	Gest. Age							
	111 day	109 day	97 day	84 day	68 day	43 day	30 day	30 day
IF Titer	80,000	200,000	400,000	200,000	150,000	1,000	800	2,000

During the second trimester, fetal animals (68–97 days) continue to produce high levels of IF. Although fetal immaturity is the likely explanation for the significantly lower levels of IF observed in the first trimester animals, the route of inoculation could be a factor. The data clearly indicate, however, that the capacity to produce interferon is present during early stages of fetal development.

The effect of early folic acid deprivation on later growth and susceptibility to Shigella infection. JOHN D. NELSON and KENNETH C. HALTALIN. *Univ. of Tex. (Southwestern) Med. Sch. at Dallas, Dallas, Texas.*

Early, brief environmental factors may have lasting effects on growth rate, adult size and responses to stress. Nutritional deprivation is one of these events. Newborn guinea pigs fed a folic acid-deficient diet for 14 days are susceptible to fatal infection with *Shigella flexneri* while optimally-fed control animals are resistant. (J. Infect. Dis. 121:275, 1970). To test the hypothesis that animals subjected to a brief period of folic-acid deficiency as newborns would show enhanced susceptibility to Shigella challenge later in life after resuming a normal diet, newborn guinea pigs randomized for sex and litter were assigned to a control group receiving optimal diet or to a test group fed the folate deficient diet for 14 days and subsequently given optimal diet. 27% of animals (9/33) receiving deficient diet died unexpectedly and without obvious cause shortly after being offered standard diet. Possibly metabolic readjustments led to fatal biochemical derangements. At 45, 75, 105 or 135 days of age when selected animals were challenged with Shigella, there was only transient fecal shedding and no differences existed between the test and control groups. There was a profound and lasting effect of early folic acid deprivation on subsequent growth. Between 125–149 days of age the average weight of the control group was 856g and of the early-deprivation group 649g. Aside from smaller body size the early-deprivation animals appeared healthy. Although previous studies have shown similar growth retardation from early periods of protein or caloric restriction and from incomplete protein feeding, it has not been noted previously with a specific dietary deficiency such as folic acid.

The effects of corticosteroids on experimental herpes simplex virus encephalitis. LAURIE N. ECKMAN and JOHN F. GRIFFITH (Intr. by Samuel L. Katz). *Duke Univ. Med. Ctr., Durham, N.C.*

This study examines the effects of corticosteroids on the ultimate survival, virus concentration and neuropathologic changes in mice with herpes simplex virus (HSV) encephalitis.

Swiss white mice were inoculated intracerebrally with 0.01 ml of a 5×10^{-4} dilution of stock Rodanis strain HSV. Virus was injected directly into the right cerebral cortex. Treatment was initiated 60 hours after inoculation of virus with either hydrocortisone, corticosterone or placebo. One group of animals was inoculated with virus and left untreated and another group was retained as an uninfected control population. Both preparations were given as 5 mg intramuscular injections every 24 hours for 5 days.

Fifty percent of the infected, untreated animals and an identical proportion of those treated with placebo, died with encephalitis. In the steroid treated group sixty percent of those receiving hydrocortisone died as compared with fifty percent receiving corticosterone. The differences were not significant.

The study relating virus concentration in brain and neuropathology to serum adrenal corticosteroid levels was done using an identical population of animals with the same inoculum. Groups of 8 animals were sacrificed by decapitation at intervals before and after institution of therapy. The blood was pooled and the plasma separated and stored at −70°C. Steroid levels were measured using the fluorimetric method. Preliminary results revealed a level of 90 μgm/100 ml for hydrocortisone treated animals and 13 μgm/100 ml for untreated animals. Two brains from each of these groups were aseptically removed and made into a 10% suspension for plaque assay. The results will be presented and discussed, stressing the survival data and the interrelationship between steroid concentration and prognosis in this illness.

Intrinsic defect of the polymorphonuclear leukocyte resulting in impaired chemotaxis and phagocytosis. RUTH L. STEERMAN, RALPH SNYDERMAN, SANFORD L. LEIKIN, and HARVEY R. COLTEN. *Children's Hosp., Washington, D.C., NIDR, Bethesda, Md., NCI, Bethesda, Md.*

Abnormalities of polymorphonuclear leukocyte (PMN) chemotaxis and phagocytosis have been described. In each instance the combined chemotactic and phagocytic defects were a consequence of an abnormality in humoral, not cellular, function. We now describe a 3½ year-old white male with recurrent pneumonia and skin infections associated with a *cellular defect* of PMN chemotaxis and phagocytosis, as well as a sex-linked form of congenital agammaglobulinemia. He had normal delayed hypersensitivity and normal levels of hemolytically active whole complement and C1 thru C5. The impairments of PMN function were demonstrated *in vitro* by an inability of his PMNS to respond to chemotactic factors, to phagocytize *S. aureus*, and by abnormal NBT dye tests. These abnormalities were not corrected by the addition of normal serum to the patient's PMNs. No evidence was obtained for a humoral inhibitor of PMN function since normal PMNs were capable of normal chemotaxis and phagocytosis in the presence of his serum. In addition to the intrinsic granulocytic defect, the patient's serum was deficient in generating chemotactic activity for normal PMNs. The parents' PMNs were capable of normal chemotaxis and phagocytosis. It is not certain whether the patient's PMN abnormalities are the result of an acquired or an inherited defect. These studies demonstrate a previously unrecognized abnormality of PMN function, namely, an intrinsic defect of the PMN resulting in impaired chemotaxis and phagocytosis.

Hemorrhagic chickenpox associated with disseminated intravascular coagulation. JAMES J. CORRIGAN, JR. and W. LORRAINE WATKINS. *Univ. of Arizona, Coll. of Med., Tucson, Ariz. and Emory Univ. Sch. of Med., Atlanta, Ga.*

Disseminated intravascular coagulation (DIC) or consumption coagulopathy has been well documented in children with bacterial septicemia but infrequently reported in viral diseases. Fibrin thrombi have been noted with the malignant form of varicella-zoster virus infections and there is laboratory evidence that DIC may be present in hemorrhagic smallpox. It is the purpose of

this report to describe the changes in the coagulation mechanism in 4 children with severe varicella infection, 3 of whom had hemorrhagic chickenpox. All cases had a malignant disease at the time of their viral infection; 2 with acute leukemia in remission, 1 acute leukemia in relapse, and 1 with metastatic retinoblastoma. All were receiving an antineoplastic drug but none were on corticosteroids. None had bacterial sepsis or shock at the time of their chickenpox. Hemorrhagic varicella only occurred in the 3 leukemic patients, and all 3 died. The non-hemorrhagic case survived. The coagulation data revealed that the patients with the hemorrhagic form demonstrated thrombocytopenia, reduced levels of coagulation factors II, V, and VIII, hypofibrinogenemia, positive fibrin split products, and normal euglobulin lysis. In the non-hemorrhagic patient all studies were normal. Heparin therapy was given to one patient with questionable improvement only noted in the fibrinogen level. Although hepatic necrosis may be found in fatal cases of varicella the coagulation data suggest that the multiple defects were due to DIC. In addition, the data further suggest that the mechanism by which this virus elicits DIC is different from bacterial sepsis since the DIC was clearly present in the absense of hypotension or shock.

The effect of toxic agents commonly ingested by children on antibacterial defenses in the lung. STEPHAINE BURLEY and GARY HUBER (Intr. by J. Klein). *Channing and Thorndike Memorial Labs, Harvard Med. Unit, Boston City Hosp., Boston, Mass.*

Kerosene ingestion, a common cause of accidental poisoning in children, is often followed by serious bacterial pulmonary infection. The effect of kerosene ingestion (10 ml/kg) on pulmonary antibacterial defense mechanisms was studied acutely (4 hr) and subacutely (24 hr) in pretreated mice exposed to an aerosol inoculum of radiotracer-tagged (^{32}P) *Staphylococcus aureus*. Intrapulmonary bacterial inactivation was determined by quantitating the change in bacterial viability and isotope clearance in the lungs of each animal. Controls inactivated 86.6 ± 1.0% of the inoculum. Kerosene ingestion resulted acutely in a depression of host defenses, with only 59.1 ± 4.5% of the inhaled bacteria cleared. In animals challenged with aerosolized bacteria 24 hours after kerosene ingestion, intrapulmonary bacterial replication exceeded inactivation and bacterial clearance did not return to normal until 96 hours after ingestion. Pulmonary histology, correlated with bacterial clearance, revealed a chemical pneumonitis, with alveolar hemorrhage, bronchial necrosis and pulmonary edema. Aspiration of the ingested kerosene increased the severity of the anatomical and functional alterations. Similar structural and functional responses were demonstrated following ingestion of other toxic agents commonly ingested by children, with acute and subacute inactivation values of 70.5 ± 3.9% and 32.2 ± 11.7% for linseed oil, 46.3 ± 5.6% and 70.4 ± 4.8% for gasoline, 73.4 ± 2.9% and 70.6 ± 5.7% for lighter fluid and 54.3 ± 6.5% and 71.3 ± 3.2% for turpentine.

The unusual severity of mycoplasmal pneumonia in children with sickle cell disease. S. T. SHULMAN, J. BARTLETT, W. CLYDE, and E. M. AYOUB. *Univ. Fla., Gainesville, Fla.; Univ. of North Carolina, Chapel Hill, N.C.*

Respiratory infection with *Mycoplasma pneumoniae* in children is uniformly considered to be mild and benign. Patients with sickle cell disease may have frequent episodes of pulmonary infection and/or infarction and are known to be unusually susceptible to pneumococcal disease including overwhelming sepsis. We recently observed 4 children (ages 4–12 years) with sickle cell disease who had pulmonary infection attended by a severe course of illness. Clinical features included diffuse pneumonia (4 patients), pleural effusion (2), prolonged febrile states (3), respiratory distress (3), moderate to marked leukocytosis (4) and pleuritic pain (3). None of these patients responded to penicillin and/or ampicillin. All 4 patients had significantly elevated cold hemagglutinin titers. *M. pneumoniae* was isolated from both patients cultured for this organism. In 3 patients serologic evidence of *M. pneumoniae* infection, as manifested by a rise in the mycoplasma complement fixation (CF) or growth inhibition (GI) titer, was obtained. One patient showed no rise in CF titer but an elevation of the GI titer. The course of this disease was of a severity rarely observed in *M. pneumoniae* infection. The reason for the unusual severity of this ordinarily benign disease in this group of patients is not clear at present but may be related to concomitant pulmonary infarction or to an underlying immune defect. In addition to pulmonary infarction and pneumococcal infection, the differential diagnosis of pulmonary disease in patients with sickle cell disease and leukocytosis must include mycoplasmal infection, especially when penicillin unresponsiveness is noted.

The EB virus infection within families of cases of infectious mononucleosis. J. H. JONCAS (Intr. by J. R. Ducharme). *Univ. of Montreal and l'Hôpital Ste-Justine, Montreal, Que., Canada.*

The incidence and rise of the EBV antibodies were measured by indirect immunofluorescence in 1033 sera from a group of 175 pediatric and older cases of infectious mononucleosis and from 344 family and social contacts. Cases of infectious mononucleosis with eleven exceptions were EBV seropositive in acute and/or convalescent sera. A rise in EBV antibodies of two dilutions or more was demonstrated in 23 of the 175 cases. The EBV antibody titres of mononucleosis sera were significantly higher than those of contacts's sera ($P < 0.01$). The incidence of these antibodies in contacts reached 35 to 67% in four different age groups. A seroconversion was demonstrated in only 9 of 110 EBV negative family contacts and a significant antibody rise encountered in only 6 additional contacts giving an attack rate of less than 15%. Interinfection or interdisease periods varied from 1 week to 2 years. The infectivity of the EB virus and its horizontal transmission seem to be as low in nature as they appear to be experimentally in the laboratory. The epidemiological behaviour of the EB virus infection suggests that its relationship to infectious mononucleosis may be analogous to that of the V-Z virus to zoster.

The ToRCH complex——perinatal infections associated with toxoplasma and rubella, cytomegol- and herpes simplex viruses. ANDRÉ J. NAHMIAS, KENNETH W. WALLS, JOHN A. STEWART, KENNETH L. HERRMANN, and WILLIAM J. FLYNT, JR. *Emory Univ. Sch. of Med., and Ctr. for Disease Control (CDC), Atlanta, Ga.*

It is difficult in most cases to differentiate clinically among perinatal infections associated with Toxoplasma (To), Rubella (R), Cytomegalovirus (C) and Herpes simplex virus, type 1 or 2 (H). To evaluate this problem, sera submitted to CDC from infants (<2 yrs.) with various abnormalities were tested for all agents in the ToRCH complex, besides those requested by the physician. Antibodies to To, R and C were measured by conventional technics, and antibodies to H type 1 and 2 by microneutralization and IgM fluorescent antibody tests. Interpretation of results were complicated by such factors as prior immunization,