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Immunoglobulin E response during viral infections

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One hundred and three patients (90 nonatopics and 13 atopics) with respiratory infections to various viral agents were studied retrospectively with respect to IgE immunoglobulin levels during acute (1 to 7 days) and convalescent (8 to 30 days) phases of infection. It was found that 59% of patients had a decrease of 20% or more in IgE level, 27% remained the same, and only 14% showed a rise of 20% or more from the acute to the convalescent phases of infection. IgE levels decreased up to 3 to 4 wk after symptoms and the degree of decrease was more apparent for the nonatopics who had higher IgE levels in their acute phase of infection. Less dramatic decrease in IgE was observed for the 13 atopics studied. The changes in IgE levels during the viral infectious period are discussed in terms of possible cellular mechanisms that may control IgE immunoglobulin.

Clinical studies dating back almost 40 yr have suggested that upper respiratory tract infections are associated with bronchial asthma and can precipitate or potentiate attacks of bronchial asthma[1, 2] and wheezing in asthmatic patients.[3, 4] Other studies have shown that killed influenza vaccine can increase bronchial sensitivity to drugs such as methacholine.[5] By viral isolations and serologic techniques, a variety of viruses including respiratory syncytial virus, parainfluenza virus, corona virus, and rhinovirus have been identified in patients with asthma. In addition, Ida et al.[6] found an enhancement of IgE-mediated histamine release from human basophils and ultraviolet-inactivated herpes simplex virus-1, influenza A, and adenovirus-1.

From the recent results of Frick et al.,[7] a possible virus infection association was found with the onset of allergic sensitization in infants. Other investigations have shown both increased[8, 9] and decreased[10, 11] levels of IgE in association with viral infections. The purpose of the present study was to examine more closely the relationship between viral infections and IgE levels. For this purpose, a retrospective study was performed on a population of patients with upper respiratory symptoms of viral origin. All patients were followed clinically, screened for viral and bacterial infections, and IgE and RAST determinations were performed during the course of their acute and convalescent phases of infection.

METHODS AND MATERIALS

Selection of patients

The records of the Regional Virus Laboratory were inspected and a list prepared of patients showing a rise ≥4-fold in antibody level (by complement-fixation test)[12] against one of the common respiratory agents, between the first and second specimens of paired sera. From this list 103 individuals were chosen (from November, 1976, to March, 1977) on the basis of having been diagnosed as having an acute upper and/or lower respiratory infection, the onset of which was 8 or fewer days before submission of the first blood specimen. Individuals with chronic viral infections and/or bacterial infections were eliminated from the study. The antigens in the test were as follows: influenza A (soluble), influenza B (soluble), parainfluenza, type I, parainfluenza, type II, parainfluenza, type III, adenovirus, respiratory syncytial virus, herpes simplex virus, psittacosis group, and myoplasma pneumoniae.

In every case, the clinical condition was sufficiently severe to warrant hospitalization of the patient. Most patients manifested bronchitis, tonsillitis or pharyngitis. Their ages ranged from 6 mo to 60 yr. About half were under the age of 15 yr and the rest between the ages of 16 and 60 yr. Clinical histories were taken, particularly noting the patients' infections (recent and past) and atopic state. All patients were screened for allergies using a radioallergosorbent test (RAST).

IgE and IgE antibody determinations

Serum IgE levels were measured using paper disk radioimmunoassay technique (PRIST; Pharmacia Diagnostics,

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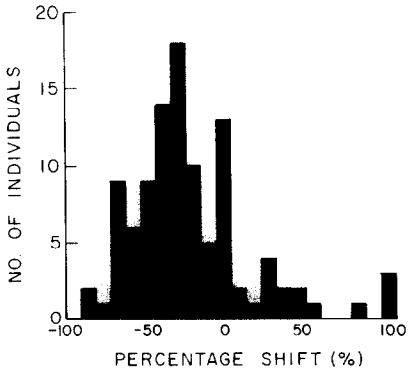

FIG. 1. Percentage shift in IgE level between acute and convalescent phase.

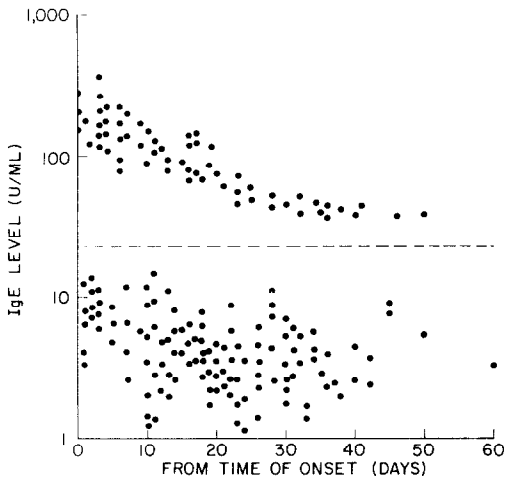

FIG. 2. IgE levels of nonatopics vs time of onset of viral infection.

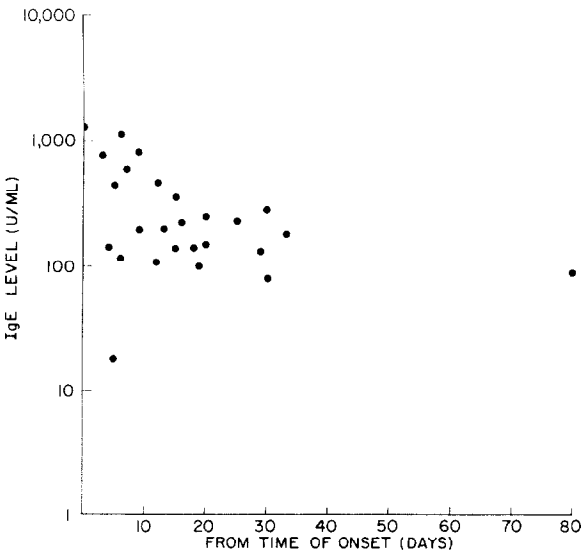

FIG. 3. IgE levels of atopics vs time of onset of viral infection.

Piscataway, N. J.). All samples were examined in duplicate. In our hands, a 20% variation was found for IgE levels over the range used in this study considering both kit-to-kit variation as well as variation with the same kit. All kits were standardized not only with the standards provided with the PRIST kit but also with several sera whose IgE levels were over the working range. Each pair of acute and convalescent sera were always run with the same kit. A change of 20% or more in IgE level was considered significant.

The Phadabas RAST for IgE antibodies was determined for acute phase samples for all patients against the more common allergens found in the Ottawa area, such as tree (maple, birch, oak, elm), grass (sweet vernal, meadow fescue, rye grass, timothy), weed (short ragweed, western ragweed, wormwood, mugwort, Russian thistle), mold (*Alternaria, Aspergillus, Cladosporium*), animal (cat, dog), food (egg, milk, fish), and house dust allergens. An individual was considered positive to RAST if a 2+ reaction was found for one or more allergens.

RESULTS

Analysis of changes of IgE levels for given individuals during acute and convalescent phases of infection are shown in Fig. 1. It was found that 59% of patients had a decrease in IgE level of 20% or more, 27% remained the same, and only 14% showed a rise of 20% or more for this immunoglobulin. Fig. 2 shows a scattergram summarizing the IgE levels of the nonatopic population as a function of time after onset of infection. For each patient, acute and convalescent IgE values were plotted. Fig. 3 shows a similar scattergram for the atopic patients. For the nonatopics (Fig. 2), 2 populations of patients emerged, one segregating at IgE levels greater than 60 U/ml (nonatopic I) and the other, below this value (nonatopic II). Figs. 4 and 5 show the average IgE value for a given time after onset of infection for the nonatopic and atopic groups respectively. Decreases in IgE levels were observed for the high and low nonatopic groups as well as for the atopic group of patients. It can be seen (Figs. 4 and 5) that decreases in IgE occurred from the time of onset of symptoms up to 3 wk after symptoms, after which the IgE values leveled off.

Table I shows the geometric mean values of IgE for nonatopic groups I and II as well as the atopic group during the acute and convalescent phases of infection. It can be seen that IgE levels decreased for all 3 groups but more dramatically for nonatopic I.

DISCUSSION

In the present study, it was found that naturally occurring viral respiratory infections modulated serum IgE levels in both nonatopic as well as atopic individuals. These results confirm those of previous

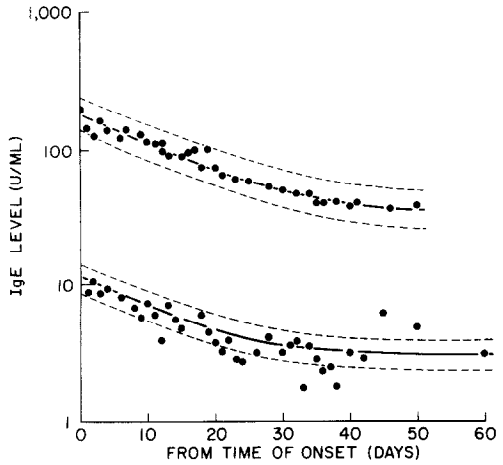

FIG. 4. IgE levels of nonatopics as a function from time of onset of viral infection. The broken line refers to the standard error observed in the PRIST.

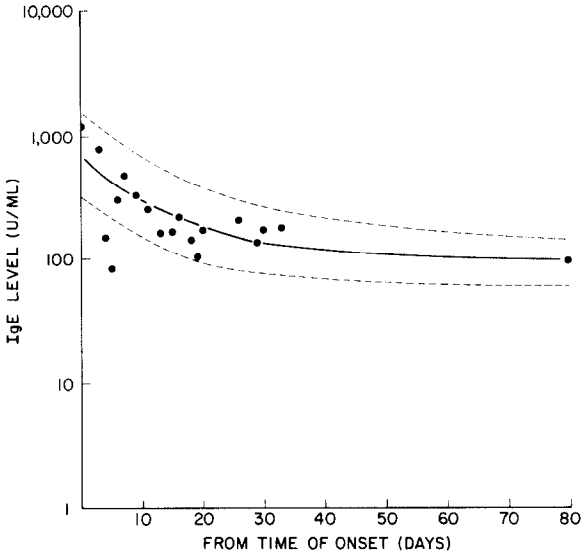

FIG. 5. IgE levels of atopics as a function from time of onset of viral infection. The broken line refers to the standard error observed in the PRIST.

studies which demonstrated either enhancement[8, 9] or decrease[10, 11] in IgE associated with viral infections. In this study, IgE levels decreased up to 3 to 4 wk after symptoms. On the other hand, the IgE levels detected in nonatopic patients during their acute phase of infection appeared elevated when compared to healthy Swedish population.[13, 14] The exact extent of elevation of IgE levels for the nonatopics awaits further studies with preinfection serum samples and controls based on a healthy population in the Ottawa area, matched for age, sex, race, past histories of allergies, etc. In addition, the exact response of IgE with respect to a particular viral agent will be determined when larger populations of patients to individual viral infectious agents are investigated. In that connection, it is interesting to note that Bahna et al.[15, 16] observed IgE response in heterophil-positive infectious mononucleosis. These investigators found that IgE changes showed a definite pattern, similar to that found in the present study, consisting of early elevation in illness, rapidly followed by a significant drop reaching a nadir by the third month after symptoms. Since in preliminary studies[17, 18] IgE antibodies to influenza and Epstein-Barr virus were detected in patients with those viral infections, it is possible that the elevated IgE levels observed in the acute phase may be due, in part, to IgE antibodies against the infectious agent and that these antibodies may be short-lived because of decreasing IgE levels into the convalescent phase of infection.

Upper respiratory tract infections due to virus are associated with the onset of bronchial asthma.[1–4] It is tempting to speculate that IgE antibodies to the infectious agent react in the respiratory tract with the viral agent to precipitate the asthmatic condition. For some individuals, the viral agent may be capable of "turning off" the formation of IgE immunoglobulin in sufficient time to prevent the development of the disease state. The degree to which this will occur will depend, in part, on the cellular mechanisms that control the formation of IgE immunoglobulins. It is possible that during viral infection T helper cells are stimulated during the acute phase of infection for both atopics and nonatopics to produce IgE immunoglobulin and IgE antibody to the infectious agent. The viruses may also activate T suppressor cells for the nonatopics during the convalescent phase to decrease IgE levels. For atopics, there is increasing evidence[19] that there is a genetically determined defect in some or all of the T lymphocytes which makes them more vulnerable to the inhibitory action of cyclic adenosine monophosphate (cAMP). This substance is considered to be inhibitory, particularly for suppressor T cells. Thus, it might be expected that during the convalescent phase of viral infection for atopics a de-

TABLE I. IgE levels of individuals with respiratory infections

Group	Geometric mean of IgE level	
	Acute	Convalescent
Nonatopic I (n = 32)	178 ± 36	97 ± 19
Nonatopic II (n = 58)	11 ± 2	8 ± 2
Atopic (n = 13)	567 ± 113	488 ± 98

fect in the T suppressor cells may lead to continual hyperproduction of IgE and hence bronchial asthma.

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