CELL MEDIATED IMMUNITY CONFERPED BY NATURAL RSV INFECTION AND KILLED VACCINE. Hyun W. Kim, Sanford L. Leikin, Carl D. Brandt, Robert M. Chanock, Robert H. Parrott. George Washington University and Research Foundation of Children's Hospital, Washington, D.C. 20009

In attempts to understand the apparent "sensitization" of individuals to respiratory syncytial virus (RSV) after inactivated RSV vaccine, in vitro lymphocyte transformation studies were carried out as a measure of cell mediated immunity in infants who had received inactivated RSV vaccine and infants who had received a similar parainfluenza 1 virus vaccine. Some infants in each group had, and others had not, undergone natural RSV infection prior to the lymphocyte studies. All infants who had received the RSV vaccine and/or who had undergone RSV infection showed RSV specific lymphocyte transformation. These findings strongly suggest that systemic RSV-specific cell mediated immunity developed after immunization with killed RSV vaccine and after natural RSV infection. As applied to understanding the pathogenesis and prevention of RSV disease these findings: 1) are consistent with the hypothesis that systemic cell mediated "sensitization" may be responsible for the altered response to natural infection occurring following use of inactivated RSV vaccine. 2) are opposed to the hypothesis that cell mediated immunity per se is important in protection against RSV infection. 3) suggest the hypothesis that transplacentally conferred lymphocyte sensitization to RSV might play a part in the pathogenesis of first infection RSV bronchiolitis.

FUNCTIONAL ACTIVITY OF THE FIFTH COMPONENT OF COMPLEMENT (C5) IN HUMAN,ANIMAL,PROPRIETARY AND SOY MILKS.THERAPEUTIC AND BIOLOGIC IMPLICATIONS.Michael E. Miller,Dept. of Pediatrics Charles R. Drew Postgraduate Medical School,Los Angeles,CA

We have previously demonstrated familial dysfunction of C5 in humans, and successful therapy of same with fresh plasma. Leiner,in 1908,suggested changing the wet nurse or substituting bottle feeding.We have therefore,measured functional C5 activity in human,cow,goat,lamb,proprietary and soy milks.A previously described assay of yeast opsonization,which requires normal function of the first five complement components was utilized.Ability of the various milks to restore opsonic activity to two separate C5 deficient serums-human and B10D2 old line mouse-was measured.Confirmation that only C5 activity was being measured was obtained by a)comparing results with those obtained by addition of purified human complement components (As little as 1.5ug/ml.human C5 will fully restore opsonic activity to C5 deficient serums);b)inhibition of opsonic restoration of the milks with highly purified anti-C5 but not with anti-C3.The data showed that all preparations tested,including soy milk had significant functional C5 activity.We conclude:1)Sources other than plasma may serve in recovery of C5 and/or therapy of abnormal C5 states;2)Functional activity of C5 lasts far longer in milks than in human plasma; 3)The finding of apparent complement activity in milk without animal protein-i.e.,soy milk has obvious major biologic implications.

POTENTIALLY IMMUNOSUPPRESSIVE FACTORS IN TUMOR CELLS AND CERTAIN FETAL AND ADULT TISSUES. William T. Kniker, Robert L. Ganaway and Kendall O. Smith. Univ. Tex. Health Science Cntr., Depts. of Ped. and Micro., San Antonio, Texas 78284.

Fetal and cancer cells have many common features, including the release of "fetal" antigens. Because fetuses and cancers escape rejection, we wondered whether such products could inhibit immunologic responses. Human fetal liver, brain, gut, lung and 8-10 week whole fetuses were homogenized in buffered saline, 10% w/v. After freeze-thawing and centrifugation, supernatants (sups.) were diluted in serum-free medium. Eleven human cancer cell lines were grown in vitro until they reached 50-95% confluency. After washing with serum-free medium and incubation for another 24 hours, sups. were aspirated. They were tested for ability to suppress lymphocyte transformation induced by mitogens, using the whole blood technique of Han and Pauly.

All but one tumor sup. suppressed 20-98% of mitogen stimulation. As compared to controls, fetal brain and gut sups. suppressed 25-50%, while fetal and adult liver suppressed 95-99% of lymphocyte response. Trypan blue exclusion ruled out cytotoxic effects. These results suggest that both fetal and tumor cells produce immunosuppressive factors that may interfere with rejection by the host. Studies with sup. derived from adult liver indicate that several distinct factors exist, capable of inhibiting lymphocyte responsiveness variably to different mitogens and antigens.

SCREENING FOR ADA DEFICIENCY, E.C. Moore and H.J. Meuwissen, (Intr. by Ian H. Porter), New York State Department of Health, Kidney Disease Institute and Birth Defects Institute, and Department of Pediatrics, Albany Medical College, Albany, New York.

Some forms of combined immunodeficiency (CID) have been shown to have deficient activity of the enzyme adenosine deaminase (ADA). Earlier detection of CID prior to infection, by ADA assay, would greatly benefit those patients, particularly if a histocompatible marrow donor were available. As the usual methods for measuring ADA are too laborious for large scale screening and require venous blood not readily available from newborns, we have developed a screening method using blood spotted on filter paper identical to the samples used in the Guthrie test for phenylketonuria. This method depends on pH reagents incorporated into a gel containing adenosine, which change color as ammonia is released in the presence of ADA. The method is about 97% accurate, and is simple to perform. The cost is about 1½ cents per sample. This technique has also been adapted for screening of serum, cultured fibroblasts, tissue hemogenates, and eluates from column chromatography with $pH < 6$.

A pilot study using this method is at present underway at the PKU laboratory of the New York State Dept. of Health, Division of Labs. and Research, in Albany, N.Y., which analyzes blood from all newborns in the eastern half of New York State.

THYMIC DYSPLASIA IN A CHILD WITH SYSTEMIC LUPUS ERYTHEMATOSUS. Nancy B. McWilliams, Jesse M. Jones, Vijay V. Joshi and Julio Martinez. (Intr. by William E. Laupus). Medical College of Virginia, Depts. of Ped. and Path., Richmond, Virginia.

Systemic Lupus Erythematosus (SLE) is associated with abnormal antibody production. Recent evidence also suggests T cell dysfunction in this disorder. The patient described had ante- and post-mortem evidence of thymic dysplasia.

A diagnosis of SLE was made in a 2 year old girl with clinical evidence of skin and joint involvement. Laboratory evidence included positive LE cells, high ANA titer, hypergammaglobulinemia and proteinuria. History of a severe reaction to smallpox vaccine suggested pre-existing T cell deficiency.

Excellent control of the disease was achieved with prednisone and cyclophosphamide for 7 months when progressive central nervous involvement began. Death occurred 1 year after diagnosis.

At autopsy the thymus was composed almost entirely of thymic epithelial cells. While depletion of lymphocytes and plasma cells may be explained by prolonged immunosuppressive therapy, the total absence of Hassall's corpuscles suggests thymic dysplasia. In this patient, there may be an abnormity of T cell modulation of B cell function resulting in formation of antibodies to non-foreign antigens.

DEVELOPMENT AND CHARACTERISTICS OF VIRAL INDUCED CELL-MEDIATED IMMUNE RESPONSES IN UPPER RESPIRATORY TRACT. A.M. Morag*, J.M. Bernstein*, K. Beutner*, B. Morag* and P.L. Ogra. Dept. of Ped., ENT and Microbiol., SUNY at Buffalo, N.Y.

The appearance of rubella specific cell-mediated immunity (CMI) in tonsillar and adenoidal lymphoid tissue and in circulating lymphocytes, and antibody activity in serum and nasopharyngeal secretions was studied in groups of children who underwent tonsillectomy and adenoidectomy (T&A) at varying intervals after natural rubella infection, subcutaneous immunization with HPV-77 or intranasal inoculation of RA27 rubella vaccine. The techniques of hemagglutination-inhibition, autoradiography, in-vitro lymphocyte transformation and assay of migratory inhibitory factor using rubella virus as the antigen were employed to determine antibody and CMI in serum and secretory sites. Serum antibody response was elicited regularly after natural or induced infection. Nasopharyngeal antibody response was observed only after natural infection or RA27 immunization. Development of specific CMI in circulating lymphocytes was regularly observed after natural infection and frequently after immunization. Natural infection or intranasal immunization with rubella vaccine resulted in the appearance of CMI in the tonsillar and adenoidal lymphoid tissue, and the response persisted for 3-4 months. Significantly however, CMI activity in tonsils and adenoids was conspicuously absent after subcutaneous immunization. These data suggest the existence of locally induced cellular immune components in the mechanism of mucosal defense against viral infections.