study of

the prevalence of asthma and allergic disorders over time. The authors sought to track changes that may have resulted from the rapid industrialization following reunification of Germany in 1990. Methods employed included a parental questionnaire as well as cold-air lung challenge and skin prick allergy tests of each child. The authors observed a significant increase in occurrence of hay fever and atopic sensitization between 1991 and 1996, but no change in the occurrence of asthma.

Wijga, A. H., H. A. Smit, M. Kerkhof, J. C. de Jongste, J. Gerritsen, H. J. Neijens, H. C. Bosshuizen, and B. Brunekreef. (2003). Association of consumption of products containing milk fat with reduced asthma risk in pre-school children: the PIAMA birth cohort study. *Thorax* 58, 567-572. (<http://thorax.bmjournals.com/cgi/content/full/58/7/567>)

Data from nearly 3000 pre-school children in the Netherlands were analyzed for this study of the effect of consumption of dairy products on asthma risk. Five questionnaires on asthma symptoms and diet were administered between 0 and 3 years of age. The authors conclude that frequent consumption of milk fat is associated with a reduced risk of asthma symptoms.

Readings and Presentations

Papers may be assigned by the instructor or selected from the list by students. If class size exceeds 24, students may work in pairs or larger groups. At least four weeks should be allowed from the time a student gets a paper until the day of the presentation. While each article is relatively short, the reading will be slow. Students should expect to reread their assigned article a number of times; each subsequent reading will yield a better understanding of the paper and all the nuances of the study. A careful reading involves highlighting key sentences or paragraphs, looking up unfamiliar terms, and rereading particularly difficult sections. Students may be encouraged to confer with the instructor during office hours as time permits. If students are working in groups, one or two class periods may be set aside for groups to meet, plan, and rehearse their presentations.

Oral presentations give students practice in valuable communication skills while also exposing the class to an entire body of asthma research. Each presentation should include an introduction, background

information, hypotheses to be tested or questions to be answered, population involved, study design, description of the kinds of data collected, summary of results, and comments on the strengths or limitations of the study.

An effective presentation requires both in-depth familiarity with the paper and its findings as well as careful attention to delivery. To assist students in preparing their own presentations, you may wish to make a model presentation based on one of the papers not assigned in that class (see the sample presentation below). Beside content, your model presentation should emphasize good organization and delivery. Stress the importance of speaking to the audience rather than reading to them. Demonstrate the use of a variety of instructional aids from the blackboard and handouts to transparencies and PowerPoint presentations. You may wish to incorporate a few obvious gaffes such as a mispronunciation, an upside-down transparency, or a sudden episode of mumbling and ask your students to critique you, a task they will take quite seriously (and with a certain amount of pleasure).

Emphasize the importance of rehearsing a presentation before a friend or family member. Advise students to time their presentations and add or delete material as needed to meet the time requirements you specify. Also urge them to become familiar in advance with the set-up and use of whatever technology they plan to employ in their presentation.

A Forum on Asthma

The module concludes with a forum on asthma at which each student or group makes a presentation of their assigned paper. Individual presentations should be 12 to 15-minutes long with another 3 to 5 minutes allocated for questions from classmates; more time should be allotted for group presentations. Total time required for the forum will depend on the number of individual or group presentations; in my community college classes of 16 to 18, forums typically extend over two 2 ½ - hour sessions.

In the last week before the forum, both excitement and anxiety will mount. Some students may need encouragement, assistance, and advice both on content and delivery. You may wish to offer help in copying transparencies and handouts or requesting audio-visual equipment.

A few days before a forum I invite to my classes as guest lecturers clinical specialists from area hospitals who can share their expertise and experiences with asthma. This seems to have a direct impact on the forum as speakers and questioners refer repeatedly to the insights gained from guest lecturers.

Some of the anxiety will be alleviated as the first few students make their presentations. For me the excitement begins when presenters reveal details of their studies to which others can draw parallels or contrasts from their studies. The ultimate payoff for student and teacher alike is a presenter, or audience member, who raises an insightful question or doubt:

"The researchers relied on parents to report whether they smoked during pregnancy; I wonder if you can really trust a parent to admit that?"

"Isn't the sample size of this study awfully small and from a very limited area? Can we really generalize

about asthma in large populations from just 55 families in a small town in England?"

"All of the papers we've read have multiple authors; my paper has ten authors. How can that many people write one paper and make any sense at all?"

"Perhaps the much higher rates of asthma deaths in minority populations in the U.S. tells us more about the inequities of our health care system than about the factors that cause asthma."

"One of the authors of my paper disclosed that he has received payments from six large drug companies. Do you think that could have influenced his conclusions?"

Whether or not I agree with comments like these, I encourage this kind of critical thinking about the papers. Those are the kinds of skills that will prove invaluable to students in the sciences or in any field of future endeavor.

Verbal feedback may be offered at the end of each presentation. I prefer to make more detailed comments on an evaluation sheet designed specifically for the presentations; students receive a copy of the evaluation sheet in advance so that they will be aware of the basis for evaluations. I include comments on content as well as delivery and try to be positive and encouraging about each student's strengths, selective and constructive about shortcomings. I always make a special point of praising a student for evidence of critical thinking.

CONCLUSION

Integrating readings from the primary scientific literature into an introductory undergraduate biology course is challenging. But carefully selected papers on a topic of wide interest can yield many benefits. Students will gain direct insight into the current thinking on a subject. They will also develop an appreciation for the many decisions that a researcher must make in designing an experiment, carrying out that design, and interpreting the results. When a number of papers on one topic such as asthma are presented, students will gain a broader sense of what the areas of scientific interest are at present, what methodologies are in vogue, and what common threads can be drawn from a large body of research.

ADDITIONAL RESOURCES ON ASTHMA

I. Video Resource

Evolution. (2001). WGBH/NOVA Science Unit and Clear Blue Sky Productions, Boston, MA.

This four-part video series examines the fundamental concepts of natural selection and evolution. Episode 3 includes material on microbial evolution and the lessons to be learned regarding treatment of conditions such as asthma and allergies. Included is a short segment profiling the work of asthma researcher Erika von Mutius. That segment may also be accessed on-line at this link:
www.pbs.org/wgbh/evolution/library/10/4/1_104_07.html

Presenting a personal profile of a researcher such as Dr. von Mutius is an excellent way to give science a human face. Here is an example:

Dr. Erika von Mutius, Head of the Asthma Outpatient Clinic of the University Children's Hospital in Munich, Germany, has co-authored over 100 papers on asthma and its causes, including five of the papers in this module. She has been particularly interested in the changes that have occurred in the eastern provinces of Germany that were reunited with West Germany in 1989 and the subsequent increase in asthma and related disorders. Her pioneering work on the relationship between asthma and farms, farming, and farm animal exposure has advanced the idea that children actually benefit from early exposure to allergens. She is often associated with the "Hygiene Hypothesis" that argues that excessive cleanliness in childhood may increase the likelihood of respiratory disorders later in life.

II. Print Resources

Marieb, E. N. (2001). *Human anatomy & physiology* (5th ed.). Benjamin Cummings, San Francisco, CA.

Navarra, T. (2003). *Encyclopedia of asthma and respiratory disorders*. Facts On File Publishers, New York, NY.

Pearce, N. (1998). *Asthma epidemiology: principles and methods*. Oxford University Press, New York, NY.

Platts-Mills, T. (1999). *Asthma: causes and mechanisms of an epidemic inflammatory disease*. Lewis Publishers, Boca Raton, FL.

Scanlon, V. C. (1999). *Essentials of anatomy and physiology*. F. A. Davis, Philadelphia, PA.

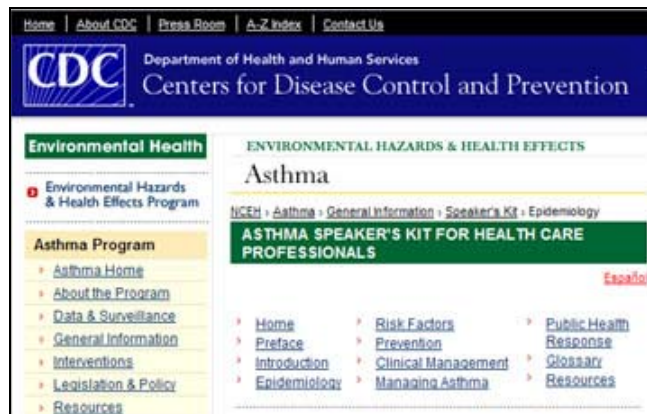


Figure 3. Centers for Disease Control and Prevention website on asthma

III. Web Resources

Enter the term "asthma" in any web search engine and you will be instantly overwhelmed with data. Some of that information is from hospitals, universities, and governmental agencies whose goal is to promote public health. But beware, much of what you find may be little more than "infomercials" designed to sell products. While the extensions ".org" and ".gov" can usually be used to guide you away from strictly commercial sites, your students will find that some companies have advertising pitches cleverly disguised to look like non-profit or governmental agencies. Learning how to tell the difference between reliable, factual information and commercial hype is a necessary skill in the Internet age (Figure 3).

www.lungusa.org/asthma. Accessed July 27, 2005.

The American Lung Association's asthma web page is an excellent source of information on the disease, symptoms, and treatment options.

www.niehs.nih.gov/airborne/home.htm. Accessed July 27, 2005.

The National Institute of Environmental Health Sciences' asthma web page provides details on many of the Institute's current research efforts on asthma as well as links to other resources both for patients and for students.

www.lung.ca. Accessed July 27, 2005.

The Canadian Lung Association's web page includes useful asthma information for families, summaries of recent research findings, and links to other resources for patients and families.

www.aaaai.org. Accessed July 27, 2005.

The American Academy of Allergy, Asthma, and Immunology maintains a web page with information on asthma for patients, families, and health care professionals including highlights of recent issues of the *Journal of Allergy and Clinical Immunology*.

www.aafa.org. Accessed July 27, 2005.

The Asthma and Allergy Foundation of America provides a web page with video tutorials and print articles such as "What is Asthma?", "Asthma Facts and Figures", "Treatment of Asthma in Children", and "Asthma and African Americans." They also provide a glossary of terms related to asthma and allergy, and a clinical trials resource center where new trials are announced.

www.socialresearchmethods.net. Accessed July 28, 2005.

The Web Center for Social Research Methods provides an excellent introduction to research design that is equally applicable to biomedical research. "Introduction to Categorical Analysis by H.-J. Cho (www.socialresearchmethods.net/tutorial/Cho/intro.htm) may be especially useful to students in understanding asthma research design.

www.cdc.gov/nchs. Accessed July 28, 2005.

The National Center for Health Statistics provides on-line access to statistics on prevalence, mortality, hospital admissions and discharges and other data for asthma by age, race, sex, year, state, and region.

IV. Model Presentation

This model presentation describes the paper "Effects of maternal smoking during pregnancy and environmental tobacco smoke on asthma and wheezing in children" (Gilliland et al 2001) The presentation may be made by the instructor, or students may be urged to read a hard copy of this transcript and use it as a guide to planning their own presentations.

INTRODUCTION: The paper that I will present today is entitled "Effects of maternal smoking during pregnancy and environmental tobacco smoke on asthma and wheezing in children." The authors are Frank D. Gilliland, Yu-Fen Li, and John M. Peters of the Keck School of Medicine at the University of Southern California in Los Angeles. The paper appeared in the *American Journal of Respiratory and Critical Care Medicine*, volume 163, in 2001.

BACKGROUND: Asthma is an increasing problem, especially in industrialized nations. It is a very common disease, and its occurrence is on the rise. Many environmental factors have been blamed including air pollution and toxins in the workplace, but there is little evidence to support a link between these factors and increased risk of asthma. Ample evidence does exist for a relationship between smoking and other respiratory disorders.

QUESTION OR HYPOTHESIS: The question researchers asked was whether a relationship exists between exposure of children to cigarette smoke in the home and the development of asthma or wheezing. They looked at both *in utero* and post-natal exposure.

POPULATION: The study included 5762 children in grades 4, 7, and 10 in the public schools of 12 communities in southern California. Most were 10 years old or younger, white, and from middle class families. The paper does not give details on how the children were selected, but they were all part of a larger long-term study of childhood respiratory health carried out by the Children's Health Study and sponsored by the Keck School of Medicine.

DATA: Two types of data were collected. First, lifetime tobacco smoke exposure was assessed for each child based on a questionnaire that asked a parent for information on smoking frequency for all adult household members and regular visitors. Second, the incidence of wheezing and asthma was judged by a second parent questionnaire asking whether the child had ever been diagnosed by a doctor as having asthma, whether the child had ever

suffered from wheezing, and the incidence of related respiratory disorders such as pneumonia, bronchitis, atopy, and allergies.

RESULTS: 1.7 % of the children in the study were themselves smokers; 18.8 % had some *in utero* smoke exposure, 39.5 % had some smoke exposure after birth; 57.5 % had either *in utero* or post-natal exposure; 16.0 % had both *in utero* and post-natal exposure.

- *In utero* exposure alone almost doubled the incidence of asthma compared to no exposure (an odds ratio of 1.8 to 1).
- But post-natal exposure alone did NOT have a statistically significant effect (1.1 to 1).
- Children with both *in utero* and post-natal exposure had a 1.3 to 1 increased risk of developing asthma, although the authors suggest that the small numbers of children in this category explain the lack of statistical significance.
- Both *in utero* exposure and post-natal exposure were significantly related to occurrence of wheezing (1.8 to 1 and 1.3 to 1, respectively)
- The strongest relationship between both types of exposure and wheeze (2.0 to 1) occurred in families with a history of asthma or atopy.

PROBLEMS WITH THE STUDY: The authors note several weaknesses in their study. First, women who smoke during pregnancy almost always smoke after giving birth, so it is not possible to separate

maternal *in utero* effects from maternal post-natal effects. Secondly, when collecting data via questionnaires, researchers relied on the memory and truthfulness of participants; the study could have been improved by providing objective measures of tobacco use and of smoke exposure.

STRENGTHS: One strength of this study is the size of the population throughout the study.

CONCLUSIONS: Among the conclusions listed by the authors were

- Parental smoking significantly increases the risk of a child developing asthma and wheeze.
- *In utero* exposure alone is strongly related to asthma, but post-natal exposure alone is not.
- *In utero* and post-natal exposure are both strongly associated with development of wheeze.
- A family history of asthma combined with exposure to smoke increases a child's risk of developing asthma and wheeze still further.

The authors conclude by stating that

"...we estimate that elimination of *in utero* exposure to maternal smoking would prevent 5 to 15 % of asthma cases in children...Reducing the burden of chronic respiratory diseases may require a stronger focus on the reduction of smoking among women during their childbearing years."

Call for Resolutions

The Steering Committee of ACUBE requests that the membership submit resolutions for consideration at the 2006 Annual meeting to the Chair of the Resolutions Committee. Submit proposed resolutions to:

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Kirksville, MO 63501,

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