5 hr at 56° in order to destroy reaginic activity led in most cases to diminished inactivation in mothers' and infants' sera, indicating that a certain amount of the antibody is reaginic in type. Absorbing the sera on anti-IgE-sepharose prior to testing confirmed that in those sera in which there were heat-labile penicillin antibodies, there were also IgE penicillin antibodies, and there was a good relationship between the amount of antibody found by the two methods. Some infants showed the presence of IgE penicillin antibodies whilst their mothers had none, indicating the fetus' ability to produce IgE antibodies. One mother had IgE penicillin antibodies while her infant had none, indicating that these antibodies did not pass through the placenta. Antibodies to DNP in a titre 25 times that of penicillin were found in all mothers and infants studied. It is concluded that the modified phage technique as an ultrasensitive method for antibody assay has advantages over other assay methods, and by using this technique we have shown that actively produced penicillin IgE antibodies may be found in newborn sera, and that IgE penicillin antibodies probably do not pass the placenta from mother to infant.

24. Skin reactivity in childhood—phytohemagglutinin(PHA) skin test and streptokinase(STK) skin test. G. R. Burgio, E. Curtoni, R. Genova and U. Magrini, *Univ. of Pavia, Italy.*

With advancing age there is a gradual increase of skin reactivity to PHA and to STK up to the youth and adult life [1, 2]. Some biopsies carried out in adolescents and adults demonstrated that the histology of both the skin reactions to STK and to PHA corresponds to that of delayed hypersensitive reactions [3].

The present investigation deals with the histology of skin reactions to STK and PHA in childhood. The following results were obtained: (*a*) in the first 2 years of life the positive reactions to STK are unusual and feeble. In this period of life the histology of the positive reactions assumes an aspecific pattern; it does not correspond to that of the delayed hypersensitive reactions. On the contrary, from the 6th to 8th year of life delayed hypersensitive reactions were obtained, comparable with those observed in adults. (*b*) As regards PHA, the reactions are always positive and many are very strong, during the 1st year of life. Nevertheless, the first small perivascular infiltrates of lymphomononuclear cell may be observed only from the 6th to 8th year of life; furthermore, this finding is much weaker than in adult life.

The results confirm the age dependency of skin reactivity and suggest the possibility of understanding why some reactive diseases have a different behavior at different ages.

1. Lancet, *ii:* 411 (1968).
2. Mschr. Kinderheilk. (in press).
3. Pathol. Eur., *4:* 138 (1969).

25. Immunological deficiency syndrome in nonidentical twins: attempts at treatment with transplantation of bone marrow and fetal thymus. H.-D. Flad, U. Genscher, G. Hochapfel, D. Krieger, E. Treppel, M. Dietrich, T. M. Fliedner, and W. Teller, *Univ. of Ulm, Germany.*

This report describes nonidentical male twins with an immune deficiency syndrome, which can not be classified into the known categories. The defect in cell-mediated immunity was characterized by lymphopenia, diminished response of lymphocytes to phytohemagglutinin (PHA) and allogeneic cells in culture, negative skin tests to various antigens, delayed rejection of a second set skin graft from a HLA-nonidentical donor. Humoral immunity was deficient in terms of diminshed production of IgG, IgA, and IgM, of isoagglutinins, and of antibody against poliovirus vaccine and tetanus toxoid. There were no plasma cells in the bone marrow. The children were kept within a sterile plastic isolator and maintained in a gnotobiotic state by antibiotic treatment from the early days of their life. In one child two thymus transplants induced a transient rise of peripheral lymphocyte count and of the response of lymphocytes to PHA. It was concluded that a humoral factor of the thymus was operative, since no cells of HLA type of the donor were found in the recipient. The second child received bone marrow cells from the mother separated in an albumin density gradient according to the method of Dicke and Van Bekkum. Fraction 3, containing 40×10^6 cells with a markedly reduced lymphocyte component was injected intravenously in this child treated before with ALG. There were no signs of secondary disease following transplantation. A transient rise of PHA response of lymphocytes, a temporarily positive skin test to DNCB, and an increased production of IgG were observed.

26. Studies on tumor-specific transplantation antigens in childhood leukemia. W. Plenert, F. Zintl, and G. Aurich, *Children's Hosp., Univ. of Jena, German Democratic Republic.*

The indirect immunfluorescence technique was applied to test vital leukemic cells (blasts from peripheral blood and bone marrow) for the existence of tumor-specific transplantation antigens on their membranes. The studies were carried out in homologous as in autologous systems. Sera gathered from leukemic children in different phases of the disease were tested for antibodies against autologous blasts in time of relapse and against homologous blasts. The sera of adult contact persons were tested for antibodies against the cells of childhood leukemia using parablasts. Antibodies were found in 11 out of 28 tested sera (11 28), monocytoid blasts (5 21), and paramyeloblasts (1 10). In relapse autoantibodies against parablasts could not be found (4 children). These are preliminary results of studies going on at the time of print.

27. Resistance mechanisms of Friend virus induced leukemia. J. M. Dupuy, O. Stutman, and R. A. Good.

Immunological resistance against Friend virus seems to be primarily mediated by antibody formation. No cell-mediated immune response against the virus was found in immunized mice. Besides immunological basis, other mechanisms play a major role in resistance and susceptibility. The possibility of a "target cell" capable of virus binding in the hematopoietic tissues of susceptible mice was studied by using a new technique. Known numbers of focus units (FFU) of Friend virus B (passaged in DBA 2 mice) were incubated with variable amounts of cells from different origins. After 30 min of incubation, the supernatant was injected intravenously in DBA/2 susceptible mice. Nine days later, the spleens were removed and the number of surface foci was counted after immersion in Bouin's fixative. The number of foci observed in these animals represents the number of FFU left in the supernatant after incubation. Controls were injected with unabsorbed virus kept for 30 min at room temperature. Using this method, we found that the Friend virus was adsorbed by spleen, bone marrow, or thymus cells of mice from susceptible strains, *e.g.*, C3H or DBA/2, but was not adsorbed by other tissues from the same strains. By contrast, when spleen or bone marrow cells from resistant strains were incubated, *e.g.*, C57BL/1, C57BL/6, C58, the virus was not adsorbed and the original number of FFU was obtained in the supernatant. These date strongly

suggest the presence of a target cell in hematopoietic tissues of susceptible mice and its absence in resistant strains.

28. Active immunotherapy as an adjunct to chemotherapy in the control of solid tumours. G. Currie. *Chester Beatty Res. Inst., Belmont, Sutton, Surrey, England.*

Active immunotherapy, used alone, is unlikely to be of value in cases of advanced malignant disease. There is evidence, however, that it may be useful in eliminating small numbers of tumour cells remaining after other forms of treatment. It was decided to test this proposal in chemically induced fibrosarcomas in mice. Various forms of active immunotherapy were tested. Nonspecific stimulation of the immune response with *Corynebacterium parvum* gave the most promising results. This was then combined in various regimens with chemotherapy. Combining cyclophosphamide with subsequent *C. parvum*, 12 days later, produced a significant number of complete and lasting regressions. The results are discussed with reference to the use of nonspecific stimulants of the immune response in man.

29. Glomerulonephritis associated with infected ventriculo-atrial shunt. Immunohistochemical examinations. H. J. Pleiss, W. H. Hitzig, and U. G. Stauffer. *Univ. of Zürich, Switzerland.*

Infectious complications in children with ventriculoatrial shunt are common. About one-half of these patients show alterations in the kidneys, usually degenerative changes, occasionally infectious microemboli. A newly recognized manifestation is diffuse glomerulonephritis. Recently we observed a 3 6/12-year-old boy who, 3 years after implantation of a shunt, developed severe signs of nephrotic syndrome. Blood cultures were repeatedly negative, but from the CSF of the valve *Staphylococcus albus* could be cultured. An open kidney biopsy showed severe subacute glomerulonephritis. The kidney disease improved after removal of the shunt. Immunohistochemical examination of the renal biopsy with Coons' indirect method demonstrated distinct precipitates in the glomeruli, containing IgM, IgG, and complement, but no IgA. However, no bacteria could be cultivated. A few cases reported so far presented identical findings. The kidney disease therefore seems to be caused by an immunological reaction of the body towards toxins produced by the low grade pathogens infecting the artificial surface of the shunt.

30. Capsular antibodies to *Escherichia coli* in relation to urinary tract infections (UTI). B. Kaijser, R. Borssén, L. Å. Hanson, J. Holmgren, and U. Jodal. *Inst. of Med. Microbiol. and Univ. of Göteborg, Göteborg, Sweden.*

Antibodies to the O antigen of infecting *Escherichia coli* strains have been studied in children with UTI. No relation between levels of O antibodies and protection against UTI has yet been ascertained in humans. We wanted to study the appearance and possible significance of capsular antibodies.

By direct bacterial agglutination with appropriate controls antibodies to K antigens could be demonstrated in a few patients with UTI. For further investigation a few well characterized K antigens of the acid polysaccharide type were isolated from *E. coli* strains by preparative zone electrophoresis. These antigens were employed to study with the passive hemagglutination technique the K antibody response in rabbits immunized with *E. coli*. A marked K and O antibody response mainly consisting of reduction sensitive 19 S antibodies was observed after a single injection of bacteria. After a booster dose a secondary type response including increased titres of 7 S as well as 19 S antibodies was obtained against both K and O antigens. The protective effect of these rabbit antibodies was evaluated in mouse protection experiments employing for challenge the homologous *E. coli* strain as well as two serologically related strains. These experiments illustrated the serological specificity of protective antibodies. The obtained data may help in the evaluation of the possible significance of the K antibodies appearing in patients with UTI.

31. Neurological maturation in small for date infants. O. Finnström. *University Hosp., Umeå, Sweden.*

Sixty newborn infants were selected for the present study according to the following criteria. (*1*) Twenty small for date infants (birth weight below −2 SD according to Swedish standards) without major anomalies or pathological neurological signs. (*2*) For each small for date infant, one full term infant with normal birth weight and of equal gestational age was selected, 20 infants in all. Their mean gestational age was the same as that of the small for date infants. (*3*) For each small for date infant, one preterm infant with the same birth weight, appropriate for the gestational age, was selected, 20 infants in all. Their mean birth weight was the same as that of the small for date infants.

All infants were examined neurologically, mainly using the technique of the French school. Thirty neurological signs were used. A neurological score was calculated for each infant.

The mean neurological score for the small for date infants was significantly lower than that for the full term infants of normal birth weight. The difference corresponds to a gestational age difference of 10 days. The mean neurological score for the preterm infants was significantly lower than that for the small for date infants. The finding of delayed neurological maturation in small for date infants is at variance with reports from the French authors. It is also at variance with our own results of motor conduction velocity studies in the same infants. Motor conduction velocity was not significantly reduced in small for date infants.

32. Maternal toxemia, fetal malnutrition, neonatal hypoglycemia and nervous activity of the newborn. F. J. Schulte, G. Schrempf, and G. Hinze. *Univ. of Göttingen, Germany.*

Twenty-one small for date newborn infants of toxemic mothers were compared as to their neurological maturation with an equal number of normal neonates matched for both age from conception and from birth. The following parameters were studied: nerve conduction velocity (degree of myelinization), EEG sleep patterns including their computer analysis (development of the cerebral cortex), sleep cycles (behavioral maturation) and electromyographic evaluation of motor activity (excitatory state of spinal motoneurones). Even in severely malnourished infants peripheral nerve myelinization was found to be normal for age whereas the EEG sleep pattern development was sometimes remarkably retarded and/or abnormal. In severely abnormal infants the development of bioelectrical coherence, *i.e.*, a linear correlation of activity between corresponding cortical areas, was markedly disturbed. The spinal motoneurone excitability was found to be lower than normal with a greater variance. The abnormal neurophysiological findings were related to the severity of the maternal nephropathy but no significant correlation could be detected to postnatal blood glucose values of the infants.

33. Later head circumference of infants weighing 1,500 g and less at birth. P. A. Davies. *Hammersmith Hosp., London, England.*

Previous follow-up surveys of low birth weight infants have shown increasing neurological and intellectual handicaps with