

larger or cortisone treated dwarfs. HGH from embalmed bodies is clinically useful. HGH, 10 U., was not more beneficial than 2 U. The craniopharyngiomas in the OH did not grow during short-term treatment with HGH.

- 95 *A Longitudinal Study of Streptococcal Antibody Dynamics Showing Unusual Seasonal Fluctuations.* EDWARD L. KAPLAN, ELIA M. AYOUB, BASCOM F. ANTHONY, FRANKLIN W. BRIESE and LEWIS W. WANNAMAKER, Univ. of Minn. Med. Sch., Dept. of Ped., Minneapolis, Minn.

A population of 160 children (mean age = 6.6 years) was followed at 2-month intervals over a 2-year period with serial determinations for 3 streptococcal antibodies: antistreptolysin O (ASO), antideoxyribonuclease B (anti-DNAse B) and anti-nicotinamide-adenine-dinucleotidase (anti-NADase). Antibody dynamics of the more than 1,100 sera collected (mean no. bleedings/child = 7.3) were examined by comparing geometric mean titers (GMT) and significant rises at different times of the year. GMTs for all 3 antibodies increased during the summer and fall when streptococcal skin infections were common but leveled off or fell during the winter and spring despite a high prevalence of respiratory illnesses and positive throat cultures for group A streptococci (up to 70%). The smallest number of rises for all 3 antibodies occurred during the respiratory season. During the summer anti-DNAse B titers tended to rise more sharply and reached maximum levels sooner than the other two antibodies. Although GMTs were lowest in the 1-3-year age group, these children also showed marked rises during the summer and fall. Rises in ASO were less frequent than responses in the other two antibodies, especially after 3 years of age. Plateauing of GMTs occurred at a later age for anti-DNAse B than for the other two antibodies. This extraordinary, inverse seasonal pattern of antibody levels and responses emphasizes the predominant influence of skin infections in this population and raises the possibility of a curious immunological unresponsiveness to streptococcal respiratory infections during the winter month, behavior which may contribute to the low frequency of acute rheumatic fever relative to acute nephritis in this population.

- 96 *Measles in Previously Immunized Children.* STEPHEN J. LERMAN and ELI GOLD, Epidemic Intelligence Serv., Nat. Communicable Disease Center, Atlanta, Ga. and Dept. of Ped., Case Western Reserve Univ. Sch. of Med. at Cleveland Metropolitan General Hosp., Cleveland, Ohio.

An outbreak of measles (rubeola) occurred in a city in Northeast Ohio during January-June, 1969, involving 14 children previously immunized with live attenuated measles vaccine and 46 unimmunized children. In one school where the attack rate was 52.4% for unimmunized children, the attack rate for children immunized by one particular physician was 14.3% compared to 2.4% for children immunized by the local health department and other physicians. Vaccine in this physician's office was exposed to temperatures that may have contributed to virus inactivation.

This study is an example of vaccine efficacy under conditions of current community use that is less than anticipated by field trial experience. Lack of initial

seroconversion is the most likely cause of these vaccine failures and deterioration of vaccine infectivity during storage is proposed as the probable explanation.

- 97 *Pathophysiology of Mycoplasma pneumoniae Infection in Human Fetal Tracheal Organ Culture.* ALBERT M. COLLIER and WALLACE A. CLYDE, Jr., Dept. of Ped., Univ. N.C. Sch. of Med., Chapel Hill, NC.

Mycoplasma pneumoniae-host cell interactions have been difficult to analyze: natural disease is limited to man, and low mortality provides little pathologic material. Data from experimental models suggest that the ciliated respiratory epithelium is the target cell of *M. pneumoniae*. Evaluation was made of fetal tracheal organ culture as a means of providing organized differentiated human epithelial cells for studies *in vitro*. Tracheas were removed from 15-20-week fetuses, obtained aseptically by hysterotomy for psychiatric indications; transverse sections were maintained in Hayflick's medium with HEPES buffer at 36°C in 5% CO₂. The effects of *M. pneumoniae* were studied by observations of ciliary function, light microscopy and immunofluorescence. Ciliary motion (which could be quantitated stroboscopically) slowed, became disorganized and ceased by 96 h. Microscopic changes included epithelial cytoplasmic vacuolization and nuclear swelling, followed by loss of cilia. Immunofluorescence identified organisms among the cilia, between cells, and in surface microcolonies. No comparable changes were produced by 4 other human mycoplasma species which were tested. These findings suggest the pathophysiology of *M. pneumoniae* disease by revealing both functional and structural changes in parasitized human respiratory epithelium. The nature of this interaction may explain many general features of *M. pneumoniae* disease, particularly the frequency of tracheo-bronchitis with protracted paroxysmal cough which commonly occurs in childhood infections.

- 98 *Altered Growth Following Gestational Viral Infection of the Placental and Aplacental Host.* JOSEPH W. ST. GEME, JR., CATHERINE W. C. DAVIS and LLOYD F. VAN PELT, UCLA Sch. of Med., Harbor Gen. Hosp., Dept. of Ped., Lab. for Microbiol. and Immunol. Research, Torrance, Calif.

Intravenous infection of 10 pregnant rhesus monkeys with mumps virus during the first trimester results in intrauterine and postnatal growth retardation. Virus may be recovered from the oropharynx of the pregnant monkey but has not been detected in the tissues of the embryo, fetus, or neonate. The maternal host develops mumps virus neutralizing antibody and delayed hypersensitivity while the infant monkey demonstrates delayed hypersensitivity alone.

Inoculation of the embryonated chick egg with mumps virus at 12 h of age results in a persistent gestational infection. At hatch virus may be recovered from the blood and organs contain virus in from 0.01 to 1.0% of their cells. Hatchling experimental and control chicks are of the same size. Within 1 week experimental chicks incur a transient growth lag which disappears by 4 weeks of age. Virus disappears from the tissues by 1 week of age. Specific antibody is present in the sera of experimental chicks at 1 month of age.

Preliminary studies reveal that parenteral mumps virus infection of the pregnant rat during early gestation results in fetal dwarfing. Virus has not been detected in late fetal tissues. Both maternal and weanling

experimental rats demonstrate mumps virus antibody and delayed hypersensitivity.

Gestational viral infection may alter growth by a direct replicative effect on fetal tissues or perhaps indirectly via dysfunction of the placental unit.

- 99 *Cytomegalovirus Infection of the Female Genital Tract.* DONALD N. MEDEARIS, Jr., ROBERT MONTGOMERY and LEONA YOUNGBLOOD, Children's Hosp. of Pittsburgh and Dept. of Ped., Univ. of Pittsburgh Sch. of Med., Pittsburgh, Pa.

Infections of the female genital tract may play an important role in intrauterine or neonatal cytomegalovirus (CMV) infections. Serum, urine (U) and cervical swab specimens (CSS) were obtained from 71 unselected pregnant Navajo women in Fort Defiance Indian Hospital, and 125 women of the prenatal clinic of Magee-Women's Hospital of Pittsburgh. Cord blood and urine specimens were obtained from 81 newborn infants delivered at Fort Defiance during the same period that the mothers were studied. CMV was recovered from 9/64 CSS of Navajo women (14%) and from 3 of 68 (4.4%) U. Virus was recovered from 5 of 112 (4.5%) CSS women in Pittsburgh and from 3 of 104 (2.9%) U. Recovery of CMV was more frequent from primigravidas (7/62 CSS; 4/57 U); 43 CSS and 41 U from women who had had more than 4 pregnancies were negative. CMV was recovered from 2% of CSS taken in the first trimester, 7% of those taken in the second trimester and 12% of the third trimester specimens from the combined population. None of the 66 urine specimens obtained from newborn infants was positive. Herpes virus was not recovered. These data revealed a surprisingly high frequency of cytomegalovirus infection of the cervix and although the differences were not statistically significant (presumably due to the small numbers studied) they suggest the possibility that infection was more frequent in young women, in primigravidas, and late in pregnancy. (Supported in part by NIH grant HD 02135.)

- 100 *Transmission of Toxoplasmosis by Leukocyte (WBC) Transfusion.* STUART E. SEGEL, MILFORD N. LUNDE, ARTHUR S. LEVINE and ROBERT G. GRAW, Jr., NCI and NIAID, NIH, Bethesda, Md. (introduced by Robert W. Miller.)

Disseminated toxoplasmosis infections without an obvious source have been documented frequently in cancer patients. Two children with acute leukemia given WBC transfusions for granulocytopenia from a donor with chronic myelogenous leukemia (CML) developed toxoplasma gondii infection. The CML donor, with no history of toxoplasma infection had received no anti-leukemic therapy prior to leukapheresis and remained clinically well. The first child was given 0.35×10^{11} CML leukocytes. Three weeks later she developed skin rash, pneumonia, congestive heart failure, hepatitis, and seizures, accompanied by a rising toxoplasma dye titer to 1:8,000 (IgM = 1:160). She expired 3 months later with disseminated toxoplasmosis. The second child received 2.5×10^{11} leukocytes over a 7-day period four weeks prior to splenectomy for an *E. coli* splenic abscess. Concomitantly, her dye titer rose to 1:128 (IgM = 1:40). Toxoplasma gondii was isolated from the spleen and a single toxoplasma cyst was found on histologic examination. She died 1 month following surgery with toxoplasma cysts found in the lung and heart at necropsy. Retrospective examination of stored serum samples from the CML donor

revealed that at the time of WBC donation she had a toxoplasma dye titer of 1:8,000 (IgM = 1:10, CF = 1:16). Leukocytes from the same donor were given to other leukemic patients. Both died within one week of transfusion without pathologic evidence of toxoplasma infection. Toxoplasma infection in two patients receiving leukocyte transfusions from a CML donor with serologic evidence of toxoplasmosis suggests the role of WBCs in the transmission of this disease.

- 101 *Splenectomy and Impaired Resistance to Pneumococcal Infection.* ROBERT H. DRACHMAN, LAI-SUNG LEUNG and GREGORY SZAL, Johns Hopkins Univ. Sch. of Med., Dept. of Ped., Baltimore, MD.

Efforts to devise an animal model in which splenectomy decreases the effectiveness of host defences against acute bacterial infection have been infrequently successful. It has been difficult to provide a challenge which sharply differentiates controls from the operated animals. A model is described in which all splenectomized rats died after intravenous (i.v.) challenge with an LD₅₀ dose of pneumococcus Type 25. Normal rats immunized with pneumococcus Type 25 formalized bacteria and then challenged i.v. 3 to 6 days afterwards, all survived, while previously splenectomized rats, similarly immunized, all died. As the interval between immunizations and subsequent splenectomy was lengthened in a stepwise fashion, the mortality following i.v. challenge fell from 80% to zero. Clearance of pneumococci from the blood stream reflected these results, more prompt disappearance of bacteria becoming evident at 1 to 3 hours after i.v. challenge in those most likely to survive. During this period of increasing antibacterial resistance both early antibody and the unique ability of the spleen to clear minimally opsonized bacteria were critical for effective antibacterial host defence. Early but delayed antibody could be detected in the immunized splenectomized rat, but was not adequate for protection in the absence of the spleen.

- 102 *Antibody Response to a Polyvalent Pseudomonas Vaccine in Children with Leukemia.* MAHROO HAGHBIN, LOWELL S. YOUNG, DONALD ARMSTRONG and M. LOIS MURPHY, Memorial Hosp. and Cornell Univ. Coll., New York, NY.

Pseudomonas aeruginosa infection accounts for 30% of gram-negative bacteremias in children with acute leukemia at Memorial Hospital. There is a mortality rate of 87% despite antimicrobial therapy. Previous studies in animals and man following severe burns suggest that *P. aeruginosa* infection may be subjected to immunological control. Active immunization of 20 leukemic children in bone marrow remission was attempted with a lipopolysaccharide antigen derived from 7 strains of *P. aeruginosa* (Fisher-Devlin immunotypes). Vaccination consisted of 4 intramuscular injections at weekly intervals. Febrile and local reactions occurred in all, but were not severe enough to discontinue the procedure. The appearance of antibody was demonstrated by 1 to 5 precipitin bands using the Ouceterlony immunodiffusion technique. This was correlated with a rise in hemagglutinating antibody titers. Sixteen children demonstrated antibody response within one month, despite the immunosuppressive antileukemic therapy that they were receiving. If this antibody proves to be protective against *P. aeruginosa* infection by further control studies in progress, vaccination of patients early in the course of leukemia would be indicated.