with periodic clinical examinations, nasopharyngeal cultures for *H. influenzae* and serum samples. *H. influenzae* strains were isolated from all at some time during the study; while 8 had type b, usually associated with clinical illness. One child had meningitis at 40 months; bacterial inhibitory substance (BIS) was present only during and immediately after the acute illness. Serum from 5 other patients had BIS within 3–4 weeks; in 2, BIS was temporary while in 3 it persisted until age 5. 11 other children had temporary BIS, 7 associated with nontype b strains and 4 without any relationship to isolations of *H. influenzae*. 18/20 of the children had BIS at some time, but it persisted until age 5 in 7/20.

Cord blood serum from 6/20 showed BIS which was lost by age 2 years in all but 2 patients.

The inhibitory effect was entirely removed from serum by adsorption with heavily encapsulated bacterial cells and partially removed by adsorption with PRP.

An increase in opsonizing antibody to type b was noted also in association with *H. influenzae* strains.

Response of children immunized with meningococcal group C and group A polysaccharides. MARTHA L. LEPOW, IRVING GOLDSCHNEIDER, and EMIL C. GOTSCHLICH. *Univ. of Connecticut Sch. of Med. Hartford, Conn., and Rockefeller Univ., N. Y., N. Y.*

To date 60 children ages 1 to 9 years have been immunized with 25 or 50 micrograms of highly purified meningococcal group-specific polysaccharide. Thirty children received the group C antigen and 30 the group A antigen by subcutaneous injection. Three immunized children developed local zones of transient erythema up to 1.8 cm. in diameter within 24 hours of injection. There were no local or systemic reactions.

Humoral antibodies were measured by bactericidal, immunofluorescence, hemagglutination and quantitative radioimmunoprecipitation assays. Complete antibody studies on 50 of the children showed that all responded within 3 weeks of immunization with the production of specific IgG, IgM and IgA antibodies against the C or A antigen in amounts comparable to those produced by immunized adults. Bactericidal and hemagglutinating antibodies were demonstrated. There was no advantage of the 50 microgram dose over the 25 microgram dose.

Previous studies with the meningococcal group C antigen in more than 40,000 military recruits has established the effectiveness of this immunization in preventing systemic meningococcal disease. On the basis of results of the current study, it appears that immunization of children with the meningococcal group A and C vaccines would be safe and immunologically efficacious in the age group tested.

Altered reactivity to respiratory syncytial virus: Description of atypical RSV illness and prospective four year follow-up of children previously immunized with an inactivated vaccine. JERRY J. ELLER, VINCENT A. FULGINITI, DANIEL C. PLUNKET, and OTTO F. SIEBER, JR. *U.S. Army Med. Research and Nutrition Lab., and Univ. of Colo. Med. Ctr., Denver, Colo.* (Intr. by Henry Kempe).

Beginning in July 1966, 424 children ranging from 6 months to 7 years of age were immunized. Mild RSV illness was documented to occur later upon natural exposure to the wild virus in all age groups. Nineteen children in the youngest age group immunized (6–23 mos) were hospitalized with an atypical illness due to RSV. Eleven were hospitalized in 1966–67, 6 in 1967–68, and 2 in 1968–69. Two children had recurrent atypical illness during separate years. The illness was characterized by high fever and pneumonia with marked bronchiolitic wheezing. Chest films showed prominent multi-segmental infiltrates usually in several lobes. Associated lung complications included: lobar atelectasis, pneumothorax, pneumomediastinum, pneumopericardium, subcutaneous emphysema, and pleural effusions. A diffuse maculopapular rash was present on the neck, trunk and proximal extremities of 8 (42%) vaccinees in contrast to 1 of 31 (3.2%) controls with hospitalized RSV illness ($\bar{X}^2 = 9.57$, $p < 0.01$). Of 9 hospitalized vaccinees available for prospective follow-up for 4 years from the time of immunization, 5 (55.6%) were diagnosed by allergists, independently of the investigators, as having either asthma (4) or allergic rhinitis (1). This was in contrast to a diagnosis of an atopic disorder made in 7 of 46 (15.2%) age-matched controls prospectively followed ($\bar{X}^2_c = 5.01$, $p < 0.10$).

Studies on immunization with three types of combined viral vaccines. ROBERT E. WEIBEL, JOSEPH STOKES, JR., VICTOR M. VILLAREJOS, JORGE A. ARGUEDAS G, EUGENE B. BUYNAK, and MAURICE R. HILLEMAN. *Sch. of Med., Univ. of Pennsylvania, Philadelphia, Pa., Louisiana State Univ., International Ctr. for Med. Res. and Training, San Jose, Costa Rica, and Merck Inst. for Therapeutic Res., West Point, Pa.*

Combined lyophilized Moraten measles, Jeryl Lynn mumps, and HPV 77 duck rubella vaccines were administered by a single injection to 715 children ages 7 months to 7 years, and susceptible to these viruses. The geometric mean antibody responses to the triple vaccine were comparable to those obtained with monovalent vaccines. The antibody seroconversion rate was 96% to measles by hemagglutination-inhibition tests, 95% to mumps neutralization tests and 94% to rubella hemagglutination-inhibition tests. Clinical reactions to the triple vaccine were no greater than those following measles vaccine given alone. Arthralgia and arthritis were not reported during the 28 day recording period. In children combined measles-mumps-rubella vaccine provides a *safe, simple* and economical means of immunizing against these three diseases. Similar findings were obtained in tests in 375 seronegative children given combined measles-rubella vaccine and in 415 seronegative children given combined mumps-rubella vaccine.

Persistent joint symptoms associated with HPV-77DK12 rubella vaccine. SPOTSWOOD L. SPRUANCE, LAWRENCE E. KLOCK, JR., and CHARLES B. SMITH. *Univ of Utah Sch. of Med., Univ. of Utah Med. Ctr., Salt Lake City, Utah* (Intr. by Lowell Glasgow).

The incidence and duration of joint complications were investigated in 2989 children who received the HPV-77DK12 rubella vaccine. Two hundred eighty-seven (287) children experienced joint symptoms within 45 days after vaccination. Two hundred twenty-five (225) of these children were contacted 6 months later and three were found to have had recurrences of symptoms.

Histories, physical examinations, and serologic studies were conducted on 11 children, including three from the study group, who manifested recurrent joint symptoms 6–9 months after receiving the dog kidney rubella vaccine. In all cases the original and the recurrent symptoms were in the knees. Symptomatic episodes were 1–4 days in duration and were characterized by pain and limitation of knee extension. On examination of the knees, abnormalities were observed in 5 children. These included limi-

tation of motion, mild tenderness or swelling, and in two cases, synovial thickening. Two other children had reactive tests for rheumatoid factor. The mean rubella HI titer 6–9 months after vaccination was 1:66 among the 11 children with recurrent symptoms. This was lower but not significantly different from the mean HI titer (1:127) of sera collected at the same time from 18 children who had joint symptoms only during the first 45 days following vaccination.

Recurrent joint symptoms may rarely be observed following administration of HPV-77DK12 rubella vaccine. Serologic studies failed to distinguish children with recurrent joint symptoms from controls.

Protective effect of antirubella human immunoglobulin. LOUIS Z. COOPER, JOAN P. GILES, ALFRED L. FLORMAN, PHILIP R. ZIRING, and SAUL KRUGMAN. *New York Univ. Sch. of Med., N.Y., N.Y.*

Previous experience with immune serum globulin (ISG) indicated 1) that it did not prevent viremia in children with rubella infection, and 2) that it did not prevent congenital rubella. This report describes the protective effect of an experimental lot of high titer antirubella human immunoglobulin (RIG) in 33 children exposed to the Brown strain of rubella virus (RV).

RIG was given to 22 of the susceptible children 24 or 96 hours after intranasal exposure to RV. Six other children received ISG. The dose of RV was either 10^4TCInD$_{50}$ or 10^1TCInD$_{50}$, and the dose of immunoglobulin was 0.3 ml/kg of body weight. In the group that received RIG: 1) passively acquired rubella antibody was detected transiently after inoculation in 15 children; 2) no detectable viremia was observed; 3) pharyngeal shedding of RV was decreased and 4) the rubella specific IgM response was depressed. RIG was more effective when given at 24 hours against low dose virus challenge, preventing or delaying seroconversion; it was less effective in modifying infection when given at 96 hours after high dose challenge. These data suggest that RIG may be useful for the prevention of congenital rubella.

Serologic responses to live further attenuated rubeola vaccine among term and low birth weight infants. J. WILKINS, P. F. WEHRLE, and B. PORTNOY. *Hastings Found. Univ. Southern Calif.-Los Angeles County Med. Ctr., Los Angeles, Calif.*

Protective antibodies against rubeola virus have been demonstrated in IgG and passive transfer of maternal antibodies against rubeola has been known to protect infants during the first several months of life. It has also been shown that the presence of this passively acquired antibody interferes with effective immunization against rubeola with live attentuated virus vaccines. For all infants there is a strong correlation between initial level of passively acquired antibody of maternal origin and its persistence. The concentration of IgG at birth is lower in low birth weight (LBW) than in term infants. This suggests that early curtailment of interuterine life is likely to result in lower IgG levels in the infant. From August 1, 1965 through March, 1968 251 infants (114 terms and 151 LBW) were inoculated with further attenuated rubeola vaccine at varying ages between six months and two years. No detectable rubeola HAI antibody was present at $<1:8$ prior to inoculation. The data indicate that the serologic responses of the two groups are better than previously recognized. Thus, the effectiveness of rubeola immunization of infants <12 months of age is such that use of this vaccine may be considered in younger infants during epidemic situations or in immunization programs in developing countries.

The acquisition of antibodies against adeno-associated satellite viruses. MARTHA D. YOW, LARRY H. TABER, JOSEPH L. MELNICK, and D. WARK BOUCHER. *Baylor Coll. of Med., Houston, Tex.*

The adeno-associated satellite viruses were first recognized in 1965. In spite of significant investigations since that time, their role in human disease remains obscure. In an attempt to define this role a longitudinal study of 42 infants (birth–2 yrs.) from a low socioeconomic group was initiated in 1968. The infants were examined at regular intervals and during illnesses. Specimens for viral isolation were collected on each occasion. Sera for antibody titers were obtained at birth and every 3 months thereafter. The purpose of this paper is to report the results of the serologic portion of this study. Neutralization tests revealed that at birth 50% of the infants had antibody to Type 1 satellite virus and 71% to the Type 2-3 complex. These percentages declined to 9% and 18%, respectively, at 6 months, remained low from 6 to 12 months, then rose sharply at 15 months. At 2 years 66% of the infants had antibody against Type 1 and 73% against Type 2-3. Mean geometric titers were high at birth, low from 6–12 months, and highest at 24 months. These data indicate the passive transfer of maternal antibody, and its decline. They also indicate infection due to adeno-associated satellite viruses early in life.

Parotitis in previous recipients of mumps vaccine. PHILIP A. BRUNELL, ANTHONY BRICKMAN, SHARON STEINBERG, and ELAINE ALLEN. *New York Univ. Sch. of Med., N. Y., N. Y.*

Between 1967 and 1970, twenty children with parotitis who had previously received mumps vaccine were studied. These children were immunized in four different Pediatric offices over a four year period so that no single lot of vaccine or immunizing procedure could be implicated as the cause of these apparent "vaccine failures." Mumps soluble complement fixing (MSCF) antibody determinations revealed that only eight of the seventeen children for whom appropriate serum specimens were available had evidence of mumps infection. Children without a detectable antibody response could not be differentiated clinically from those who developed MSCF antibody. Parotitis occurred in two siblings without a MSCF antibody response suggesting that these illnesses might have an infectious etiology. Neither mumps nor any other virus could be recovered from five children without an antibody response or from three children who could not be classified serologically. These findings confirm the multiple etiology of parotitis and indicate that serologic studies are required to identify true mumps vaccine failures.

Host resistance to virus infection in the fetus: I. Interferon (IF) production. J. C. OVERALL, JR. and L. A. GLASGOW. *Univ. of Utah Coll. of Med., Salt Lake City, Utah.*

The mechanisms underlying impaired host resistance of the fetus and newborn infant to virus infections are poorly understood. Immaturity of the IF system has been suggested as one major determinant of this enhanced susceptibility. Our previous studies demonstrated that the third trimester (140–117 days) fetal lamb (normal gestation 150 days) produced markedly higher levels of serum IF (27,000–250,000 units/ml) than adult sheep (180–250 μ/ml) following intravenous (IV) inoculation with Chikungunya virus (CV). The present report extends these studies to fetuses in the second and first trimester, the period during which greatest damage from virus infection occurs. Second and third trimester fetuses were inoculated by the IV, and first trimester by the intraperitoneal route. Highest IF titers (μ/ml of serum or gram of tissue) were present 2–4 hours following inoculation: