

The ALLERGY ARCHIVES

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Pioneers and Milestones

Cooke and Vander Veer on heredity and sensitization

While habits of mind and character were entirely independent of initial mental force and early education, the body was so much a creature of parentage and circumstances, that no punishment for ill health should ever be tolerated.

—Samuel Butler

Erewhon, Ch 14, 1872

Robert A(nderson) Cooke (Fig 1) was born in 1880 in Holmdel, New Jersey. Whether heritage or childhood illness was the major influence in pointing him to the study of medicine was never a question; the dye had been cast for both factors to play motivating roles during his intellectually formative years. His professional medical lineage traced through 3 successive generations, from his great-grandfather, who served as a physician with the Colonial forces during the Revolutionary War, to his father, a founder of the New Jersey State Medical Society.

Robert, at age 8, had intractable asthma. He would later recall being “an asthmatic child ... continuously ... inhaling little volcanos of (burning) Himrod’s asthma powder and vomiting from (medications) syrup of ipecac and squill. Adrenalin was not yet known.” So too was allergy then an unknown, by name, definition or mechanism, as the cause of his asthma. Ultimately, the first of responsible factors, environmental circumstance of association with residence on the family’s estate farm, revealed itself. On entering boarding school, Robert immediately became asthma free only to experience return of symptoms during vacations



FIG 1. Robert A. Cooke, MD (1880-1960). Courtesy of National Library of Medicine. Note scar on forehead at the site of surgery for treatment of his frontal sinusitis and associated asthma.



FIG 2. Horse-drawn New York City ambulance, late 19th-early 20th century. Courtesy of Bellevue Hospital Archives. “What is food (*succor*) to one is to others bitter poison (*potent allergen*).” Lucretius (Titus Lucretius Carus [99-55 B.C.]). *De Rerum Natura*, Bk 4, l1.

spent at home when in contact with horses and exposed to the stables. Robert Cooke himself would establish a second factor, heredity, 28 years later.

While attending Rutgers University (A.B. 1900, M.A. 1904) and Columbia University College of Physicians and Surgeons (P&S; M.D. 1904), Cooke’s unavoidable contact with laboratory animals and experiences with respiratory tract infections expanded his appreciation of asthma-triggering agents. Subsequently, during his Presbyterian Hospital internship, every horse-drawn ambulance call he made (Fig 2) created an asthmatic problem. Relating to hypodermically administered adrenalin—introduced into clinical medicine only within the previous 2 years—he recalled “six-months as a bus surgeon would not have been possible were it not for my Adrenalin kit. ... I put as much adrenalin under my skin as any human being.” Related difficulty reached a critical height in 1907 when, as a research fellow at Cornell University Medical College and assistant attending physician at Bellevue Hospital, he assisted in an emergency tracheotomy on a patient with diphtheria. A prophylactic immunizing injection of equine-source antitoxin resulted in an immediate reaction of collapse, a 10-hour loss of consciousness, and impaired breathing that necessitated artificial respiration and adrenalin. He had served as his own model of common allergen content in horse dander and horse serum and of the human counterpart of animal anaphylaxis that was described only 5 years previously by Portier and Richet.

In his first position as research physiologist in the Cornell Department of Experimental Therapeutics, his initial studies, published between 1907 and 1914 dealt with diabetes, fat metabolism, and paroxysmal hemoglobinuria. At that time, the field of immunology and preliminary observations on experimental hypersensitivity were just beginning to emerge. The

imprints of his disabling asthmatic attacks and near-fatal anaphylactic shock soon turned his interest to awareness of relevant scientific developments. On coincident entry into medical practice, he began to explore applications of new laboratory-derived knowledge for the diagnosis, treatment, and prevention of the asthma, hay fever, and eczema group of disorders then known as “protein sensitization, human hypersensitization, and clinical anaphylaxis.” Cooke’s affiliation with Cornell took on an added dimension in 1910 with Arthur Coca’s appointment to the school’s Department of Experimental Pathology. Coca’s background in pathology, bacteriology, and chemistry provided the basis for common interest and collaborative studies in sensitization phenomena. In this setting an early initiative followed up the Noon (1911) and Freeman (1911, 1914) pollen “inoculation”/“vaccination” reports. A 1915 study, the “Treatment of hay fever by active immunization,” Cooke’s first publication in the nascent field of allergy, (1) conceptualized clinical manifestations of protein sensitization to environmental antigens as a result of antibody fixation to tissue, in contrast to protective immunity effected by circulating antibody, and thus hay fever to reflect localized anaphylaxis; (2) described a method for preparation of allergen extracts with a special protein-extracting fluid developed by Coca; and (3) introduced the intracutaneous technique of skin testing and its advantage over the conjunctival method.

In 1918, the combination of formal affiliation of Cornell and the New York Hospital, with Coca’s appointment to establish a Division of Clinical Immunology within the unit, enhanced the Cooke-Coca collaboration. Meanwhile, Cooke had been joined in practice by Albert Vander Veer, Jr (1878-1959), a Columbia P&S classmate and hay fever sufferer, who, like Cooke, had a family background of medicine. His father had served as a surgeon with the Union Army during the Civil War and then successively was Professor of Surgery and Dean at Albany Medical College and Chancellor of the University of the State of New York. From the early Cooke-Vander Veer association, a 1916 seminal publication, “Human sensitization,” reported observations on 621 patients that pointed to inherited predisposition to transmission of the development of hypersensitivity disorders.

In addition to conducting research on animal models of sensitization, Coca’s laboratory provided a base for immunochemical studies of allergens. The availability of joint facilities for the preparation of diagnostic and therapeutic materials and for hospital outpatient space enabled Cooke, in 1920, to seize the opportunity to establish the first US multistaff asthma and allergy clinic. Advance notices and publicity in the news media brought a long waiting line of patients on opening day. With a combination of intellectual fervor, imagination, and initiative, Cooke

moved to the forefront of work aimed at the understanding and management of sensitization phenomena and disorders.

Within 2 years, the clinic’s original attending staff of 3 physicians had increased to 10, and its sessions increased from 2 to 4 half days a week; progress in meeting objectives in patient care, research, and teaching was well underway. Academic outreach activities in the clinic were integrated into a required Cornell third-year student course in immunology. A longtime associate whose introduction to Cooke began as a student recalled “the intensity and purpose he emanated while lecturing. You just knew that medical history was being made in front of your eyes. Something truly great was happening” (Bengtsson).^{*} At the postgraduate level, courses were offered, and visiting physicians were welcomed to instruction by Coca on laboratory methods and preparation of allergenic extracts and to learn special techniques of diagnosis and therapy. Cooke’s energetic initiative had expanded into a resource from which physicians and materials were provided to seed allergy services in other hospitals in and beyond New York (eg, Boston, St Louis, Philadelphia, Baltimore, and Pittsburgh).

Meanwhile, Cooke and colleagues, joined by other pioneers of hypersensitivity (eg, Warfield Longcope, Chairman of Medicine at Columbia P&S and Presbyterian Hospital, and his research assistants in the study of immunologic disease; Oscar Schloss, Chairman of Pediatrics at Cornell, who described food allergy and the scratch test; and Rufus Cole of the Rockefeller Institute, working in infection and immunity) provided the nucleus for the first professional allergy society. From a discussion group of 13 that gathered in Cooke’s office 1 or 2 evenings a month, a national organization, the Society for the Study of Asthma and Allied Conditions, evolved in 1923. Cooke’s 2-year term as its first president was only a formal beginning for his leadership and influence in clinical, research, academic, and organizational arenas. As the Society became the Eastern parent of the American Academy of Allergy, his stance was intense and dynamic, his strong voice heard, and his behind-the-scene dominant activities heeded in making judgments and setting policies: creating practice standards, developing certification of clinics, performing collaborative research, electing members, preparing publications, founding the *Journal of Allergy*, championing allergy’s recognition as a separate segment of medicine, and establishing a corresponding subspecialty board within the American Board of Internal Medicine for certification of its practitioners. In serving 13 years as a founding member of the board, his controversial firm position of restricting eligibility to only those who were certified by the parent American Board of Internal Medicine was uncompromising. Despite engendered antagonism, he had little if any sympathy and concern for

the cause of establishing certification in allergy for pediatricians being denied by their own American Board of Pediatrics.

By 1932, 14 years after its founding, the clinic had expanded beyond size, scope, and facilities able to accommodate its 200 daily patient visits. As many as 20 professional staff and visiting physicians worked in small cubicles among many patients, all within a small and crowded space. On invitation from Roosevelt Hospital, with cooperative release from New York Hospital, attending staff and resources were moved to the new Roosevelt base (later named the Institute of Allergy). The integration of facilities for patient care, laboratory and clinical investigations, and training of fellows and resident physicians served as the prototype and model for nationwide allergy clinics and centers. The day of National Institutes of Health grants for research and training in allergy was yet to arrive. Nor were there hospital institutional funds available to support Cooke's programs. Undeterred, as a personal mission through varied initiatives, he himself generated the resources to provide for purchases of equipment and laboratory supplies and salaries for the fellows (Reed).*

Although housed in new and larger quarters, the Roosevelt clinic continued in the same layout as developed in its New York Hospital original site. With reason, "laboratories were interspersed with examining rooms, and everyone was within shouting distance. The end point of most of the investigation that had gone on in the clinic and was continuing was the skin of patients or donors; the reagin (or skin sensitizing antibody) was the basic element of atopic disease, and up to this time had never been demonstrated in vitro. This meant all serum fractions made to isolate the reagent needed to be tested on skin. All allergy extracts and fractionation were standardized on the skin. The animal model of non-precipitable antibodies and identity of the factor causing cold urticaria were tested on the skin" (Seebohm).*

"Although there was no question he was the Boss in his private office, the clinic and his inpatient hospital service, for those around him his authority, however, was more revered than feared. He was always addressed as Dr. Cooke even by Bill Sherman, his close associate" (Seebohm). To a scientist outside of the Roosevelt circle, he projected the image of a "patrician."

Cooke's expertise and tireless energies were concurrently devoted to research. With the internist and otorhinolaryngologic practice and clinic associates and chemistry laboratory coworkers he brought into the field, Cooke's 91 single and coauthored publications covered a wide range of original contributions. Among those opening or pioneering new areas of study—as reflected in his 1947 textbook *Allergy in Theory and Practice*—were chemistry and fractionation of allergens, hyposensitization therapy, sensitiza-

tion mechanisms, identification and measurement of blocking antibody, design of protein nitrogen units for standardization of allergenic extracts, identification of new environmental allergens and their sources (including house dust), drug reactions, diagnostic materials and methods, skin test methods, constitutional reactions, differences between immediate and delayed hypersensitivity, lymphocytes in experimental contact dermatitis, serologic changes in immunotherapy, and, with Coca, classification of hypersensitiveness and the concept of atopy.

Cooke's observations on the association of many asthmatic patients with infection—especially his own troubles with recurrent asthma and paranasal sinus disease (Fig 1)—led him to pioneer the possible bacterial sensitivity theory of causation. In reflecting on the pre-corticosteroid and pre-volume-controlled respirator era of problematic status asthmaticus and dependence on intravenous aminophyllin drip, Seebohm* recalled: "He treated them with vaccines of bacteria cultured from their sinuses and carried out extensive searches for foci of infection particularly found in surgical extirpation of the ethmoids and or the maxillary sinuses. When antibiotics became available, and when we received reports of subacute bacterial endocarditis being cured with massive doses of penicillin, we tried the same treatment on several 'infective' asthmatics. It didn't work . . . Penicillin was helpful in the treatment of secondary infections, but of little help in attacking the asthmatic state . . . Cooke's conviction about the bacterial cause was further weakened."

Additionally impressive were Cooke's concurrent activities in the out-of-the-clinic-and-laboratory world. Eminent missionary and representative for an emerging field, he was a trustee of Rutgers University and distinguished as a medical scientist with clinical orientation elected to membership in the selective American Association of Immunologists. True to his tenet "Physician first, allergist second," he moved among the elite in internal medicine as an elected member of the prestigious Association of American Physicians and American Clinical and Climatological Association, and as vice president and regional governor of the American College of Physicians, and associate editor of the *Annals of Internal Medicine*. As consultant to the Surgeon General of the US Army during World War II, he played an authoritative role in establishing guidelines and criteria for evaluation and disposition of issues relating to asthma and allergic disease (eg, questions pertaining to draft registrants and enlistees and problems of personnel whose illnesses developed while in service). Maintaining interests in activities back on the farm, he was a founder and president of the New Jersey Aberdeen Angus Breeders Association.

Robert Cooke died in 1960 at age 79. Within his legacy was mentorship of a whole generation of physicians trained for entrance into a newly born spe-

cialty and who established and developed clinical, academic, and research sections of asthma and allergy in institutions worldwide. His last publication, an undelivered intended address printed posthumously in a 1960 issue of the *Journal of Allergy*, expressed his dedication to research, an insightful understanding of allergic disease and asthma, and foresight in recommending a broadening of interests in other immune systems mediated disorders.

The father of allergy, Robert Cooke; who else?

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Paul M. Seebohm, MD. Fellow in Allergy, Roosevelt Hospital, 1948-1949.

Otella J. Bengtsson, (1898-1995), MD. Cornell, 1922. Practice associate of Robert Cooke, quoted by Janet M. Werkmeister, MD, President, New York Allergy Society.

Charles E. Reed, MD. Resident in Internal Medicine, Roosevelt Hospital, 1948-1951.

Robert Cooke and Albert Vander Veer and the genetics of allergy

Our knowledge of the pathogenesis of asthma and allergies has unfortunately been woefully inadequate until recent times. This is because to understand the biology of a condition such as asthma, you have to know its genetics; however, to understand the genetics, you have to know the biology. On the basis of studies performed around the turn of the 20th century regarding human sensitization and genetics, Cooke and Vander Veer¹ investigated their interrelationship. This signaled the beginning of the modern studies of the genetics of asthma and allergies.

Allergy and genetics

In ancient times, traits were traced through generations. Blood was thought by Aristotle to be the basic element of heredity in humans.² He believed that blood flowed from parents to offspring, carrying hereditary traits. Heredity is the passing on of characteristics from parents to offspring. Genetics is the science of heredity. Although human traits and diseases, such as asthma and hay fever, have been known to be familial for years, the science of genetics is young. The observations of many generations of plants by Gregor Mendel at the beginning of the 20th century

led to his formulation of the first law of heredity, resulting in the founding of the science of genetics.³ Investigators initially used plants and then animals to develop and understand inheritance. It became apparent that these laws of biologic inheritance described by Mendel might be applied to humans.

A relationship between allergy and familial and genetic factors was suggested by early reports, including those of Hippocrates.^{4,5} Wyman described a family predisposition for autumnal catarrh, and Floyer noted in 1698 that asthma was familial.^{5,6} Through the years, it has become evident that familial, if not genetic, factors are involved in allergic conditions, such as asthma, hay fever, and eczema.⁵ On the basis of this information, Cooke and Vander Veer performed their investigations, applying the ideas of Mendelian genetics to the human conditions of asthma and allergies.

Allergy and the immune system

Although descriptions of allergic conditions, such as asthma, rhinitis, and anaphylaxis, date back to ancient times, their pathogenesis was not understood. In the early 1900s, as pointed out by Cooke and Vander Veer,¹ little had been published regarding the human sensitization to foreign protein. The concept that the immune system, which had been shown to protect our bodies, could cause adverse reactions was difficult to accept. The relationship between the immune system and allergy was suggested in 1837 with Magendie's description of what we now call anaphylaxis.² Blackley,⁷ who in 1873 noted skin reactivity to grass pollen with hay fever, suggested a connection between hay fever and asthma and the immune system. The word "anaphylaxis" was introduced by Richet to designate a hypersensitive state as one strictly opposed to prophylaxis and distinctly disadvantageous to the host.⁸ The relationship between anaphylactic antibodies and hay fever was established by Wolff-Eisener in 1906 and with asthma by Meltzer in 1910.^{9,10} At the same time, another theory stating that toxins play a major role in the pathogenesis of hay fever and asthma was suggested. The role that anaphylactic antibodies and toxins had in the development of asthma and hay fever was being debated at this time.^{1,5}

Cooke and Vander Veer

Against this background, suggesting that there is a heritable factor in the development of allergies, such as hay fever and asthma, which involve an immune mechanism, Cooke and Vander Veer investigated the pathogenesis of these conditions. They stressed the role genetics might be playing. Their findings and thoughts were published in an article entitled "Human sensitization" in the *Journal of Immunology* in 1916.¹

This was the first systematic study of the genetics of allergic disease. It marked the beginning of the modern investigation into the genetics of complex diseases, such as allergies. Their study was a thoughtful clinical investigation of certain phases of anaphylactic reactions. They discuss the 2 suggested theories (toxin vs sensitization or anaphylaxis) regarding the pathogenesis of these conditions, such as asthma, hay fever, and hives, and they concluded that these were conditions of sensitization and not toxin.

The data contained in their article included histories of 621 cases of human sensitization the authors observed over a 5-year period. They described the heritability of the clinical manifestations of sensitization of conditions, such as bronchial asthma, hay fever, urticaria, angioneurotic edema, and acute gastroenteritis after the ingestion of certain foods. They excluded the diagnosis of eczema because they thought the methodology used to identify this condition was too sensitive and not specific. As a result, they believed its inclusion would falsely influence their results. The authors suggest that further studies were needed. It is apparent, at the present time, that atopic dermatitis, probably a form of eczema, usually has family history of allergy as a major criterion for its diagnosis. Recent studies have demonstrated that atopic dermatitis has heritability.^{5,11}

Cooke and Vander Veer sought to determine, by using family histories, what part inheritance plays in the clinical manifestations of sensitization, such as hay fever, asthma, urticaria, angioneurotic edema, and acute gastroenteritis. They initially investigated the frequency of human sensitization. Sixty-eight randomly selected individuals, along with both of their parents, were evaluated. A total sample of 204 subjects was included. Five of the 68 probands evaluated provided a history of sensitization. In the total group of 204 individuals, 14 (7%) provided a history of sensitization. They conclude that the frequency of human sensitization with clinical manifestation is probably not greater than 10%. This compares with the current estimation of the prevalence of atopy being 10% to 30%, that of asthma being 3% to 15%, and that of hay fever being 10% to 41%.¹²

The role of inheritance as a factor in sensitization was then investigated. They excluded the 5 proband cases of the 68 families initially studied. There was a family history of allergy in 6 (9.5%) of the remaining 63 probands without clinical manifestations of allergies. Seventy-six additional individuals with no history of sensitization were also studied. Of these, 11 (14.5%) provided a family history of sensitization. They next evaluated 621 cases of sensitized individuals. In these the family history for sensitization was negative in 260 subjects, positive on one side in 205

subjects, and positive on both sides in 39 subjects. In other words, of 504 cases with a history of allergies, there was positive family history in 48.4%. This is in comparison with the 9.5% and 14.5% prevalences of a positive family history of allergy in the 2 groups of subjects ascertained with probands not having a history of allergy. They concluded that there was a heritable factor in the pathogenesis of allergies. The influence of inheritance on the age of onset of clinical symptoms of sensitization was further investigated in 500 of the cases in which age of onset was given. They observed that inheritance had a distinct effect on the age of onset of symptoms. The more complete the inheritance, the earlier the manifestations.

Nature of inheritance

The question of whether individuals inherited the tendency to have an allergy or the specific disease and immune response was also evaluated. They studied the offspring of parents and observed that those of an allergic parent were not born sensitive. Furthermore, it was observed that parents might transmit a tendency for sensitization without themselves being sensitized. A comparison of sensitization of antecedents and descendants was performed in nuclear and small extended families and twins. They concluded "that sensitized individuals transmit to their offspring not their own specific sensitization but an unusual capacity for developing bioplastic reactivities to any foreign proteins."¹

Further analysis of their database revealed that a large number of their cases had clinical evidence for more than one sensitization. Of 551 cases of sensitization, 42.3% had evidence for multiple sensitization. This suggested to the authors that these "individuals, as a group, possess a very peculiar capacity to become sensitive in a natural way to certain proteins in their environment and habit of life frequently expose them." To further investigate this question, natural sensitization to pollen and artificial sensitization to horse serum in the form of antitoxin was studied. Although the numbers were small, they concluded that artificial sensitization, even in individuals with an abnormal capacity to be sensitized, is not easily obtained. It was suggested that the type of clinical sensitization that develops in allergic individuals is dependent on factors in addition to those of exposure. These findings have been confirmed by many investigators, who stress that many factors, both environmental and nonenvironmental, might influence the sensitization process.¹²

Mode of inheritance

Once having determined that there was heritability of conditions such as asthma and allergic rhinitis,

TABLE I. Sensitization in children and parents

Inheritance	No. of families	Total children	Children sensitized		Average age of total	% Sensitized at average age	Estimated sensitized children	
			No.	% Total			No.	% Total
Both parents	26	70	39	55.7	23.0	82.6	47.2	67.5
One parent	52	150	77	51.3	27.5	84.5	91.2	60.0
Negative	148	631	205	32.4	35.0	84.0	244.0	38.6

Cooke and Vander Veer then investigated their mode of inheritance. Cases of double, single, and negative family histories of allergies were studied to determine whether they conform to the Mendelian laws, either as a dominant or as a recessive trait (Table I). The predicted estimates of the number of sensitized children were based on their "age of onset curve." By using a dominant model, 67.5% instead of the theoretical 75% for bilateral inheritance and 60% instead of 50% for unilateral inheritance was found. They concluded that this was sufficiently close to suggest that sensitization is inherited as a dominant characteristic. However, they could not explain the 38.6% of the patients who had sensitization, but there was an absence of sensitization in the family history. They suggested that their results were in part the result of a failure to find the antecedent sensitization because of the limitation of their methods of ascertaining the family histories. To date, there are no adequate studies regarding the mode of inheritance of asthma or allergies. Dominant, codominant, and recessive modes of inheritance have all been suggested. It is now apparent that these conditions are complex and multifactorial in origin. They do not fit a simple Mendelian mode of inheritance.^{3,13}

Genetics of asthma and allergies after Cooke and Vander Veer

The heritability of allergy has been established on the basis of the investigations of Cooke and Vander Veer. Many investigations have been performed to identify which genetic loci are linked to asthma and atopic conditions. The main methods used to identify the genetic loci of complex phenotypes such as these include the positional and candidate gene approaches. These genetic mapping methods have included the evaluation of gene-gene and gene-environment interactions. We are starting to see further improvements in the methodology and technology, such as the use of single nucleotide polymorphism and microarrays to investigate and understand complex conditions, such as asthma and allergy. It is apparent that the present methods of the study and analysis of the complex diseases of asthma and allergy have their limitations.¹⁴

Many chromosomal sites and suggested candidate genes for asthma and atopic phenotypes are now being reported. These have included CTLA4 on chro-

mosome 2q33. Chromosome 5q has been reported to have many possible genes, including the cytokine cluster consisting of IL-4, IL-13, IL-5, IL-3, and IL-9, as well as CD14, GM-CSF, the β_2 -adrenergic receptor (ADRB2), and the corticosteroid receptor. Linkage of these phenotypes with TNF- α and TNF- β on chromosome 6 have been noted. Chromosome 11q has been found to have linkage of asthma and atopic phenotype with the β chain of the high-affinity IgE receptor (Ig ϵ RI) and glutathione S-transferases (GTSTP-1, GSTM1, and GSTT1). Chromosome 12q has been suggested to have linkage involving INF- γ , stem cell factor, insulin-like growth factor, and STAT-6. Linkage on chromosome 14q has been reported with the T-cell receptor. An Iceland study detected linkage of asthma to chromosome 14q24. One of the candidate genes in this area is a disintegrin. Chromosome 16q has been noted to have linkage of the asthma and atopy phenotypes with the IL-4 receptor α subunit (IL4RA). Recently, chromosome 20p13, containing a disintegrin and metalloprotease (ADAM33), has been observed to have linkage with asthma and asthma-associated phenotypes.^{12,14-21}

It is evident that asthma and allergic phenotypes are very complex and polygenic conditions. We most likely have several genes (ie, gene a, b, and c) involved in the development of atopy. Having only 2 of these genes, such as a and b or b and c, alone will not result in the development of the defined atopy phenotype. All 3 are needed. In addition, to develop another phenotype, such as asthma, you might need the atopy genes (eg, genes a, b, and c), as well as other genes (eg, genes d, e, and f) that are required for the ultimate clinical expression of the disorder. These other genes might be needed to localize the process, such as in the lung. In addition to having the genetic predisposition for asthma and its associated conditions, environmental interactions are needed. These environmental factors might shift the balance between protection and development of the clinical picture. Asthma and atopy appear to be a genetically determined condition involving several genes that appear to interact with each other, as well as with the environment.

Since Cooke and Vander Veer's initial study regarding the genetics of asthma and atopic conditions, many investigations have confirmed their observations.^{1,12} With the development of a variety of techniques in various disciplines, including

immunology, biochemistry, molecular biology, and statistics, the specific genetics of allergic conditions are being further defined. The understanding of the genetic basis initially evaluated by Cooke and Vander Veer and the role of environmental interactions with these genes will result in a better understanding of asthma and allergies and provide improved methods to diagnosis and treat these conditions. As a result of the knowledge gathered in different areas, we are increasing our understanding of the genetics and biology of allergies. This information will enable us to (1) identify genetic factors, (2) define environmental cofactors, (3) characterize how genes and the environment work together to cause disease, and (4) design treatment and prevention measures, including drugs designed for the individual's genetic make up.

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