Unusual Elevation of IgE Levels During Childhood

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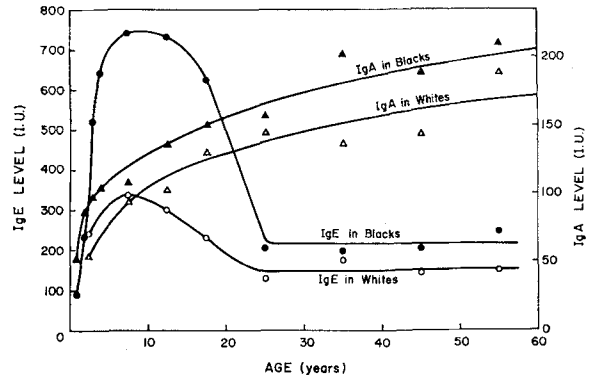
Summary. IgE levels in children 5 to 15 years of age were much higher than in their parents. The high IgE levels may result in part from a compensation for low IgA levels in children and in part from intestinal infestations.

Immunoglobulins IgE and IgA have the properties in common that both are synthesized in submucosal cells and both are secreted along the mucosa and secretory glands[1]. The major function of IgA is assumed to concern the defense of membranes of the respiratory and the gastrointestinal tract. Although no beneficial function is as yet known for IgE, it has become of obvious interest to allergists. A population study has provided evidence for marked elevation of IgE levels in children. This evidence is summarized in this report.

Serum samples were obtained from normal members of families of the Black and White populations of Virginia as described in detail elsewhere[2]. Families for the study were ascertained through the Medical College of Virginia Hospital records by selecting mothers of blood group 0 who were there for delivery, and who at that time were married, had at least 3 children and lived in the city of Richmond or surrounding counties. The families were originally selected in connection with a project on ABO hemolytic disease of the newborn and the variation of isoantibodies anti-A and anti-B levels[2]. A total of 369 individuals who were members of 59 families were included in the present study. IgE was measured by the commercially available RIST test (Pharmacia Laboratories, Piscataway, NJ) and IgA was determined by radial diffusion plates (Helena Laboratories, Beaumont, Texas)[2,3]. The IgE and IgA levels according to the age of the individual are shown in the Figure. It shows that IgA and IgE levels were higher in Black Americans than in White Americans, as was also the case for IgG and IgM levels[2].

The Figure shows that IgE levels increased very rapidly early in childhood and reached a maximum between 5 and 10 years. Late in childhood, the IgE levels decreased rapidly to a fairly stable adult level. For the individuals 5 to 19 years, the mean IgE level was 711.5 (*ln* 5.80 $\pm$ 0.12) and 299.8 (*ln* 5.80 $\pm$ 0.12) for Blacks and Whites, respectively. The corresponding values for individuals 20 years of age and older were 208.6 (*ln* 4.77 $\pm$ 0.13) and 151.4 (*ln* 4.39 $\pm$ 0.14). Statistical tests based on the natural log (*ln*) of IgE revealed highly significant differences between adults and children aged 5 to 19 years both in Blacks and Whites ($p < 0.001$). The natural log transformation was used for statistical analyses of IgE data because the frequency distributions of the raw data were strongly skewed to the left and were, therefore, unsuitable for the application of analyses assuming normal distribution of variables. Transformation to natural logarithm [*ln* (*x*)] was found to convert the data into suitable form[3]. The Figure also shows the IgA levels which increased rapidly at first and then more gradually. In another study[4], a steady increase was found up to old age when IgA values amounted to several times those of young adults.



Serum IgE and IgA levels in International Units (IU/ml) according to age of the individuals. The dots and triangles represent the means per dedade for individuals 20 years of age and older and for shorter intervals below 20.

From 28 children and their parents, a second serum sample was collected 3 years later. Testing the sample from the 2 collections side by side revealed little change except for 3 of the children who were 17 years of age at the first time of collection and 20 at the second. In these 3 individuals the levels decreased during the period. Within the ages 5 to 15 years, the high levels thus seem to persist for some time and are not just short-lived spurrious increases.

Evidence of higher IgE levels in children than in adults was also found in studies in South Africa[5], California[6], and in Canada[7]. Even the data of BERG and JOHANSSON[8] published in 1969 show the trend of high values in normal children. However, these authors elected to eliminate 6 high values in normal children in order to obtain their anticipated trend of a steady increase throughout childhood.

The age changes in IgE are unusual and different from the other classes of immunoglobulins which increase rapidly early in life and then either remain relatively stable (IgM) or continue to increase throughout life (IgA)[4]. Evidently, starting early in childhood and lasting for several years some factors cause an increase in IgE but do not affect the other immunoglobulins.

The reason for the high IgE levels during childhood is not known, but the following factors might be responsible for the elevated levels: 1. Larger amounts of IgE are synthesized during childhood to compensate for an inadequate synthesis of IgA. 2. Infestation by intestinal para-

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sites causes an elevation of IgE levels during childhood.

A compensation of IgA by IgE early in childhood appears an attractive hypothesis because it provides also an explanation for the existance of this class of immunoglobulins as it is difficult to imagine the evolution of a protein for which no useful function can be established. Indirect evidence of an interrelation between IgA and IgE is provided by the fact that atopic disease occurs more frequent in IgA deficient than in normal individuals[9,10].

JOHANSSON et al.[11] found higher levels of IgE in Ethiopian children with verified infections with *Ascaris lumbricoides* than in children with a negative stool. However, in a study in California, no uniform elevating of the serum IgE level was found in individuals with ascariasis[12]. It appears unlikely, therefore, that in the present study the elevated levels in children did result from ascariasis alone inasmuch as infestation occurs also in adults[13]. The present data do not permit to establish to what extent the high IgE levels in children might result from ascariasis and to what extent it might represent a compensation for the relatively low IgA levels but likely both factors contributed to the elevated IgE. The large difference between Black and White children might in part also result from a difference in *Ascaris* infestation in addition to a racial difference as it was found for the other classes of immunoglobulins[2]. The data clearly show that age of the individual should be considered in studies on IgA and IgE levels.

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Failure of SV40-Transformed Lizard Cells to Induce Tumors in Autogeneic or Allogeneic Hosts

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Summary. Lizard cells from the tails of geckos were readily morphologically and antigenically transformed in vitro by SV40 virus. Neither autografts of these cells nor allografts of SV40 transformed gecko embryo cells produced tumors in animals under observation from 1 to 3 years.

Recently we reported that poikilothermic cells from two species of lizards, *Gekko gecko* and *Eublepharis maculatis*, could be cultivated in vitro and both morphologically and antigenically transformed by SV40[3,4]. To determine if these cells were also malignantly transformed, transplantation experiments were performed using the leopard gecko, *Eublepharis maculatis*. Since inbred lizards were not available, implants of transformed cells were made into allogeneic hosts and also into autogeneic hosts whose tail tissue had been cultured in vitro and transformed by SV40 virus. This report gives the results of these experiments.

Material and methods. The Leopard geckos, *Eublepharis maculatis*, used in this study were bred and reared in captivity. SV40 (RH911) propagated in CV-1 cells had a titer of 2×10^8 plaque forming units per milliliter (PFU/ml) in CV-1 cells. Assay for the SV40 T antigen was performed by the indirect immunofluorescence method[5].

Cell lines were derived from young adult geckos' (less than 6 months old) autotomized tail tissue. After removal of the epidermis, muscle and connective tissue were minced and dispersed with a trypsin-versene solution 0.25% trypsin and 0.1% versene in Ca^{2+} and Mg^{2+}—free PBS at room temperature (22–25 °C) for 20 min. The digest was filtered, pelleted and planted in flasks in Eagle's basal medium containing 10% fetal calf serum (BME-FCS 10) at 30 °C. The origin and methods of cultivation of the gecko embryo cell line, GE-1 and its transformation by SV40 have been reported elsewhere[2].

For transplantation, cells were dispersed with trypsin-versene solution, counted, pelleted, and resuspended in less than 0.5 ml of BME-FCS-10. GE-1 cells transformed by SV40 were used for allografts. Animals were inoculated either subcutaneously in the leg or intraperitoneally. In some animals non transformed cells at the same passage level were inoculated in the opposite leg to serve as controls.

Results. Cell cultures from the tail tissue of 4 animals were infected in suspension at high multiplicity at their first passage (3rd passage for T-8) with SV40 virus which produced little or no cytopathic effect. The SV40 infected cells and noninfected cells of the same culture that served as controls were subcultivated at about weekly intervals and monitored for the presence of SV40 T

Table I. Percentage of gecko cells exhibiting SV40 T antigen

Cell line	Virus multiplicity of infection	Cell passages after infection									
		1	2	3	4	5	6	7	8	17	18
T1	127	2			14	[a]		100			
T4	160	0		6		98[a]			100		
T5	480	[a]	91							100	
T8	80	4			12		55[a]				100

[a] Onset of morphologically transformed appearance.

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