Immunoglobulins and Lymphocyte Populations

On the elaboration of an immunological response of a humoral type, the cooperation between the thymocytes and the bone-marrow lymphocytes derived, at least, in the presence of certain antigens such as sheep's erythrocytes and bovine seralbumin is necessary[1-3].

On the other hand, the condition is notable of the experimental thymectomy[4-6] giving rise to a depletion of the antigen Theta carrying lymphocytes, while the percentage of immunoglobulin-carrying lymphocytes, which carry it in their membranes, detected by immunofluorescence, increases. A similar picture is observed in some clinical circumstances as occurs in Di George's syndrome[7,8] and in primary immunodeficiencies[9,10]. Between these two conditions there is a clear difference in the normal concentration of immunoglobulins in the first case, which is frankly diminished in the second.

With these premises, and keeping in mind that with the elderly person[11,12] there is a clear diminution of both the primary and secondary humoral response in the presence of exogenous antigens, the purpose of this study has been to relate the concentration. Of immunoglobulins with lymphocyte populations of a group of healthy elderly people.

Material and methods. We have studied the concentration of seric immunoglobulins and the state of the T and B lymphocyte populations in a group of 43 healthy elderly people, using as a control group 16 young people whose ages varied between 18 and 29 years. Of the 43 elderly people, 20 were males whose ages varied between 52 and 84 years (average: 68.5) and 23 women whose ages varied between 52 and 92 years (average: 73.6).

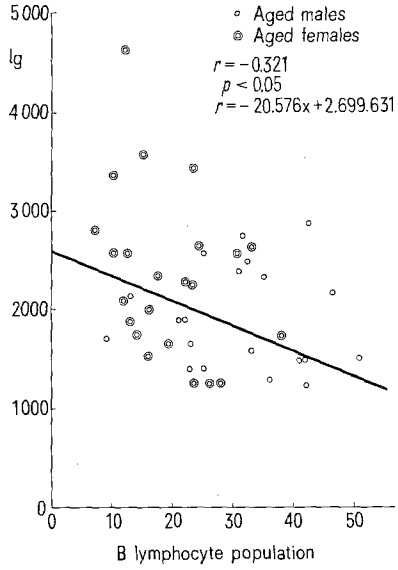
The appraisal of the thymo-derived population was made by determining the percentage of blastic transformation in vitro cultures of lymphocytes in the presence of phytohemagglutinin. The bone-marrow derived population was studied by means of the direct immunofluorescence of lymphocytes[13] by using monospecific immunoserums (anti-IgG, anti-IgM and anti-IgA) marked with isothiocyanate of fluorescein.

The concentration of immunoglobulins in the serum (IgG, IgM and IgA) was determined by means of the techniques of radial immunodiffusion by using Hyland immunoplates.

Results and comments. The percentage of blastic transformation in the presence of phytohemagglutinin is notably diminished with relation to the values obtained with the control group of young people (Table I) with the observation that this diminution is less with the elderly women. The B lymphocyte population, on the other hand, is greater in the elderly people, an increase which is significantly greater in the elderly men.

The values of seric immunoglobulin are found to be within normal limits for both sexes, although the percentage of all the immunoglobulins in the elderly women is increased in relation to the men, which is statistically significant ($p < 0.05$), while no statistical difference between each class of Ig was found separately (Table II).

In view of these results, we observe that in elderly people there is a depletion of the thymic function reflected by the lower index of blastic transformation which affects



Correlation between the percentage of B lymphocyte and concentration of all immunoglobulins.

[1] H. N. CLAMAN, E. A. CHAPERON and R. F. TRIPLETT, Proc. Soc. exp. Biol. Med. *122*, 1167 (1966a).
[2] R. B. TAYLOR, Transplant. Ref. *1*, 114 (1969).
[3] J. F. MILLER and G. F. MITCHELL, J. exp. Med. *128*, 861 (1968).
[4] M. C. RAFF, Immunology *19*, 637 (1970).
[5] E. R. UNANUE, H. M. GREY, E. REBELLINO, P. CAMPBELL and J. SCHMIDTKE, J. exp. Med. *133*, 1188 (1972).
[6] E. RABELLINO and H. M. GREY, J. Immun. *106*, 5 (1971).
[7] K. J. GAJL-PECZALSKA, W. D. BIGGAR, B. H. PARK and R. A. GOOD, Lancet *1*, 1344 (1972).
[8] R. A. GOOD, W. D. BIGGAR and B. H. PARK, *Progress in Immunology*. First Congress International of Immunology (Ed. B. AMOS; Academic Press 1971), p. 699.
[9] J. L. PREUD'HOMME and M. SELIGMAN, Lancet *1*, 442 (1972).
[10] M. D. COOPER, A. R. LAWTON and D. E. BOCKMAN, Lancet *2*, 791 (1971).
[11] M. J. ROWLEY, H. BUCHANAN and I. R. MACKAY, Lancet *2*, 24 (1968).
[12] T. MAKINODAN and W. T. PETERSON, Devel. Biol. *14*, 112 (1966).
[13] M. PAPAMICHAIL, J. C. BROWN and E. J. HOLBOROW, Lancet *2*, 850 (1971).

Table I. Percentage of blastic transformation in the presence of phytohemagglutinin

	Blastic transformation rate (%)	Total B lymphocyte population (%)
Young males	75,2 ± 4.1	17.8 ± 6.9
Young females	72.0 ± 5.5	12.9 ± 6.9

Table II. Increasing immunoglobulins in elderly women

	Blastic transformation rate (%)	Total B lymphocyte population (%)	Total Ig concentration (mg/100 ml)
Aged males	39.6 ± 19.4	31.8 ± 19.4	1867.4 ± 459.6
Aged females	52.2 ± 15.4	19.7 ± 8.11	2403.5 ± 822.5

Mean ± S.D.

elderly men to a greater degree. The thymic depletion maintains an inverse relationship with the percentage of lymphocytes which carry immunoglobulins on their surfaces as demonstrated by the condition in which, with the men in whom the blastic transformation is less, a greater percentage of B lymphocytes is found. These differences between both lymphocyte populations are statistically significant ($r = 0.477$; $p < 0.01$).

The concentration of seric immunoglobulins is not significantly related to the index of blastic transformation; however, there does exist a significant inverse relationship ($r = -0.303$; $p < 0.05$) between the percentage of B lymphocytes and the concentration of all the seric immunoglobulins (Figure).

These results suggest that in elderly people the reduction of the T function would influence the concentration of seric immunoglobulins through the action which it exercises on the B lymphocyte population in the sense of facilitating their transformation to plasmatic cells. This would explain why in elderly women a greater concentration of seric immunoglobulins coincides with a smaller percentage of bone-marrow-derived lymphocytes.

It proves difficult to explain, if we admit the collaboration between the thymo- and bone-marrow-derived cells in the production of antibodies, how with a thymic reduction elderly people show a concentration of normal seric Ig. It might be thought that the immunoglobulin concentration would be normal, provided that a response in the presence of an antigen were not required at which moment the thymic cells would fail when faced with this exigency. Thus, we could explain the smaller response in elderly people in the presence of exogenous antigens.

Resumen. Se ha estudiado la relación existente entre la concentración de Ig. sericas y las poblaciones linfocitarias T y B en un grupo de sujetos ancianos, encontrandose un notable descenso de la transformación blasticá al tiempo que se incrementa el porcentage de linfocitos portadores de Ig. en su membrana. De nuestros resultados parece deducirse una relación entre el nivel de Ig. sericas y la población medulo-derivada.

R. Velasco Alonso, J. Prieto Valtuena, M. A. del Pozzo Perez, M. I. Gonzales Guilabert and L. Corporales Lopez

Department of General Pathology, University of Valladolid (Spain), 28 December 1972.

IgM Levels of Newborn in Hawaii

IgM is generally not thought to be transported actively across the 'placental barrier', probably due to its molecular size. For this reason cord blood IgM levels are considered to be of fetal origin. Elevated IgM levels in the cord blood has been suggested by Alford et al.[1,2] to reflect the immune response of the neonate, indicating perhaps chronic intrauterine infections of rubella, syphilis, cytomegalovirus or toxoplasma. In a variety of cases, asymptomatic infections which had begun in utero were diagnosed by elevated IgM levels in cord blood. Based on these findings it has been suggested that cord blood IgM levels be screened routinely for asymptomatic infections acquired in utero. The purpose of this investigation is to evaluate such a screening program for infections of newborns in Hawaii.

Materials and methods. Cord blood was obtained at time of delivery and the sera were frozen prior to testing. Samples from newborns were obtained generally by heel prick. IgM determinations were performed within 2 or 3 days of collection, using single radial immunodiffusion with Kallestad 'Quanti-Plate' kits (Kallestad Laboratories, Inc., Minneapolis, Minnesota).

Results. 523 cord blood IgM level determinations were performed. There was no history of maternal infection in any instance. The mean IgM levels was determined as 17.0 mg/100 ml. 20 of the 523 specimens were more than 2 standard deviations above the mean (> 37.4 mg/100 ml). 5 of the 20 had some perinatal problem. The remaining 15 patients had completely uneventful hospital courses.

A number of patients without significantly elevated IgM levels at birth but who subsequently developed infections were followed up with IgM level determinations. These tests were carried to demonstrate the sera in IgM levels in newborns with chronic infections from the normal range determined in the study.

A-32-week-gestation male developed pneumonia at 3 days but responded to antibiotics. IgM level was 45 mg/100 ml at age 10 days (elevated in comparison with normal IgM levels for this age reported by Alford[3]).

A-36-week-gestation boy developed an *E. coli* sepsis at age 3 days. Subsequent course was complicated by a recurrence of sepsis followed by meningitis, subdural effusions, and hydrocephalus. IgM level was 65 mg/100 ml at 12 days and 12 mg/100 ml at 15 days.

Six other patients with pneumonia were studied. In 5 of these, IgM levels were measured before 48 h of age and their average was 23.9 mg/100 ml. In the sixth, the first measurement done at age 6 days (2 days after clinical onset of pneumonia) was elevated at 77 mg/100 ml.

Twelve patients of the 523 were born after the membranes had been leaking or ruptured for more than 24 h. IgM levels were determined in the first few days of life and the average was 15.5 mg/100 ml. 2 infants of this group who subsequently developed pneumonia had initial IgM levels of 13 and 29%. The others remained asymptomatic.

One patient was born with a full-blown rubella syndrome confirmed by the presence of specific IgM antibody against rubella virus antigen. IgM levels were subsequently shown to be between 100 and 200 mg/100 ml over the first 2 months of life.

Discussion. Mean values of cord blood IgM levels from various reports in the literature[3–10] have ranged from 5.8

[1] C. Alford, J. Schaefer, W. Blankenship, J. Straumfjord and G. Cassady, N. Eng. J. Med. *277*, 437 (1967).

[2] C. Alford, W. Blankenship and J. Straumford, The diagnostic significance of IgM-globulin elevations in newborn infants with chronic intrauterine infections. Intrauterine Infections in Birth Defects Original Article. Published by the National Foundation – March of Dimes. IV (7) Dec. 1968, p. 5–19.

[3] C. Alford, J. Foft, W. Blankenship, G. Cassady and J. Benton, J. Pediat. *75*, 1167 (1969).

[4] G. McCracken jr., J. Pediat. *75*, 1204 (1969).

[5] S. Korones, J. Roane, M. Gilkeson, W. Lafferey and J. Sever, J. Pediat. *75*, 1261 (1969).

[6] E. Stiehm and H. Fudenberg, Pediatrics, N. Y. *37*, 716 (1966).

[7] R. Buckley, J. Pediat. *75*, 1143 (1969).

[8] W. Blankenship, G. Cassady, J. Schaefer, J. Straumfjord and C. Alford. J. Pediat. *75*, 1271 (1969).

[9] C. Ichida, M. Yamakido, M. Yokoyama and H. S. Uyemura, Hawaii med. J. *28*, 377 (1969).

[10] M. Yokoyama, M. Yamakido, S. Chandor and R. E. Rogers, Z. Immun. Allergie klin. Immun. *139*, 445 (1970).