affect the frequency of ahaptoglobinemia, a finding which argues against an isoimmune process as the cause of this condition in the newborn. Finally, no association was found between the frequency of ahaptoglobinemia and the ABO or Rh (D) phenotypes of the infants. These data permit us to tentatively conclude that the frequency of ahaptoglobinemia in the newborn is stable in various populations. Moreover, the data support the contention that ahaptoglobinemia of the newborn represents impaired or absent synthesis of functional haptoglobin. (SPR)

26 *Deletion of Chromosome No. 18 (Long Arm). A New Syndrome.* WLADIMIR WERTELECKI*, ANNE M. SCHINDLER* and PARK S. GERALD, Children's Hospital Medical Center, Boston, Mass.

Four unrelated examples of partial deletion of the long arm of chromosome No. 18 have been briefly reported by us (Lancet *ii:* 641 [1966]). These patients have now been studied in detail.

The typical features of this syndrome are mental retardation, short stature, impaired hearing with atretic or narrow ear canals, prominent antihelix, mild microcephaly, typical facies manifested by prominent forehead—perioral areas and deep set eyes, proximal implantation of the thumbs, increased number of whorl fingerprint patterns, hypotonia, vertical tali, fundoscopic anomalies and asymptomatic congenital heart anomalies.

Relatives of three of the patients had normal chromosomes. The father and two siblings of the fourth patient had one metacentric No. 18, interpreted as a pericentric inversion. The deletion in this last patient probably arose by a crossover in the father between the metacentric and the normal No. 18 ('aneusomy by recombination').

These four patients represent partial monosomy No. 18 but nonetheless the findings are not obviously the antithesis of the trisomy 18 syndrome.

The retardation and morbidity associated with this chromosome disorder are less severe than those found with the usual autosomal trisomies. Since survival does not seem to be affected by this disorder, these patients will likely be found among older children. (SPR)

27 *Abnormal Organ and Cellular Growth with Various Chromosomal Disorders.* RICHARD L. NAEYE*, Univ. Vermont, Coll. of Med., Burlington, Vt. (introduced by Jerold Lucey).

It is known that newborns with a variety of chromosomal disorders are subnormal in weight for gestational age at birth but their growth disturbance has received little attention, major consideration having been directed toward the characteristic organ and body malformations. The present study was designed to explore the prenatal growth disturbance in such infants. Using line sampling, planimetry and other quantitative, histologic methods, this intrauterine growth disturbance was found due to a subnormal number of cells in many body organs in six neonates with trisomy D_1, eight with trisomy E and 21 newborn mongoloid infants. Each of the three trisomic disorders appears to have a rather characteristic growth pattern in individual organs. The spleen, kidneys, and adrenals are relatively enlarged in infants with trisomy D_1, a pattern not found in neonates with a wide variety of other disorders associated with intrauterine growth retardation. Newborns with trisomy E have relatively large hearts while spleen, adrenals, and thymus are small for body weight. Newborn mongoloid infants have relatively large hearts and spleens while their livers, kidneys, adrenals and thymus glands are small for body weight. Disparate growth of individual cell lines in the various organs is responsible for these abnormalities in growth. Both a slowed rate of cell multiplication and a shortened lifespan of some cells may contribute to the growth disorders. (SPR)

28 *Long-term Administration of 5-Hydroxytryptophan in Down's Syndrome.* MARY BAZELON*, RICHMOND S. PAINE* and VALERIE COWIE*, Children's Hospital of the D.C., Washington D.C., and Medical Research Council Psychiatric Genetics Unit, London, England (introduced by Robert H. Parrott).

Patients with trisomy-21 Down's syndrome have been demonstrated to have a depression of whole blood 5-hydroxytryptamine (serotonin) (5HT). In older mongol children 5HT levels are usually around 50 % of normal while in the newborn a wide variation of levels from normal to as low as 10 % can be demonstrated. Fourteen hypotonic babies with trisomy-21 have been given 5-hydroxytryptophan (5HTP) in an attempt to raise the whole blood 5HT. Oral 5HTP was begun in early infancy and has been continued since then in each patient. The level of 5HT in whole blood and 5-hydroxyindoleacetic acid (5HIAA) in the urine was monitored. Serial neurological examinations were recorded by motion picture and on forms identical with those of the M.R.C. Psychiatric Genetic Unit's study of 73 trisomic mongols (all those ascertained within one geographical area in a year).

In all patients, after an initial period of fluctuation, the level of whole blood 5HT was maintained at normal or near-normal values and 5HIAA in the urine rose to high- or above-normal values. Following an increase in whole blood 5HT levels, an improvement in muscular tone was noted, often within 24 hours (motion picture demonstration). This improvement was consistently demonstrated compared to the M.R.C. group. No child has remained severely hypotonic. The effects of overdosage are projectile vomiting, diarrhea, opisthotonos and rigidity, motor restlessness and hypertension. Turning over at an earlier age than normal appears to be due to a combination of rigidity and motor restlessness. It can be stopped by reducing the dose. The children in this series are too young for any statement to be made about developmental milestones. No implications as to intelligence are warranted. (APS)

29 *The Distribution of Chromosome Aberrations in Time: Chromosome Studies in Newborn and Spontaneous Abortion Populations.* E. PERGAMENT* and T. KADOTANI*, Dept. of Pediatrics, Michael Reese Hosp., Chicago Med. School, Chicago, Ill. (introduced by J. Metcoff).

In a 36 month period involving 9000 newborns, three clusterings of autosomal chromosomal trisomies were recognized. Using the last menstrual period for estimating time of conception, the first cluster extended from October through December, 1963, and included 3 cases; the second cluster, June and July, 1964, 3 cases; and the third cluster, December, 1964 through June 1965, 5 cases. In the remaining 24 months, only 2 other cases were observed. Retrospective studies for the first cluster revealed: 1. 8 additional trisomies in nearby Chicago hospitals; 2. a significant increase in the number of stillbirths and conceptions that expired with

congenital malformations at Michael Reese Hospital; 3. a similar clustering of chromosome abnormalities in newborns in Denver, Colorado (PUCK and ROBINSON, Science [1965]) and in spontaneous abortions in London, Ontario (CARR, personal communication). For the second cluster there was a corresponding increase in the abortion population in Canada. There was no statistically significant increase in the reported incidence of 9 infectious diseases including rubella or infectious hepatitis, relative to the three clusterings defined in the newborn population. Prospective studies on the distribution of chromosome aberration in time have been conducted since November, 1964, and reveals that when the spontaneous abortion and newborn populations are considered as one conceptual population, the distribution of chromosome aberrations in time appears random. These findings indicate that either the factors responsible for nonrandom distribution of chromosome aberrations were not operating during the time period covered or that onrandom distribution of chromosome aberrations does not occur in the human population. (APS)

30 *Chromosomes of Couples with Repeated Spontaneous Abortions.* R.J. MCKAY, Jr., W.E. HODGKIN* and E.H. WITTE*, University of Vermont College of Medicine, Burlington, Vt.

Because a 20–25 % incidence of chromosomal abnormalities has been reported among spontaneously aborted fetuses, it was decided to study the chromosomes of couples who have had 3 or more spontaneous abortions. Using a commercial kit method for culturing peripheral blood leukocytes, approximately 750–1000 metaphases were scanned in each patient in order to obtain 50 satisfactory for counting. For each patient, all metaphases with abnormal counts and 5 with normal counts were photographed and karyotypes made. Among 4 couples with repeated abortions and one or more children with multiple anomalies, 2 husbands showed a balanced translocation in all metaphases studied. Among the other 38 couples studied a number showed abnormalities in a few cells (trisomy, partial trisomy, balanced and unbalanced translocations, fragments, dicentrics, endoreduplication, tetraploidy, XO, long-armed Y, quadriradials and triradials). Partially trisomic cells were seen approximately 5 times as frequently among the women as among the men, and 6 patients were observed to have a single metaphase with a quadriradial chromosome. (APS)

31 *The 'Impotent Neutrophil' Syndrome.* L.L. KAHLE.* H- MORENO*, and E. KAUDER*, Dept. of Pediat. Univ. of Cincinnati, Cincinnati, O. (introduced by A.M. Mauer).

Leukocyte function was studied in a 2–2,5-year-old Negro male with the history of repeated abscesses, cervical and inguinal adenitis, recurrent pneumonia, seborrheic eczema of the scalp, hepatosplenomegaly and anemia. An appropriate leukocytosis with neutrophilia occurred with each infection, absolute neutrophil counts ranging from 3,900 to 24,500/mm^3. IgG, IgA and IgM globulins were present in increased amounts. Lymph node biopsy contained caseating granuloma. Skin tests and cultures for all types of acid fast bacilli and fungi were repeatedly negative. These findings are characteristic of the syndrome of chronic granulomatous disease of childhood. There was a normal flux of leukocytes into Rebuck skin windows and exudate fluid. Leukocytes appeared normal with alkaline phosphatase, peroxidase and Wright's stain and were normally vacuolated after bacterial phagocytosis. Normal leukocyte motility and phagocytosis followed by degranulation were seen with phase microscopy. Decreased bactericidal activity of the patient's leukocytes during in vitro incubation with Staphylococcus aureus and Aerobacter aerogenes was repeatedly demonstrated in the presence of the patient's serum or normal serum. To determine the nature of this defect a citric acid extract of the patient's leukocyte granules was compared with control specimens and decreased bactericidal activity was found. The deficient or abnormal phagocytin activity of the patient's leukocytes, demonstrated by this study, could account for his clinical syndrome. (SPR)

32 *Defective Lymphocyte Response to PHA in Congenital Rubella.* J.R. MONTGOMERY*, M.A. SOUTH*, W.E. RAWLS* and J.L. MELNICK*, Depts. of Ped., Med., and Virology, Baylor Univ. College of Med.; and G.B. OLSEN*, P.B. DENT*, and R.A. GOOD: Ped. Res. Labs., Variety Club Heart Hospital, U. of Minn., Minneapolis, Minn. (introduced by Martha D. Yow).

Persistent viral carrier state in congenital rubella remains an enigma. Defective cellular immune mechanisms may play a role in this persistence. To investigate this possibility the response of leukocytes to phytohemagglutinin (PHA) was studied. 2×10^6 peripheral leukocytes were cultured in routine media. PHA was added to achieve a concentration of 0.025 ml/ml of media. Quadruplicate cultures were incubated at 37° C for 72 h and treated with C^{14} labeled thymidine for 5 h prior to termination. Cellular response was estimated by measuring the cellular content of C^{14} in a standard liquid scintillation system. A decreased PHA responsiveness of leukocytes was demonstrated in 8 of 14 congenital rubella patients studied, despite evidence in these patients of normal delayed hypersensitivity. PHA response returned to normal later in the course of each patient. To test whether this lack of responsiveness is due to an intrinsic defect in lymphoid cells from these patients or to direct effects of rubella virus, a normal adult's leukocytes were cultured with rubella virus. PHA response was dramatically reduced in every experiment; this effect could be eliminated by pretreatment of the virus preparation with rubella neutralizing antibody. Inhibition was also produced when Newcastle disease virus was substituted for rubella virus. These studies indicate that leukocytes from some congenital rubella patients show a defective response to PHA. The defective response can be reproduced in normal leukocytes by the addition of rubella virus or Newcastle disease virus *in vitro*. The prolonged persistence of virus and the defective reactivity to PHA in babies with congenital rubella may be interrelated. (SPR)

33 *A Mitotic Inhibitor Produced by Rubella Virus Infection of Human Fibroblasts.* STANLEY A. PLOTKIN, Wistar Institute and Department of Pediatrics, University of Pennsylvania, Philadelphia, Pa.

When infected with rubella virus, many human diploid fibroblast cell strains show mild to marked degrees of mitotic inhibition (PLOTKIN *et al.*: Amer. J. Epidem. *81:* 71 [1965]); cell strains derived from infected fetuses divide more slowly than normal (RAWLS and MELNICK: J. exp. Med. *123:* 795 [1966]); and infants congenitally infected with rubella show mitotic