

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. I. PLÜSS, 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. KÄLSJER, 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 myelination), 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 motoneurons). Even in severely malnourished infants peripheral nerve myelination 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

decreasing birth weight; and there is a known correlation between head circumference and cellular growth of the brain in early life. Over one hundred surviving infants of birth weights 1500 g and less cared for at Hammersmith Hospital between 1961-1968 inclusive have been studied. Approximately one third had birth weights below the 10th percentile for their gestational age. At later follow-up, significantly more of these small for date children were found to have head circumferences below the 10th percentile than those whose birth weight was appropriate for gestation. In the years 1965-1968, fewer children of the latter group had head circumferences below the 10th percentile than in the years 1961-1964. The incidence of neurological abnormality among them was lower, and it is concluded that their brain growth may have been more satisfactory.

34. Long lasting effects of intrauterine undernutrition. A comparative study of twins of dissimilar birth weight. L. HÖHNAUFER. *Univ. Kinderklinik, Innsbruck, Austria.*

Among 26,138 consecutive births (1952-1965) 30 twin pairs were found which matched the criterias: (1) difference in birth weight 300 g or more, (2) identical sex, (3) gestational age 36 weeks or more, (4) no gross abnormalities. Voluntary breast milk intake at day 5 was 73.5 ± 14.7 in the stunted twin vs 62.3 ± 14.1 in the larger one (mean \pm sd, P 0.01). Twenty of them could be reexamined (9 identical, 11 dizygous) at a mean age $8\frac{1}{2}$ yrs (range: $4\frac{1}{2}$ to $17\frac{1}{2}$). Physical "catch up" (height and weight) had occurred in 10 pairs at a mean age of $3\frac{1}{2}$ years. The following differences were found:

Stunted twin	Inferior	Equal	Superior	N	P†
Head circumference	17	0	3	20	0.01
Arm circumference	15	0	5	20	0.05
IQ (Krauer)	16	(1)	1	17	0.001
School achievement	9	(1)	0	9	0.05
First free walking	11	(8)	1	12	0.01

†Sign test for comparison of pairs.

Intellectual performance at home as judged by the mother was equal in 10 but inferior in 10 stunted twins ($P = 0.01$). In all 7 pairs aged 11 years or more a disadvantage of the formerly smaller one was evident.

Growth retardation at birth was significantly correlated with suboptimal performances later in life. Since genetic and environmental differences between test and control subjects are practically excluded, the handicaps are ascribed to the prenatal undernutrition. The nutritional deficit is emphasized by the neonatal drinking behavior.

35. Respiratory reflexes in the newly born. G. BODEGÅRD and G. H. SCHWIELER. *St. Görans Hosp. and Karolinska Inst., Stockholm, Sweden.*

The Hering-Breuer inflation reflex (H.B.i.r.) and the thoracic respiratory reflex (th.r.r.) have been studied in 17 babies of different postmenstrual ages ($30\frac{1}{2}$ to 13 weeks). Pronounced development of the strength of the reflexes have been found indicating the existence of differences in the mechanoreceptor regulation of the breathing between infants of this maturity level and adults.

The H.B.i.r. was studied by tidal volume inflation obtained by occluding the airways at the height of an inspiration. The strength of the reflex was assessed by relating the relative increase of the length of the breathing cycle to the transpulmonary

pressure at the moment of occlusion (thus the pressure which simultaneously stimulates the pulmonary stretch receptors). The reflex was found to be very weak at a postmenstrual age of 32 weeks. It increased to a maximum strength at a postmenstrual age of 36 to 38 weeks. Later on there was a decline of the strength of the reflex.

The th.r.r. was studied as the reflex respiratory response to an added respiratory load and recorded as the change in amplitude of the intrasophageal (=intrapleural) pressure swings caused by airway occlusion. It has earlier been shown in adults that an increase of the respiratory load leads to an increased power generation of the respiratory muscles reflected as an increasing amplitude of the intrapleural pressure swings. In the babies studied the response to an increased respiratory load was found to increase gradually with increasing postmenstrual age indicating increasing maturation of the thoracic respiratory reflex system.

In some babies estimations both of the strength of the H.B.i.r. and the th.r.r. were made at repeated occasions and the same principal development of the reflexes was seen in the single baby as was seen from cross-sectional data in all the infants studied.

Furthermore there was found a dip in the development of the th.r.r. at the time when the H.B.i.r. reaches its maximum which might indicate some kind of competition between the two reflex systems. Such a competitive interaction could also explain why the H.B.i.r. decreases in strength after 38 weeks of age when the th.r.r. continues to increase in strength.

36. Respiratory patterns in newborn infants related to postconceptive age (fetal age + neonatal age). U. SELSTAM and T. OLSSON. *Univ. of Göteborg, and Chalmers Univ. of Technol., Göteborg, Sweden.*

The aim of this paper is to present a method of analyzing respiratory patterns in newborn infants and to present variations of respiration related to postconceptive age, i.e., fetal age + neonatal age. The equipment consists of a tetrapolar impedance plethysmograph with an alarm unit, a Mingograph 81 (Elema-Schönander), and a computer (PDP 12). The respiratory movements are detected from variations in the transthoracic impedance signal. The time intervals between adjacent detections of respiration are recorded in the memory of the computer, programmed for a time interval histogram analysis. Different parameters in the program are clinically estimated. The infants are studied during sleep, shortly after feeding. Other factors influencing respiration, for example, surrounding temperature, light, and background sound, are kept as constant as possible. Data are treated statistically.

With increasing age there is a decrease in the mean frequency of respiration and a decrease in the frequency of periodic breathing and apneic episodes. The top of the histogram, i.e., the most frequent frequency of respiration, increases. When the periodic breathing, which usually is very regular, ceases, there is a period of rather irregular breathing, again followed by increasing regularity of respiration.

37. Alveolar and capillary permeability in the lung of the fetal lamb. I. C. S. NORMAND, R. E. OLVER, E. O. R. REYNOLDS, and L. B. STRANG.

Radioisotope-labeled, metabolically inactive molecules of varying radii (2-13 Å) were used as probes to investigate the permeability properties of the internal cellular lining of the lung in exteriorized fetal lambs (mean gestational age of the two groups: 127 and 140 days). By placing the isotopes in the blood or lung liquid compartments and serially collecting samples of blood,