In our study of the ecology and significance of the normal bacterial flora of the human pharynx we have noted in the cultures of 4 individuals an organism which elaborates a substance(s) producing wide clear zones in agar overlays containing staphylococci. Growth of the organism, a slow growing coccus (or coccobacillus), is inhibited *in vitro* by some ingredients of normal flora. The organism, which is sensitive to commonly used antibiotics such as penicillin, coexists in the pharynx with its inhibitors and with staphylococci and may play a role in maintaining the normal interrelationships between species. The antistaphylococcal substance(s) produced by it is filterable, heat stable and has a limited antibacterial spectrum. All staphylococci tested, including those resistant to methicillin, are highly sensitive (1/400 to 1/800 dilution of an autoclaved broth supernatant incorporated in blood agar). Using the same preparation, enterococci are moderately sensitive (1/50 dil) and all other species examined are either weakly sensitive (1/10–1/25 dil) (Group B and C β -hemolytic streptococci, *N. catarrhalis* and some viridans streptococci) or resistant (Group A, β -streptococci, some viridans streptococci, other *Neisseria* and all gram-negative bacilli tested including *H. influenzae*). The antibacterial agent is bactericidal for staphylococci; persisters remain sensitive. No resistant mutants have been selected. The antibacterial capacity for the staphylococcus is not destroyed by exposure to trypsin, chymotrypsin or peptidase, or a range of pH from 9.4 to 4.3. This organism may play a significant ecological role in the pharynx; its antistaphylococcal substance is potentially useful.

- 112 *Local Infection and Bacteremia from Scalp Vein Needles and Polyethylene Catheters.* GEORGES PETER, FREDERICK H. LOVEJOY, Jr. and JOHN D. LLOYD-STILL, The Children's Hosp. Med. Center, Boston, Mass. (introduced by David H. Smith).

The risk of infectious complications is generally assumed to be less frequent with intravenous infusions given via scalp vein needles (SVN) than those administered by polyethylene catheters (PCT). To assess this assumption, the incidence of bacteremia and local infection (positive needle/catheter tip culture) from SVN and PCT was prospectively studied on 2 general medical wards. Bacteremia occurred only with PCT (2/25, 8%). The overall incidence of local infection with SVN (12/142, 8.5%) was significantly less ($p = 0.06$) than that with PCT (6/25, 24%). Although the incidence of SVN local infection increased with the duration of use, up to 120 h it was clearly lower than that with PCT in this study and previous reports. After 120 h of use, the incidence of local infection was similar in both groups (SVN, 3/11 vs. PCT, 4/14). However, pathogenic bacteria were recovered significantly less frequently and non-pathogenic bacteria ('skin contaminants') more frequently from the SVN tips than those with PCT ($p < 0.001$). This difference may explain the greater safety of SVN in comparison to PCT. This safety is borne out by the 2 cases of PCT-associated bacteremia during a 3-month study and 2 cases in the preceding 6 months in contrast to no cases associated with SVN. This study re-emphasizes the inherent risk of venous catheterization and documents that SVN are a relatively safe alternative.

- 113 *Fluorocarbon Emulsions as a Blood Substitute.* LE-
LAND C. CLARK, Jr., SAMUEL KAPLAN and FER-

NANDO BECATTINI, Dept. of Ped., Coll. of Med., Univ. of Cincinnati, Cincinnati, Ohio.

In 1966 CLARK discovered that animals breathing certain perfluorinated liquids can transfer enough oxygen and carbon dioxide to sustain life [Science 152: 1755, 1966]. This suggested that these liquids may serve as valuable intravascular gas transport agents. Inert organic compounds having a high oxygen and carbon dioxide solubility were emulsified by intense sonication in the presence of surfactants to produce opalescent liquids having metabolic gas transport capabilities resembling whole blood. During intravenous infusion and ventilation with O_2 the mixed venous pO_2 rose to between 150 and 300 mm Hg while the arterial pCO_2 and pH were normal. A fourfold increase in brain oxygen cathode current was demonstrable. The increase in mixed venous pO_2 was initially related to the fluorocarbon content of the circulating blood. Since dogs survived in apparent good health these preparations may ultimately be used as a blood substitute or for organ preservation. (Supported in part by NIH HE-12419.)

- 114 *Effect of Heparin on Mortality Rate in Septicemia with Associated Diffuse Intravascular Coagulation.* JAMES J. CORRIGAN, Jr. and CHARLES M. JORDAN, Dept. of Ped., Emory Univ. Sch. of Med., Atlanta, Ga.

That diffuse intravascular coagulation (DIC) occurs in septicemia has been well documented and reported to occur almost exclusively in patients with hypotension. Heparin has been shown to effectively correct this coagulation defect but the efficacy of this agent in changing the high mortality rate in this group of patients has not been reported. The purposes of this investigation were to determine the frequency of DIC and to evaluate the effect of anticoagulation on the mortality rate in this group. Twenty-six children with septicemia and systolic blood pressures below 80 mm Hg had detailed coagulation studies performed and 24 were anticoagulated with heparin. Therapy also consisted of antibiotics, plasma expanders, IV fluids, transfusions and Isuprel. Two patients were given corticosteroids. No complications secondary to heparin occurred. The studies showed that all patients had abnormally long partial thromboplastin and prothrombin times, and all but one had thrombocytopenia. Classical DIC (thrombocytopenia with reduced factors II, V, VIII and fibrinogen, positive fibrin split products and normal euglobulin lysis time) was clearly present in 40% and highly probable in 96% of the cases. The overall mortality rate was 62%. Although 72% of the fatal cases had severe hypofibrinogenemia as compared to 25% who eventually survived, no correlation could be shown between the severity of the DIC and the mortality rate. These data again suggest that most, if not all, patients with sepsis and low blood pressure have DIC. Even though anticoagulation could correct the coagulation defect in most of the cases, heparin did not appear to significantly affect the mortality rate.

- 115 *Functional Studies of Young Versus Old Platelets in a Patient with Chronic Thrombocytopenia.* CHRISTINE A. JOHNSON, CHARLES F. ABILDGAARD and IRVING SCHULMAN, Univ. of Illinois Coll. of Med., Dept. of Ped., Chicago, Ill. and Univ. of California Davis Sch. of Med., Dept. of Ped., Davis, Calif.

The reproducible platelet production cycle following infusion of fresh frozen plasma (FFP) in a girl with

chronic thrombocytopenia [Blood 16: 943, 1960] provided a unique opportunity to study the functional capacity of young and old platelets. Study cycles were initiated by infusing FFP when the patient's platelet count was less than 20,000/mm³. 'Young' platelet studies were done 4 days after FFP (average platelet count, 200,000/mm³); 'old' platelet studies were done 21 days after FFP (average platelet count, 200,000/mm³). All studies were repeated during several such cycles. In association with a young platelet population, were normal Ivy bleeding times, normal or increased platelet adhesiveness, normal aggregation to ADP and collagen, and normal platelet factor 3 availability (PF-3a). By contrast, when the patient's circulating platelets were old, she was found to have long bleeding times, abnormally low adhesiveness *in vivo* and *in vitro*, and decreased PF-3a. Aggregation to ADP and collagen was slightly decreased but remained within normal limits. No abnormalities were seen by electron microscopy on platelet samples obtained throughout the cycle. (Performed by Dr. JAMES WHITE, Univ. of Minn.) It is of interest that on several occasions the patient experienced mild bleeding manifestations at the end of a cycle but while her platelet count was still normal. These episodes correlated with the findings of long bleeding time and decreased adhesiveness.

- 116 *Bilirubin-induced Platelet Staining, Aggregation, and Adenine Nucleotide Release.* HAROLD M. MAURER and JOYCE CAUL, Med. Coll. of Virginia, Richmond, Va. (introduced by W.E. Laupus).

Our previous studies have shown that free indirect-reacting bilirubin (B) even at low concentration (0.5 mg%) causes yellow staining and aggregation of washed platelets, whereas B bound to albumin and photoxidized B have no demonstrable platelet effect. The effect of B on platelet adenine nucleotide content was studied. Washed human platelets were incubated with either B (4 mg%) or buffered saline in the presence of CaCl₂ and KCl₂, and then platelets and supernatant were separately assayed for ADP and ATP. Approximately 40–80% of ADP and ATP was released from the platelets with bilirubin. Released ADP and ATP were present in the supernatants. B bound to albumin had no effect on platelet ADP and ATP content. The results indicate that platelet staining and aggregation by free B are associated with adenine nucleotide release. Released ADP is probably the underlying mechanism in B-induced aggregation.

- 117 *The Enzymatic Defect in Congenital Erythropoietic Porphyrria: Demonstration in Heterozygotes and in Non-erythropoietic Tissue of Homozygotes.* GIOVANNI ROMEO, MICHAEL M. KABACK, BERTIS L. GLENN and EPHRAIM Y. LEVIN, The Johns Hopkins Univ. Sch. of Med., Baltimore, Md., and the Oklahoma State Univ. Coll. of Vet. Med., Stillwater, Okla.

Activity of the enzyme uroporphyrinogen III cosynthetase in hemolysates from human or bovine subjects with congenital erythropoietic porphyria is much lower than the activity in control hemolysates. The partial deficiency of cosynthetase is probably a primary genetic defect in this disease and explains the pathological overproduction of uroporphyrin I. Cosynthetase activities in hemolysates from asymptomatic bovine carriers of porphyria are intermediate to those of normal and porphyric animals. This observation is consistent with the known autosomal recessive mode

of inheritance of the disorder. Similarly, in two human families parents or children of the porphyric propositus had the cosynthetase activities expected for a heterozygote state; but in a third family, these activities were in the normal range. Hence, there may be some genetic heterogeneity in the human disease. Also, the specific activity of cosynthetase is lower in extracts of fibroblasts grown in tissue culture from skin biopsies taken from patients with porphyria than in similar extracts from non-porphyric cells. This indicates that although the metabolic error in porphyrin formation is expressed only in erythropoietic tissue, the hereditary defect in the enzyme activity occurs in other tissues as well.

- 118 *Erythrocyte Sodium Flux in Hereditary Spherocytosis: Its Significance.* ALVIN ZIPURSKY and LYONEL G. ISRAELS, Dept. of Ped., McMaster Univ., and Dept. of Med., Univ. of Manitoba, Canada.

We have studied five families in whom one or more children have hereditary spherocytosis (h.s.). In the affected patients, erythrocyte ouabain-insensitive sodium efflux was significantly greater than normal in intact cells and isolated membranes. This is consistent with an increased permeability to sodium of these cells.

In each of the five families, neither parent had clinical or hematological evidence of h.s. Four of ten parents had erythrocyte sodium efflux patterns identical to that found in classical h.s. compared to three of thirty normal controls with similarly elevated values ($X^2 = 4.6$; $p < 0.05$).

These findings suggest:

1. The increased sodium permeability of h.s. erythrocytes is unrelated to their shortened life span, since similar sodium flux can be found in erythrocytes with normal life span.

2. The gene for h.s. can manifest as an increase in erythrocyte sodium permeability with no abnormality in morphology or life span of the red blood cell. (Supported by a grant from the Medical Research Council of Canada.)

- 119 *Selective Destruction of Reticulocytes (Retics) in Pyruvate Kinase (PK) Deficiency.* WILLIAM C. MENTZER, LAWRENCE N. BUTTON, STEPHEN H. ROBINSON and DAVID G. NATHAN, Children's Hosp. Med. Center, Boston, Mass.

PK retics lack adequate glycolysis and are peculiarly susceptible to irreversible damage in the spleen because they are dependent upon mitochondrial function for which splenic venous PO₂ is insufficient [Blood 34: 861, 1969]. The fraction and mass of PK deficient retics immediately trapped in the spleen should therefore influence clinical severity. A 22-year-old male (J.P.) with icterus and splenomegaly and with RBC PK 0.25 units (normal > 2.0 units) Hgb. 13.3 g % and retics 7 % illustrates this mechanism. Mean RBC life span was approximately 100 days ($T_{1/2}^{51Cr} = 33$ days), but bilirubin turnover (³H bilirubin) was 5× normal yielding mean RBC life span of only 20 days. Ferrokinetics with ⁵⁹Fe showed plasma iron turnover 5× normal; rapid marrow ⁵⁹Fe uptake, but low cumulative RBC ⁵⁹Fe and immediate splenic sequestration of newly labeled cells. These data provide evidence that the majority of J.P.'s newly formed retics were immediately sequestered in the spleen. The remainder survived normally and these were sufficient in number to provide 13.3 g % hemoglobin. That the low PK level in circulating mature J.P. cells did not limit their survival