

- 103 *Plasma Adrenocorticosteroid Levels During Experimental Infections.* STANFORD B. FRIEDMAN, LOWELL A. GLASGOW and LEE J. GROTA, Univ. of Rochester Sch. of Med., Rochester, NY.

Adrenocortical function during infection has not been well defined in man, and patient care itself may interfere with meaningful steroid measurements. Animal models provided the opportunity to relate plasma adrenocorticosteroid (corticosterone - CS) levels to the natural course of fatal infections in mice inoculated IP with (1) a malarial parasite—*P. berghei*, (2) a bacteria—*D. pneumoniae*, or (3) 2 strains of a murine enterovirus—encephalomyocarditis (EMC) virus. In *P. berghei* infection animals survived through day 6, and CS levels increased 4- to 6-fold on day 5 and 6. Enlargement of the spleen and parasitemia precedes this rise in CS by 24 h. In the more acute infection with *D. pneumoniae* (deaths occurred within 72 h) increases in CS levels of a similar magnitude were found at both the 'peak' and 'trough' of the adrenocortical rhythm. CS levels and virus titers were determined in individual animals infected with one LD₅₀ of EMC virus, and correlated with the outcome of infection. Modest elevations of CS occurred only during the terminal phases of infection. Elevation of CS did not occur during the viremic phase, and were observed only after clearance of virus from the blood. A more virulent strain of EMC virus which was lethal in 48-72 h resulted in marked elevation of CS by 24-48 h.

- 104 *Leukocyte Maturation: G-6-PD Activity and NBT Dye Reduction.* JOSEPH A. BELLANTI, BRIGITTE E. CANTZ, MEI C. YANG, HORST VON THADDEN and ROBERT J. SCHLEGEL, Georgetown Univ. Sch. of Med. and Stanford Univ. Sch. of Med.

Evidence was presented at these meetings last year that human leukocyte G-6-PD activity decayed at significantly greater rates in newborns than in adults. Quantitative NBT dye reduction was correspondingly low provided collection, incubation and measurement times were carefully controlled. The present studies reflect longitudinal maturation of these functions as shown in the table.

| Age | New-born | 1-2 mos. | 6-12 mos. | 12-18 mos. |
|----------------------------------|-------------|------------|-------------|------------|
| No. tested | 20 | 11 | 16 | 11 |
| NBT (mean ΔOD) | 0.125 | 0.092 | 0.097 | 0.119 |
| No. tested | 9 | 6 | 5 | 6 |
| G-6-PD (mean) (μmoles/g protein) | 78 | 27 | 9.7 | 55 |
| Age | 1.5-4 years | 4-10 years | 10-14 years | Adults |
| No. tested | 18 | 19 | 8 | 18 |
| NBT (mean ΔOD) | 0.144 | 0.139 | 0.175 | 0.206 |
| No. tested | 15 | 14 | 6 | 24 |
| G-6-PD (mean) (μmoles/g protein) | 56 | 98 | 148 | 141 |

These results show a fall in both G-6-PD activity and NBT dye reduction during early months of life followed by a continuous increase with maturation. In contrast, levels of 6-PGD activity remain constant. Lability of G-6-PD and diminished NBT dye reduction are also present in chronic granulomatous disease, an immune deficiency disorder associated with defective bactericidal activity of leukocytes [BELLANTI *et al.*, *Pediat. Res.* 1970]. These findings offer an explanation for the increase in resistance known to occur with age.

- 105 *Zoster Immune Globulin.* P. A. BRUNELL, A. ROSS, L. MILLER, M. COHEN and A. SCHMERLER, NYU Sch. of Med. and Meadowbrook Hosp.

It has been reported that susceptible children were protected against varicella if they received two ml of zoster immune globulin (ZIG) within 72 h following household exposure. In a double blind study to determine the minimum *modifying* dose of ZIG, 0.5 ml of either ZIG or immune serum globulin (ISG) was given to exposed household contacts. It was found that the four children who received ISG developed 161, 285, 286 and 407 vesicles while the children who received ZIG had 0, 2, 4 and 4 vesicles. All seven children who developed vesicles had rises in complement-fixing (CF) antibody. The ZIG which was used in these studies was prepared from plasma of pretested convalescent zoster donors who had CF antibody titers of 1:256 or greater. Pretesting of donors was eliminated subsequently in order to expedite the production of ZIG. Although plasma was obtained when highest antibody titers were expected, only 20 of 35 plasma collections had CF titers high enough (≥1:128) to be used for ZIG preparation. The dose of this and subsequent lots of ZIG will be estimated by comparing their antibody content with that of the reference lot for which the minimum protective dose was determined in these studies.

- 106 *Growth in Agarose of Human Cells Infected With Cytomegalovirus.* DAVID J. LANG and LUC MONTAGNIER, Duke Univ. Med. Center, Dept. of Ped., Durham, N.C. and Institut du Radium Biologie, Orsay, France.

Cultured cells transformed by certain DNA and RNA viruses develop the ability to multiply when suspended in a medium gelled with agarose. Normal fibroblasts obtained from human diploid lines do not grow in agarose medium but will do so after being transformed by Rous sarcoma virus. We report here that after infection by human cytomegalovirus (CMV) human diploid fibroblasts acquire the capacity to grow in agarose medium for several generations. Clones of infected cells grew for weeks although in every case they ultimately underwent lysis, apparently related to persistent replication of virus. Virus was inoculated at very low multiplicities (high dilution) in an effort to select non-infectious defective virions still capable of inducing cell stimulation. Viral suspensions were also irradiated (UV-CMV) to preferentially suppress infectivity. Dilute or irradiated virus yielded similar colonies of replicating cells although permanent transformation was not achieved. One clone derived from UV-CMV infected cells was passaged four times before undergoing lysis. During these passages the cells exhibited alterations in morphology and orientation. Our inability to obtain permanently transformed cells after inoculation with irradiated or diluted CMV may be due to complementation or the failure of the CMV DNA to achieve integration with the cellular genome. If permanent cellular transformation by human CMV is achieved in subsequent experiments, it will still remain to demonstrate whether this phenomenon bears any relationship to neoplasia in man. It is of interest that CMV is taxonomically related to EB and Herpes simplex type 2 viruses which have been associated with human cancer.

- 107 *Sex and Susceptibility.* SUMNER BERKOVICH, State Univ. of New York, Downstate Med. Center, Dept. of Ped., Brooklyn, NY.