enzyme and cystathionine synthase were present. None of these enzymes of transsulfuration was present in the placenta. Thus cyst(e)ine may be an essential amino acid in the immature human until sometime after birth. A single full term infant who died at 7 hr had 7% of normal cystathionase activity in the liver. Amino acid analyses of simultaneously obtained maternal and fetal blood, amniotic fluid, placenta, fetal liver, and fetal brain were performed. No consistent trends were noted during the period studied. However, the fetal-maternal ratio of all plasma amino acid concentrations at time of abortion was high (as at term). The highest ratio, by far, was that of cystine. In some cases, cystine was not measurable in the blood of the mother. Furthermore, in contrast to the mature human, cystathionine, the substrate for cystathionase, was *higher* in fetal liver than in fetal brain. In spite of this accumulation of cystathionine in fetal liver, there was none measurable in fetal or maternal blood nor in amniotic fluid. These studies suggest that the human fetus is entirely dependent on a maternal source of cyst(e)ine and that prematures and perhaps even full term newly born infants are dependent upon dietary sources of cyst(e)ine. Human milk is a high cyst(e)ine, low protein formula, whereas cow's milk is a low cyst(e)ine, high protein formula. Thus, these studies suggest that premature infants fed a high protein cow's milk formula retain more nitrogen and grow faster than infants fed a cow's milk formula containing lower amounts of protein, closer to that found in human milk, because the amount of cyst(e)ine, rather than total nitrogen, may be a limiting factor for protein synthesis. These results may also afford an enzymatic explanation for the transient hypermethioninemia seen in infants on high protein diets.

20. a_1-Fetoprotein, an index of maturation? R. Lardinois, D. Anagnostakis, and M. Ortiz. *Centre de Recherches Biologiques Neonatales, Paris, France.*

It is known that in the human conceptus, serum a_1-fetoprotein reaches a maximal concentration at approximately 13 weeks, then decreases and disappears 1 or 2 weeks after birth. In the first step of this work, the existence of a_1-fetoprotein has been studied in the serum of three groups of neonates (premature, full term, and small for date). Electrophoresis on polyacrylamide gels and immunoelectrophoresis with a specific antibody against human a_1-fetoprotein have been chosen: since they have a different degree of sensitivity, they can be used as a semiquantitative test. At birth, small for date infants have no a_1-fetoprotein or a very low concentration; the concentration is higher in full term babies and still higher in prematures. These observations suggest that a distinction between small for date and premature babies is possible by such a procedure. In the second step of this study, Mancini's immunochemical method for a_1-fetoprotein quantitative estimation is in process in order to see, especially in premature babies, whether serum a_1-fetoprotein concentration at birth is directly related to the length of gestation. If so, we shall have a simple biological test for the assessment of the gestational age of newborn infants.

21. Effects of varying severity of growth retardation on organ weight and cell population in fetal rats. J. S. Wigglesworth. *Hammersmith Hosp., London, England.*

Recent experimental studies have shown that a growth-retarding stress applied early in life results in diminished cell populations of all organs whereas a similar stress applied later on causes reduction predominately in cell size. The object of the present study was to determine the effects on cell size and population of organs of varying the severity of stress at a single time interval in pregnancy. Unilateral uterine ischemia was induced surgically in rats on the 17th day of pregnancy to produce a range of fetuses with birth weight reduced by up to 45% of the values for fetuses from the control uterine horns. Cell size and populations at term were estimated from the figures for organ weight and total DNA. A close correlation was shown between the severity of growth retardation and the degree of reduction in organ weight and cell population although the size of the effect varied for different organs. Reduction in fetal weight by 45% reduced liver weight by 60% and liver cell population by 50%, whereas brain weight was reduced by only 20% with a 12% reduction in cell population. No consistent change was seen in weight or cell population of the placenta. It is concluded that for a growth-retarding stress acting at a single time interval in pregnancy the reduction in cell size and populations of different internal organs is directly related to the reduction in birth weight.

22. IgA deficiency—hereditary aspects. P. Pelkonen and E. Savilahti. *Children's Hosp., Univ. of Helsinki, Finland.*

Familial cases of selective immunoglobulin A deficiency have been documented, but the mode of inheritance remains unsettled. The propositus of the present study, a 9-year-old girl with a past history of frequent upper respiratory tract infections, had an unusually low serum IgA level, between 0.5 and 2.0 mg/100 ml (*i.e.*, IgA detectable by double diffusion but not by the radial immunodiffusion technique). The mother of the patient showed a total lack of serum IgA and suffered from chronic urinary tract infection. The father and brother of the propositus and the maternal relatives tested had normal IgA levels. Both patients had normal karyotypes. In the propositus, IgA was detected in saliva and intestinal juice, but IgM was present in higher concentrations in these secretions. Direct immunofluorescent studies of both rectal and small intestinal mucosa revealed IgA-containing cells, but IgM-containing cells were predominant. In the mother, no IgA was detectable in whole saliva concentrated 20 times, and the rectal mucosa was completely devoid of IgA-containing cells, whereas IgM-containing cells were abundant. These findings suggest that IgA deficiency may differ in degree of severity. The daughter in this family could be heterozygous for a recessive trait, while the mother is homozygous. On the other hand, an autosomal dominant mode of transmission with variable gene expressivity cannot be ruled out.

23. Penicillin and dinitrophenyl antibodies in newborns and mothers detected with chemically modified bacteriophage. S. Levin, Y. Altman, and M. Sela. *Kaplan Hosp. and The Weizman Inst. of Sci., Rehovot, Israel.*

The development of newer, highly sensitive techniques for the detection of small amounts of antibodies opens new fields for investigation. The immunospecific inactivation of chemically modified bacteriophages by antibodies directed toward the attached hapten or protein allows for the detection of as little as 0.2–2.0 ng antibody/ml. Likewise, minute amounts of hapten or protein may be detected and measured by their ability to inhibit the inactivation of the chemically modified bacteriophage by the antihapten or antiprotein antibodies. We have studied the presence of penicillin and DNP antibodies in the sera of newborn infants and their mothers by the use of penicilloylated and dinitrophenylated-T4-bacteriophage. In almost every paired sera studied, evidence was found for the presence of penicillin antibodies. Premixing the sera with penicillin eliminated the penicillin-T4-phage inactivation. Preheating the diluted sera for

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. Aubrich. *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