Contrary to the depression observed in the production of the cellular infiltration of the thyroid, the neonatally thymectomized rats developed circulating titers of anti-bovine thyroglobulin which were equivalent to the titers seen in the sham operated animals. The production of circulating antibody to bovine thyroglobulin seems to be independent of the presence of thymus shortly after birth.

In these experiments it appears that both thymus-dependent and thymus-independent activities are involved in the response to bovine thyroglobulin. The thymus dependent mechanisms are mainly those that are involved in the direct cellular response in the thyroid, while the thymus-independent ones are primarily involved in the production of antibodies[12].

Résumé. Les rats Sprague-Dawley ont developpé une thyroïdite autoimmune caracterisée par l'infiltration de cellules lymphoïdes dans la thyroïde, qui fait suite à l'injection de thyroglobuline bovine, d'adjuvant complet de Freund et de *Bordetella pertussis*. Les rats nouveau-nés thymectomisés révélèrent une tendance nettement moindre à développer la thyroïdite.

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[12] Supported in part by research grants from the Rutgers Research Council and a Bio-medical Sciences Support Grant No. FR-7059 from the National Institutes of Health.

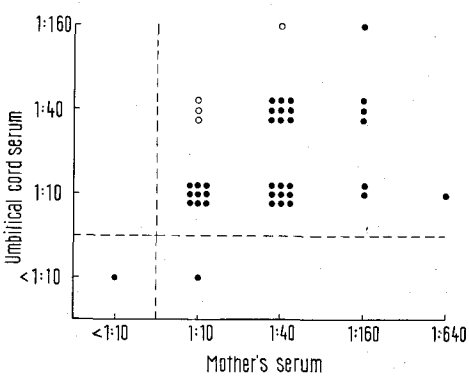
Simultaneous Determination of Antibody to Epstein-Barr Virus in Prenatal Mothers and New-Born Infants

Serological studies on the antibodies to EPSTEIN-BARR virus (EBV), originally found in cultures of Burkitt lymphoma[1], have suggested a close association of this agent to certain diseases such as Burkitt lymphoma[2], carcinoma of the posterior nasal space[3], infectious mononucleosis[4,5] and sarcoidosis[6]. Furthermore, anti-EBV antibody has been demonstrated in healthy persons living in different parts of the world[2,7-9]. The etiological role of EBV, however, in the above diseases and some of lymphomas and leukemias in man is not fully understood and the mode of its natural transmission remains largely uncertain. This communication reports the result of simultaneous determination of anti-EBV antibody titers in paired serums from a prenatal mother and her newborn infant.

Anti-EBV titers in test serums were determined by the method of other workers[2,6]. Cells of the P3HR-1 clone of the African Burkitt lymphoma-derived Jijoye cell line were used as a source of EBV antigen and indirect immunofluorescence was performed with serum diluted at 1:10, 1:40, 1:160, 1:640 and, if necessary, 1:2560. Mother's blood was withdrawn shortly before delivery and umbilical cord blood at the time of childbirth.

As shown in the Figure, in 38 of 40 pairs of mother and infant, both had detectable levels of anti-EBV antibody; the titers of mother's serum ranged from 1:10 to 1:640 and those of cord serum from 1:10 to 1:160. In 34 of the 38 pairs (closed circles) the mother's titers were equal to or exceeded the infant's titers, while in the other 4 (open circles) the infant's titers were higher than the mother's titers by a fourfold dilution. In one out of the 40 pairs, both mother and infant lacked anti-EBV antibody and in the last pair only the infant lacked antibody at a serum dilution of 1:10.

The present experiment has shown that the Japanese newborn infants had a 95% prevalence of anti-EBV antibody in the cord serum when tested at a dilution of 1:10 or higher, and there was a fairly good correlation between titers of mother and infant. Since anti-EBV antibody is restricted to IgG immunoglobulin, it would be readily transmitted from mother to infant through the placenta. Also, HINUMA et al.[9], in a study of Japanese population



Correlation of anti-EBV antibody titers in 40 pairs of mother and infant at the time of delivery.

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of various age groups, have observed a high incidence (85%) of positive antibody in the cord serum. The frequency of positive serum, according to their study, decreased to 30–40% between 1 and 24 months old but again increased to about 80% by 3 years of age. It remains to be seen whether such a sharp rise of antibody prevalence is due to de novo infection by EBV during the early infancy or immunological reactivity of the infants to latent EBV transmitted vertically in utero.

Zusammenfassung. Antikörpertiter gegen EBV wurden in 40 gepaarten Seren von pränatalen Müttern und Neugeborenen gleichzeitig mit indirekter Immunofluoreszenz bestimmt. In 95% hatten sowohl Mütter als auch Neugeborene den Antikörper. Die Titer der Mütter waren mehrheitlich gleich oder höher jenen der Neugeborenen, woraus geschlossen wird, dass der Antikörper gegen EBV von der Mutter diaplacentar auf den Fetus übertragen werden kann.

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A Comparison of the Degree of Chimaerism Produced when Allogeneic Cells from Four Different Tissues are used to Create Tolerance in the Mouse

Immunological tolerance, the specific non-reactivity to a foreign antigen initiated by contact with that antigen, was first described by BILLINGHAM, BRENT and MEDAWAR[1]. For tolerance to persist, the antigen must remain[2], and when the antigen is in the form of whole cells, these should be detectable in the tolerant individual[3]. In the mouse, using a chromosome marker, quantitative estimates of the degree of chimaerism have been made. However, conflicting findings have resulted. Some workers have found 80–90% of allogeneic i.e. donor cells in the organs of the recipient mice[4], whilst others have been unable to detect any[5]. An explanation for these differences may lie in the fact that there has been no uniformity in the various experiments for such factors as the source of the tolerogenic tissue, the route of entry of the cells or the histocompatible relationship between host and donor.

The present work examines the possibility that the source of the tolerogenic tissue may influence the degree of chimaerism achieved.

The donor mice were a pure line CBA/H-T6T6 strain, the T6 chromosomes were used as cell markers since they were not possessed by the recipients. The recipients were +/+ mice of the W-series, phenotypically completely normal.

For the preparation of the tolerogenic cells, either one spleen, or the thymus together with the subcutaneous and mesenteric lymph nodes (referred to as lymphoid tissue) from one adult CBA mouse, or the livers from a litter of 16–18-day-old CBA foetuses, were removed and placed in Hanks' B.S.S. A suspension of single cells was produced as described previously[6]. In the case of bone marrow, 2 adult femurs and tibiae with the ends removed were in turn attached to a 14G hypodermic needle on a 1 ml syringe, and the marrow flushed out with Hanks' B.S.S. Cell clumps were broken up by aspiration through a 27G hypodermic needle. Following centrifugation at 1500 *g* and resuspension in Hanks' B.S.S., the cells were counted, and the dilution of the cell sample adjusted so that 5×10^6 cells were present in 0.02–0.04 ml of solution.

Neonatal +/+ mice were injected i.v. with 5 million cells of one of the tissues. At 10–12 weeks of age each was challenged with a skin graft from a female CBA mouse, using the technique of BILLINGHAM and MEDAWAR[7]. In untreated mice such grafts were rejected in a mean time of 11.2 days[8]. Those mice which did not reject the skin grafts were accepted as having been rendered tolerant. At least 6 weeks after grafting, when the graft had a good growth of hair, the mice were subjected to mitotic chromosome studies after an injection of Colcemid (Ciba), using the method of FORD[9]. Chimaerism was sought in the bone marrow, spleen, thymus and lymph nodes of each animal.

The results were compared statistically using the Student's *t*-test, and differences were regarded as significant if $p < 0.05$.

The Table shows the results obtained. Overall, the degree of chimaerism was very low, the acme for all tissues being reached by the foetal liver cells, but even then, the highest value, found in the lymph nodes, was only 10.7%. Statistically, this level of chimaerism produced by the foetal liver cells was significantly higher than that produced by lymphoid cells in each of the 4 recipient tissues examined. When foetal liver was compared with spleen cells as the donor tissue, there was a significantly greater degree of chimaerism in the bone marrow, spleen and thymus, and when bone marrow was used as the source of donor cells, the chimaerism produced by the foetal liver was only significantly higher in the recipient bone marrow and spleen. Foetal liver cells apart, bone marrow, and spleen and lymphoid cells all produced the same very low level of chimaerism in the recipient tissues.

The chimaeric mice were quite healthy at the time of sacrifice, occasionally, individuals were found to have slightly enlarged spleens, which is regarded as one of the signs of graft versus host disease.

The present experiments have shown that when a mouse is made tolerant to allogeneic cells, their descendents will be found in all of the lympho-myeloid tissues of the recipients, albeit at a low level of chimaerism. If the tolerogenic tissue source is varied, foetal liver cells produce a higher degree of chimaerism in the recipients

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