ROLE OF RETICULOENDOTHELIAL SYSTEM (RES) MACROPHAGES IN HOST RESISTANCE TO VIRAL INFECTIONS. Lowell A. Glasgow, and Ann Murrer. Depts. of Pediatrics and Microbiology, Univ. of Utah College of Medicine, Salt Lake City, Utah.

Although phagocytic cells of the RES have been identified as a critical determinant of host resistance in certain viral diseases, the mechanism remains only partially defined. We utilized an in vitro experimental model system to better define the capacity of macrophages to control a virus infection in the absence of other components of the host's defense mechanism. Progression of a vaccinia virus infection in cultures of mouse embryo fibroblasts was partially controlled, as evidenced by decreased (1) foci of cell destruction (CPE) and (2) extracellular virus, in cultures receiving mouse peritoneal macrophages and lymphocytes. This protective effect was shown to be predominantly mediated by the macrophages after separation on a Ficoll density gradient. Nonspecifically activated macrophages (from BCG immunized mice) had a significantly enhanced capacity to control virus replication. Interferon could not be detected and the suppression of virus replication occurred in the absence of significant virus uptake by the macrophages. These data support the concept that (1) RES cells contribute to host resistance in certain virus infections and (2) suggest that macrophages may directly interact with virus-infected cells and block production or release of progeny virus.

SCALDED SKIN SYNDROME (SSS): DELINEATION OF THE GENETIC CONTROL FOR EXFOLIATIVE TOXIN PRODUCTION IN STAPHYLOCOCCI. Lowell A. Glasgow, Marvin Rogolsky, Richard Warren, and Bill B. Wiley. Depts. Pediat. & Microbiol., U. of Utah Coll. Med., SLC, Utah.

SSS has been associated with group II phage type S. aureus which produce an exfoliative toxin (ET) capable of causing separation of desmosomes in the granular cell layer and exfoliation of superficial layers of the epidermis. Development of an animal model made possible a study to delineate the genetic control for ET production. Unlike diphtheria toxin we were unable to associate ET production with a lysogenic phage. Loss of ET after treatment with ethidium bromide or growth at 44C suggested the gene was extrachromosomal (a plasmid). Failure of co-elimination of genes for ET production, penicillin and cadmium resistance indicate they are not on the same plasmid. Another extracellular protein which is bacteriocidal for other microorganisms (a bacteriocin), however, was coeliminated with ET suggesting their genes may be on the same plasmid. Isolation of labelled DNA from an ET^+ and ET^- strain (CsCl-density gradient) resulted in differences in the density profile which suggest the presence of plasmid DNA in the ET^+ strain. These data suggest (1) the possible unique situation of control for a specific staphylococcal product which is directly related to production of human disease on a plasmid and (2) raises the possibility of transfer of ET producing capability to other strains of staphylococci.

SIGNIFICANCE OF PNEUMOCOCCI AND HEMOPHILUS INFLUENZAE CULTURED FROM THE NASOPHARYNX OF CHILDREN. W.P. Glezen, A.M. Collier, and F.A. Loda, Frank Porter Graham Child Development Center and Dept. of Ped., Univ. of N. C., Chapel Hill.

Significance of pneumococci and H. influenzae (H flu) in the nasopharynx is obscured by their occurrence in well children and during disease caused by other pathogens. In longitudinal studies of children in group day care the microbial flora of the nasopharynx has been monitored by culturing for viruses, bacteria and mycoplasmas. Over 1400 cultures were studied during illnesses and 2062 cultures when asymptomatic. The frequency of isolation of pneumococci (including specific serotypes) and H flu was correlated with age or severity of illness. H flu was isolated from 27% of all illnesses (30% of otitis media) but only 15% of well cultures; this difference was greater in children <4 years old. Pneumococci were recovered from 60% of illness cultures and 47% of well cultures; however, when a pneumococcus was the only bacterial pathogen, the rates were 39% and 33% with little difference regardless of age or severity of illness. When the same comparisons were made for specific serotypes, some were associated more frequently with illness in infants. In children <4 years both pneumococci and H flu were recovered from 18% of illnesses and only 6% of well cultures; the illness:well ratio was slightly higher than that for all H flu. Cultures which yielded a virus also showed a slight excess of both bacteria. These data suggest that pneumococci are opportunistic pathogens while H flu may have greater propensity for primary invasion.

EFFECT OF PASSIVE ANTIBODY ON EXPERIMENTAL INFECTION WITH PARAINFLUENZA VIRUS TYPE 3 (PARA3). W.P. Glezen and G.W. Fernald, Dept. of Ped., Univ. of N. C., Chapel Hill.

Infants frequently develop bronchiolitis caused by Para3 in the presence of passively-acquired antibodies. Immune mechanisms have been implicated in the pathogenesis of bronchiolitis caused by both Para3 and RS viruses. To examine this hypothesis, hamsters were infected with Para3 one day after an intraperitoneal injection of 0.5 ml of pooled human γ-globulin (γG). At the time of infection serum titers were about 1:16. Histologic examination of the lungs consistently showed less cellular infiltrate in γG-treated animals than controls. Lungs of γG-hamsters yielded 6500 plaque-forming units/gm compared to 12,400 pfu/gm in controls.

When similarly-treated groups of hamsters were reinfected 30 days later the histopathology of γG-hamsters was similar to the first infection but reinfected controls had negligible infiltrates. Neither group had detectable virus in lung suspensions. The antibody titers at the time of reinfection were distinctly different: animals that received γG had a geometric mean titer $\log_2$ of 1.4; controls had a GMT $\log_2$ of 4.5.

These experiments did not show enhancement of the pathology by infection in the presence of passive antibody; instead there was a suggestion of some protection as has been observed in cattle which share Para3 with humans as a natural pathogen. The results warrant further investigation of the pathogenesis of both Para3 and RS virus before extensive trials of vaccines.

EXPERIMENTAL HSV ENCEPHALITIS: EFFECTS OF TREATMENT WITH CYTOSINE ARABINOSIDE. John F. Griffith & Sandra Casagrande. Duke Univ. Med. Ctr., Dept. of Ped., Durham, N. C.

The effects of cytosine arabinoside (cytarabine) on survival and brain virus concentration were studied in groups of young mice with experimental herpes simplex virus (HSV) encephalitis. Toxic dosages of drug were purposely employed in order to ensure maximum anti-viral activity in the brain. Encephalitis was established by direct intracerebral innoculation of previously titered virus, known to be sensitive to this drug in vitro. Treatment was begun at intervals prior to and following introduction of virus. The concentration of virus per gram of brain was determined at intervals during the 4 day treatment course and on completion of drug administration.

During the initial 3 days of infection, the brain virus concentration in treated animals was significantly lower than in the infected, untreated control group. This was also noted when a more concentrated drug dosage was used. There were no survivors in either group although the clinical courses differed. The brains of infected animals showed a necrotizing encephalitis with polymorphonuclear and mononuclear cells, focal hemorrhage and rare inclusion bodies.

Large doses of cytosine arabinoside administered in this way have a significant but transient effect on brain virus concentration but do not alter the clinical course of disease. This is the first in vivo demonstration of the activity of this agent against HSV replication in the CNS.

DISTRIBUTION OF RUBELLA VIRUS IN THE SKIN DURING ACUTE RUBELLA WITH AND WITHOUT RASH. Alfred D. Heggie (Intr. by LeRoy W. Matthews). Case Western Reserve Univ. Sch. of Med., Univ. Hosps. of Cleveland, Dept. of Ped., Cleveland, Ohio and Naval Medical Research Unit No. 4, Great Lakes, Illinois.

In a previous study to assess the role of rubella virus in the pathogenesis of the rubella exanthem, virus was isolated from cell cultures of skin biopsy specimens of the rash in 13 of 14 patients with this disease. It was postulated, therefore, that although other factors might be involved, the presence of virus in the skin was essential to evolution of the rash. To further investigate the association of virus with rash, punch biopsies were performed concurrently on areas of skin with and without rash. Cell cultures were prepared from the skin specimens and the resulting cell monolayers were tested for rubella virus. From paired skin specimens from 16 patients, virus was isolated from sites of rash in 12, and from the uninvolved skin in 10. In another patient who was shown by serologic response and recovery of virus from the pharynx to have rubella without a rash, virus was also isolated from the skin. These data indicate that in acute rubella the virus is generally distributed throughout the skin irrespective of the presence or distribution of the rash. It is concluded, therefore, that although the presence of virus in the skin appears to be a constant feature of the disease, it is only one of the factors essential to evolution of the rubella exanthem.