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Intrapair Similarity of Immunoglobulin Levels in Twins

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Abstract. Levels of immunoglobulins IgG, IgA, IgM and IgE were determined in 8 MZ and 14 DZ twin pairs at the ages of 6-11 years, 12-17 years and 15-20 years. Intrapair similarity in immunoglobulin levels was found to be higher in the MZ than in the DZ twins, especially in the case of immunoglobulins IgA and IgM.

Key words: Immunoglobulins, Twins

INTRODUCTION

The principal genes regulating humoral and cell-mediated immune responses in humans and certain experimental animals have been shown to be located in the major histocompatibility complex (MHC), which in humans resides in chromosome six [1]. The mechanisms by which MCH-linked genes and others influence immune responses are at present best known in mice [9]. The clonal selection theory presupposes that approximately 1000 genes are necessary for the capacity to form all the specific antibodies belonging to the five immunoglobulin classes. Are they inherited or do they arise by mutation during ontogeny (or later)? The results reported by Wigzell [12] indicate that both mechanisms may be involved. The formation of antibodies after a certain antigen stimulation is stopped by suppressor cells, but there are also other factors (eg, the amount of antigen) which influence antibody levels. The functions of suppressor cells in humans are controlled by HLA-linked genes [8], and it is clear that the presence or absence of anti-

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bodies (in congenital immunological deficiency states) is linked to an abnormal code. One form of combined immunodefiency is associated with lack of expression of HLA-antigens [11]. Whether genetic factors influence individual levels of antibodies in normal human subjects is still an open question, though the high IgE levels in atopic individuals have been thought to be caused by genetically abnormal regulation of the antibody response [2,4].

Some strains of laboratory mice are high responders to certain antigens, while others always give a low response, although even in these the response may depend on the dose of the antigen [3].

The present ten-years longitudinal study on the levels of immunoglobulins in pairs of monozygotic (MZ) and dizygotic (DZ) twins was initiated to clarify further the role of genetic factors in the regulation of antibody levels.

MATERIAL AND METHODS

Subjects

Twenty-three pairs of twins of the same sex, 8 MZ pairs and 15 DZ pairs, were available for examination. Zygosity was determined by a similarity diagnosis focused upon 15 traits [6] and by questionnaire method [7].

The first part of the study was carried out when the twins were 6-11 years old, and the tests were repeated at the ages of 12-17 years and 16-21 years. Nineteen of the original 23 pairs (7 MZ and 12 DZ) took part in the second round of tests and 18 pairs in the third round. The twin pairs had lived in identical environments in the first two phases, but 4 MZ pairs and 5 DZ pairs had moved apart between the second and third round of tests.

Determination of Ig levels

Serum levels of immunoglobulins A, G and M were measured by an immunodiffusion method [5]. Levels of IgE were measured by a radioimmunosorbent technique (Phadebas IgE BRIST, Pharmacia Diagnostics Ab, Uppsala).

Statistical methods

Statistical significance was tested by calculating the intrapair differences for the MZ twins and the DZ twins separately and transforming these to logarithmic values and by comparing the means of these for the two groups using Student's t-test.

RESULTS

The serum immunoglobulin levels in the MZ and DZ twins are presented in Figs. 1-4. The intrapair differences in IgG were almost significantly smaller in the MZ group at the age of 12-17 years (Fig. 1), and the IgA values were significantly more similar in MZ pairs than in the DZ ones at the age of 6-11 years and almost significantly more similar at 12-17 years (Fig. 2).

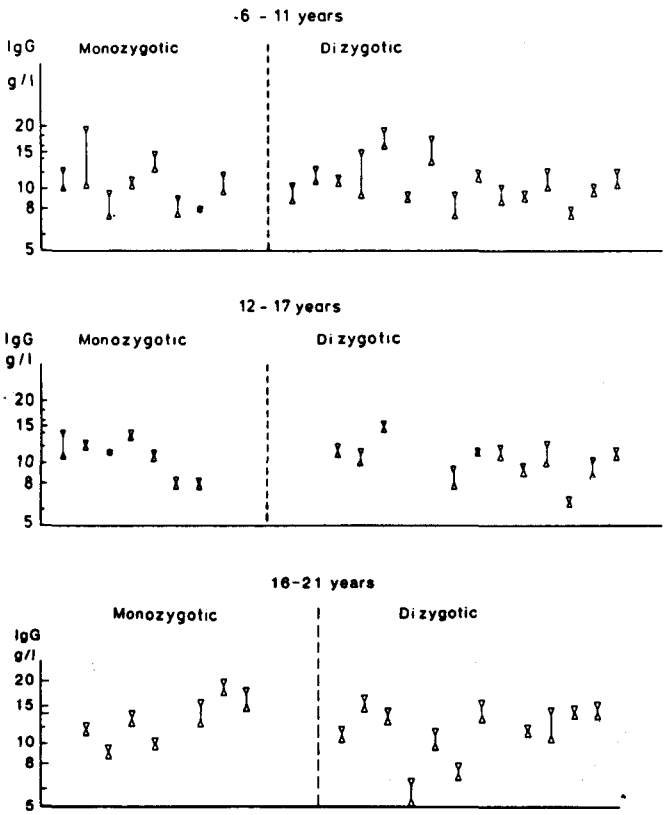

Fig. 1 - Serum IgG levels in twins at different ages. The mean of log (intrapair difference + 1) is almost significantly smaller in the MZ pairs than in the DZ pairs at age 12-17 years, $P = 0.3264$, 0.0409 and 0.3640 (Student's t-test) in the first, second and third set of tests, respectively.

No differences were found with regard to IgM at the youngest and oldest ages, but the intermediate levels were significantly more similar in MZ than in DZ twins (Fig. 3).

The MZ twins did not have any greater intrapair similarity in IgE values than the DZ twins at any age (Fig. 4).

DISCUSSION

This long-term follow-up study showed serum immunoglobulin levels to be more similar in pairs of MZ twins than of DZ twins, this being especially true of IgA levels, and in 12-17 year-old subjects, of IgM and IgG. The variation in Ig levels at different stages may derive from environmental factors, especially infections, the latter being recorded in several of the pairs of twins at various stages, especially in the MZ twins in the youngest age groups, which may explain the deviating IgM levels at that age. IgM antibodies are formed

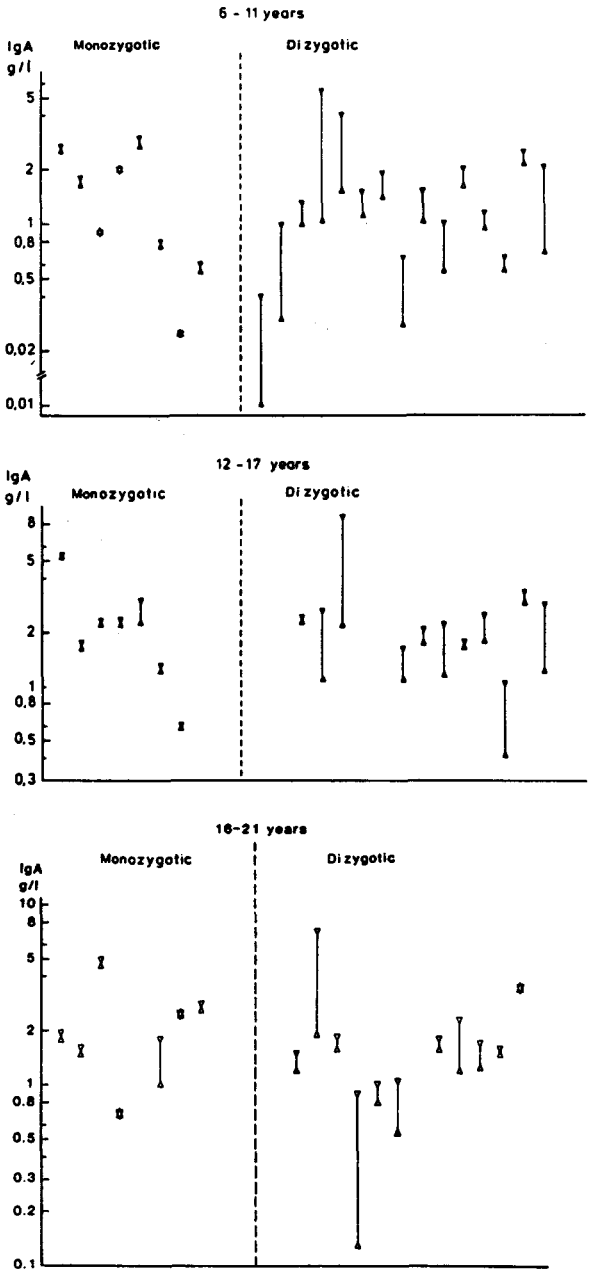

Fig. 2 - Serum IgA levels in twins at different ages. The mean of log (intrapair difference + 1) is smaller in the MZ pairs than in the DZ pairs at the first two ages. P = 0.0054, 0.0201 and 0.1007 (Student's t-test) in the first, second and third set of tests, respectively.

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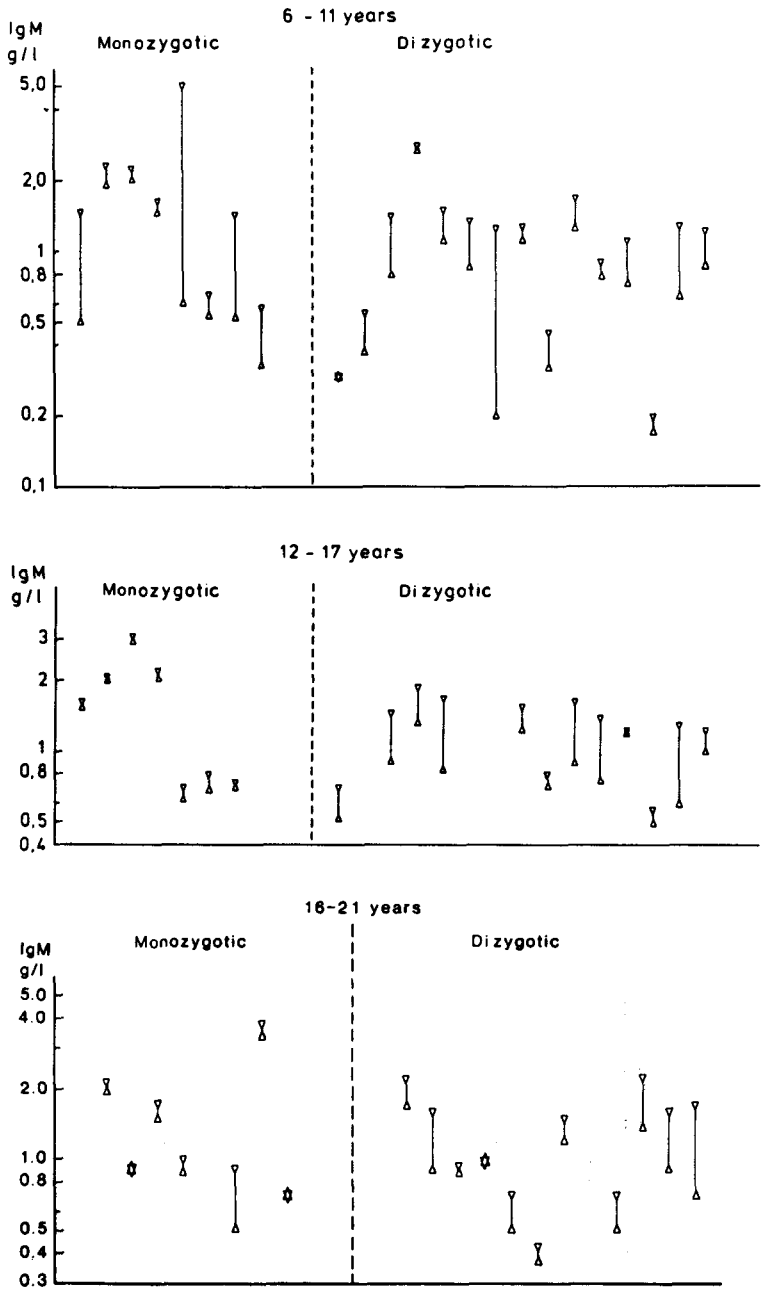

Fig. 3 - Serum IgM levels in twins at different ages. The mean of log (intrapair difference + 1) is smaller in the MZ pairs than in the DZ pairs at age 12-17 years. $P = 0.0645$, 0.0061 and 0.0535 (Student's t-test) in the first, second and third set of tests, respectively.

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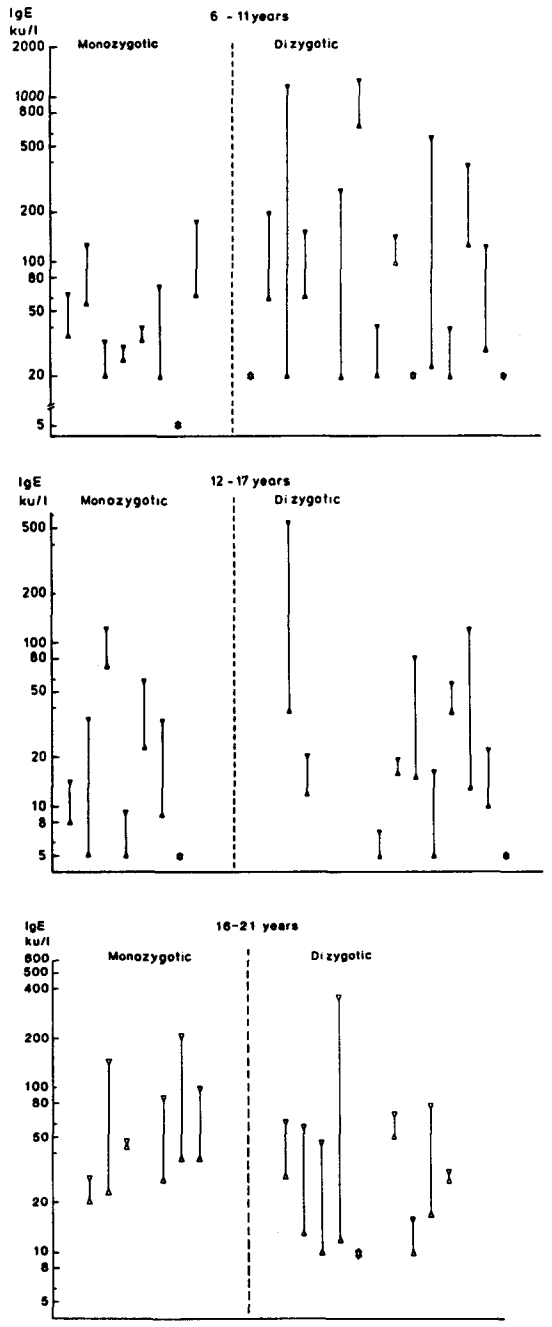

Fig. 4 - Serum IgE levels in twins at different ages. The mean of log (intrapair difference + 1) does not differ significantly between MZ and DZ pairs at any age. P =0.1389, 0.3559 and 0.2327 (Student's t-test) in the first, second and third set of tests, respectively.

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rapidly at the onset of an infection and also disappear rapidly, their half-life being 5 days.

No similarities in IgE levels could be seen here between the MZ twins, but the number of cases was admittedly small. No cases of severe atopy were found in the series, which confirms the findings of Sistonen et al [10] that there is a wide range of phenotypic expression for each genotype.

As a whole, this survey, spread over a long observation period, provides further evidence that IgA and IgM levels at least are influenced by the genetic code. As far we know there are no relevant quantitative studies on specific antibody responses in pairs of human MZ and DZ twins, but the present results indicate a need for such studies.

REFERENCES

1. Dorf M (1981): The Role of the Major Histocompatibility Complex in Immunobiology. New York: Garland STPM Press.
2. Hamburger RN (1982): The immunogenetics of IgE provides predictive value for the development of allergy. Ann Allergy 49:9-11.
3. Jormalainen S, Mozes E, Sela M (1975): Genetic control of the immune response. The dose of antigen in aqueous solution is critical in determining which mouse strain is high responder to poly (LTyr, LGlu)-poly(LPro) - - poly(LLys). J Exp Med 141:1057-72.
4. Kjellman N-JM (1976): Predictive value of high IgE levels in children. Acta Paediatr Scand 65: 465-71.
5. *Mancini G, Carbonara AO, Heremans JF (1965): Immunochemical quontitation of antigens by* single radial diffusion. Int J Immunochem 2:235-54.
6. Newman HH, Freeman FN, Holzinger KJ (1973): Twins: A study of Heredity and Environment. Chicago: University of Chicago Press.
7. Sarna S (1977): Zygosity Diagnosis in Epidemiological Twin Studies. Publications from the University Departments of Public Health in Finland M23.
8. Sasazuki T, Nishimura Y, Muto M (1984): MHC-linked immune suppression genes and their role in immunological disorders. In Sasazuki T, Tada T (eds): Immunogenetics. Its Application to Clinical Medicine Tokyo: Academic Press, pp 21-37.
9. Schwartz RH (1984): The role of gene products in the major histocompatibility complex in T cell activation and cellular interactions. In WE Paul (ed): Fundamental Immunology, Chapter 15. New York: Raven Press.
10. Sistonen P, Johnsson V, Koskenvuo M, Aho K (1980): Serum IgE levels in twins. Hum Hered 30:155-158.
11. Tourain J-L, Beruel H, Touraine F (1984): The bare lymphocyte syndrome. In C Griscelli, J Vossen (eds): Progress in Immunodeficiency Research and Therapy. Amsterdam: Elsevier.
12. Wigzell H (1973): Is it all coded for by the germ line genes? Scand J Immunol 2:199-206.

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