Important Advances in Clinical Medicine

Epitomes of Progress—Allergy

The Scientific Board of the California Medical Association presents the following inventory of items of progress in Allergy. Each item, in the judgment of a panel of knowledgeable physicians, has recently become reasonably firmly established, both as to scientific fact and important clinical significance. The items are presented in simple epitome and an authoritative reference, both to the item itself and to the subject as a whole, is generally given for those who may be unfamiliar with a particular item. The purpose is to assist the busy practitioner, student, research worker or scholar to stay abreast of these items of progress in Allergy which have recently achieved a substantial degree of authoritative acceptance, whether in his own field of special interest or another.

The items of progress listed below were selected by the Advisory Panel to the Section on Allergy of the California Medical Association and the summaries were prepared under its direction.

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Immunological Defenses in Cancer

THERE ARE MANY SIMILARITIES between the human body's defenses against intracellular infections (tuberculosis, toxoplasmosis, fungi and many viruses) and its defenses against cancer. The two types of immunological defense against infection and cancer are cellular and humerol.

Cellular immunity depends on specifically sensitized lymphocytes which can kill the sensitizing cancer cells specifically. After combining with the antigenic tumor cell, lymphocytes may (1) kill by contact, (2) release factors (lymphokines) which kill cells nonspecifically and (3) induce production of activated macrophages. Once macrophages are activated, they can kill intracellular organisms or tumor cells nonspecifically. Activated macrophages are important in protection from diseases such as toxoplasmosis and tuberculosis, as well as cancer. Macrophages may be activated by a variety of factors such as bacille Calmette Guérin (BCG), chronic toxoplasmosis and endotoxin. Several studies indicate that BCG vaccination in large numbers of children may decrease future rates of mortality from leukemia.

Recent studies indicate that most cancer has tumor specific antigens. Release of small quantities of these antigens, as from slow growing cancers, may induce both circulating immunoglobulin antibodies and cytotoxic lymphocytes. If a large quantity of tumor antigen is released, the sites of antibody production may be overpowered and immunological paralysis ensues. In these cases the cancer may continue to grow rapidly. Soluble tumor antigen may also combine with cytoxic lymphocytes to neutralize them, which is a frequent occurrence in late cancer.

If the immunological response to the tumor antigen is principally circulating noncomplement binding immunoglobulin antibodies, these may coat the surface of the tumor cells and block the cytotoxic effects from any subsequent antitumor lymphocytes. Development of cancer immunity might best be obtained by methods which minimize the production of noncomplement binding immunoglobulin antibodies and encourage the delayed immune system to produce specific antitumor lymphocytes, and possibly to produce complement binding antibodies which may also kill cancer cells.

As in many types of infection (that is, intracellular) the tumor may persist if it is in a portion

of the body away from ready access to antibodies. Immunological defenses are much less effective in large tumors, as antibodies cannot reach the inner malignant cells. Therefore, immunological defense in cancer (immunosurveillance) is much more effective in the beginning stages of cancer or after most of the tumor mass has been removed by surgery, radiation or chemotherapy. Unfortunately, the latter two modes of therapy may cause a pronounced reduction in the patient's immune capacity.

The human body is probably faced with numerous neoplastic mutations, but rarely develops clinical cancer. The successful operation of the nonspecific and specific immune system is probably largely responsible for this level of protection.

Research in this area has produced a number of recent advances in our understanding of cancer immunology. It is anticipated that this new knowledge will add to and modify the information in this epitome.

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Indoor Air Pollution: Effects on the Non-Smoker of Tobacco Smoke Indoors

Smoke from an idling cigarette, "sidestream smoke," contains almost twice the tar and nicotine as does smoke inhaled while puffing on a cigarette, "mainstream smoke."

Furthermore, the carbon monoxide in the air near a smoker can be increased from an atmosphere value of perhaps one to three parts per million (ppm) to transient peaks exceeding 90 ppm. Two other components of any tobacco smoke are hydrogen cyanide and nitrogen dioxide. The latter, an acutely irritating gas, exists in cigarette smoke in amounts 160 times greater than levels considered safe for extended exposure.

Thus, the tobacco smoking minority of our population is the source of a unique and hazardous form of indoor air pollution which can best be discussed by using such special terms as *sidestream, mainstream* and *passive* smoking. Tobacco smokers who smoke indoors clearly put upon their more numerous non-smoking colleagues by worsening allergic rhinitis, bronchitis, asthma and other respiratory diseases.

Passive smoking by the non-smoker in a poorly ventilated room or car has been shown to result in carboxyhemoglobin levels well within the range known to cause impairment of visual acuity and faulty time interval discrimination. It is possible that such levels could be lethal for the bystander who suffers from arteriosclerotic heart disease. It is no cause for wonder, then, that the Surgeon General of the United States has declared a Bill of Rights for the non-smoker.

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Coexistence of Asthma in Children with Cystic Fibrosis

A CHILD with such recurrent, chronic symptoms as cough at rest or exertion, wheezing, fever, dyspnea or nasal obstruction may well have asthma, cystic fibrosis or both. This similarity of symptoms is a reflection of similar responses to the pathophysiology involved in both diseases.

It is well known that bronchial obstruction in patients with asthma is due to bronchoconstriction, submucosal edema, and increased bronchial secretions, and that patients with cystic fibrosis have highly viscid secretions. What is usually not appreciated is that nearly 50 percent of children with cystic fibrosis have exercise-induced bronchoconstriction and that a significant number have improved pulmonary function after inhalation of the bronchodilators epinephrine and isoproterenol. Therefore, bronchoconstriction as well as abnormal bronchial secretions, play a role in the clinical symptoms of both asthma and cystic fibrosis.

Asthma has been reported to occur in 7 to 10 percent of children with cystic fibrosis. This is similar to the incidence of asthma in the pediatric population in the United States. Therefore, it is important to realize that in some patients, both cystic fibrosis and allergy may be causing the symptoms and that treatment for both is necessary.

Recently, Caplin et al found interesting similarities between aspirin-induced asthma and cystic