

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, encontrándose un notable descenso de la transformación blástica al tiempo que se incrementa el porcentaje 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 ALFORD³).

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 literature³⁻¹⁰ 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).

to 13 mg/100 ml. The upper limit of normal levels has generally been around 20 mg/100 ml although there have been wide ranges reported.

MCCRACKEN³ reported 2 standard deviations above the means as 44 mg/100 ml; ALFORD² found 10% of his values to be greater than 19.5 mg/100 ml; SEVER¹¹ reported only 0.8% of his values greater than 20 mg/100 ml and MILLER¹² found 4% of his values greater than 16 mg/100 ml and 2% greater than 20 mg/100 ml.

The high IgM mean level in this study may be related to a number of reasons, one of which may be the racial composition of the sample population. Of the 20 patients with IgM levels greater than 2 standard deviations above the mean, 5 were shown to have some perinatal problems, but none were shown to have a definite infection.

All patients, reported by ALFORD³ with elevated IgM level were followed up with bacterial cultures of the throat, stool, urine, blood and cerebrospinal fluid; viral cultures for rubella and cytomegalovirus; X-ray of the chest, skull, and long bones and examination of the cerebrospinal fluid; and, where indicated, a VDRL, FTA-ABS test for syphilis, Sabin-Feldman dye dilution test for toxoplasmosis and hemagglutination-inhibition (HIA) test for rubella. He found a 34% incidence of infection in the group with elevated IgM levels as compared to 0.8% with infection in the control group. These were primarily infections due to cytomegalovirus, toxoplasma, aseptic meningitis and infections of the urinary tract.

MILLER¹² was able to find only 1 infection out of 37 elevated cord IgM levels in a study of 5006 blood samples. In this study, as in MILLER's, infections were not actively sought in asymptomatic infants.

The contention that elevated IgM in the newborn would indicate asymptomatic infection prior to clinical onset is

not warranted by the results reported here. It appears that newborns who later develop infections and elevated IgM levels appear within normal range at birth. Elevated IgM levels are not indications of imminent clinical of infections^{5, 8, 13}.

Zusammenfassung. Es wird eine Radial-Immun-Diffusionsmethode verwendet, um durch Vergleich der IgM-Antikörper im Nabelschnurblut zu bestimmen, ob in den homologen mütterlichen Proben eine asymptomatische Infektion stattgefunden hat. Es ergab sich, dass das benutzte Verfahren nicht zur Klärung der gestellten Frage geeignet ist.

W. WANG, C. SPRAGUE, M. YOKOYAMA and
H. S. PARK^{14, 15}

Kapiolani Maternity Hospital and Kuakini Medical Research Institute, 347, North Kuakini Street, Honolulu (Hawaii 96817, USA), 9 February 1973.

¹¹ J. SEVER, J. HARDY, S. KORONES, M. GILKESON, L. CORRIGON, A. LEY, H. TZAN and D. YARNCK, *J. Pediat.* 75, 1224 (1969).

¹² M. MILLER, P. SUNSHINE and J. REMINGTON, *J. Pediat.* 75, 1287 (1969).

¹³ W. KHAN, V. RUSSELL, M. WERTHMANN and S. ROSS, *J. Pediat.* 75, 1282 (1969).

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The Effect of Lipids from *Listeria monocytogenes* on Immune Response in Mice

The author's previous work has shown that *Listeria monocytogenes* cells, given to mice together with sheep red blood cells (SRBC), cause an acceleration, increase in number and prolongation of time of the multiplication of hemolytic plaque-forming spleen cells (PFC)¹. The adjuvant effectiveness of listeria organisms was found in primary and secondary responses, but it was more pronounced in the former one. Some authors claim that the adjuvant property of listeria cells depends on the lipid fraction obtained from these bacteria².

The present experiments have been designed to observe the effect of lipids from listeria cells on multiplication of hemolysin-producing spleen cells and on the level of these antibodies in the sera of mice immunized with SRBC.

Materials and methods. The experiments were performed on male Porton mice (about 20 g body wt.). The lipid fraction of *Listeria monocytogenes* cells was obtained using a technique described by CARROLL et al.³. The lipid fractions extracted with chloroform and methanol were mixed and stored in chloroform. They were given to mice i.p. in emulsion². The number of 19 S hemolysin-producing spleen cells was determined per 10⁶ spleen cells, using the method

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² N. F. STANLEY, *Austral. J. exp. Biol. med. Sci.* 28, 109 (1950).

³ K. K. CARROLL, J. H. CUTTS and E. G. D. MURRAY, *Can. J. Biochem.* 49, 889 (1968).

Influence of lipids from *Listeria monocytogenes* on the development of plaque-forming cells (PFC) in secondary response

1st challenge	2nd challenge	Days after the 2nd challenge			
		3	4	5	6
		Mean \pm S.E.	Adjuvant index	Mean \pm S.E.	Adjuvant index
SRBC+lipids	SRBC+lipids	1208 \pm 320	4.2	2652 \pm 563	4.1
SRBC+lipids	SRBC	541 \pm 67	1.9	1834 \pm 324	2.7
SRBC	SRBC+lipids	668 \pm 128	2.3	1436 \pm 384	2.1
SRBC	SRBC	286 \pm 50	1.0	639 \pm 76	1.0

Mice were immunized i.p. with 5×10^7 SRBC. The lipids were given by the same route (50 μ g per mice). 40 days after the 1st challenge the animals were repeatedly injected with SRBC only or along with lipids. The figures represent number of PFC per 10⁶ spleen cells.