We have also been able to confirm—probably the same specimen that you analyzed—the difference in distribution of acid mucopolysaccharides in the Hurler amniotic fluid.

There is only one problem that is still a little bothersome to us, and that is the question of expressing the results in terms of volume, since I am not quite sure whether there might be differences in concentration, water content, of amniotic fluid which might artifactually influence the results.

Dr. MATALON: I have discussed this problem previously with you, Dr. SCHAFER, and I agree with you that one might add more criteria for expressing these data.

I would like to stress again that in the Hurler amniotic fluid the problem is not a problem of concentration only, but it is again a problem of total different distribution. In none of the amniotic fluids did we find any suggestion of this amount of heparitin sulfate; as you will recall, normal amniotic fluids have almost 80% of their polysaccharide as hyaluronic acid.

The second thing you mentioned is that you detected some heparitin sulfate. We did the same thing you mentioned, and found a reactive substance in all the amniotic fluids; however, this substance was not true heparitin sulfate, because it gave reaction in the zero time, which heparitin sulfate does not.

5 *Intravascular Coagulation and Fibrinolysis in Human Renal Disease.* E. RICHARD STIEHM, JON I. SCHEINMAN, CARL W. TRYGSTAD, LINDA S. KUPLIC and DAVID T. UEHLING, Dept. of Ped., Univ. of Wisc. Med. Sch., Madison, Wisc. (introduced by Arthur J. Moss).

JAMES J. CORRIGAN, Jr. (Emory University School of Medicine, Atlanta, Ga.): What happens to the fibrolytic split products in inflammatory disease in general? Can you venture a guess as to what the half-life of the split products might be? And, in studies that we have done and reported by others, we have noted that there is a high titer of a material that is antithrombin in the alpha-2-macroglobulin fraction in addition to the antiplasmin; so that thrombosis in the nephrotic syndrome is probably not simply on the basis of elevated antiplasmins.

Dr. STIEHM: Fibrin split products increase in inflammation and infection. Using a sensitive technique like hemagglutinin inhibition, elevations of fibrin split products are frequently noted; this may be a useful test for sepsis. The half-life of fibrin split products is from 3 to 6 h. Limited studies on antithrombin levels in the nephrotic syndrome have disclosed no abnormalities; I will await your data with interest.

LYMAN A. PAGE (Stanford University School of Medicine, Palo Alto, Calif.): Is defective fibrinolysis seen as nonnephrotic hypoalbuminemia and analbuminemia?

The second question is whether you have tried to correlate the presence of fibrin split products in the urine with the extent of renal failure. It seems to me you are drawing some important inferences from the absence of correlation between urinary and plasma fibrin split products.

Dr. STIEHM: In patients with chronic renal disease with low albumin, there was no defect in fibrinolysis. We have not studied any patients with analbuminemia.

In any type of chronic renal failure urine fibrin split products may be elevated; therefore, when one is using urine fibrin split product levels as an indicator of transplant rejection, one should take into consideration the degree of azotemia. A urine fibrin split product level is significant only if it is markedly above what we would expect from other uremic patients with the same degree of renal failure. Currently we are relating levels of azotemia with urine fibrin split product levels.

HAROLD M. MAURER (Medical College of Virginia, Richmond, Va.): Have you used the ethanol gelation test to detect intravascular coagulation? How sensitive is this test compared with the test for fibrin split products in serum?

Dr. STIEHM: We have had limited experience with this procedure. The ethanol gelation test is positive in marked intravascular coagulation with defibrination. I do not believe, on the basis of limited studies, that it is of value in the study of subtle and localized intravascular coagulation.

GERALD S. GILCHRIST (Children's Hospital of Los Angeles, Los Angeles, Calif.): I noticed that 37% of the patients had fibrin split products in their serum. Larger numbers have it in their urine. Can you explain the large percentage of serum positive patients in the light of the apparent defect in fibrinolysis? Secondly, with regard to the hemolytic-uremic syndrome, I find difficulty in accepting your classification of the syndrome as a manifestation of generalized intravascular coagulation. Most studies would support the concept that this is a localized phenomenon with no consistent evidence of vascular involvement outside of the kidney.

Dr. STIEHM: There is a disagreement whether fibrin split products can occur in the presence of a defective fibrinolytic system. In my experience, I have never seen a fibrinolytic system so defective that fibrin split products are not generated even in the presence of markedly decreased plasminogen levels. Fibrin split products may be falsely negative if insensitive techniques such as agar diffusion are used. Secondly, I regard the hemolytic-uremic syndrome as an illness not limited to the kidney, with central nervous system and peripheral vascular involvement. At autopsy I believe there is evidence for intravascular coagulation.

JACK RESNICK (Naval Hospital, San Diego, Calif.): What type of correlation do you find between the biopsy evidence of fibrin or fibrinogen in the kidney, and the urine and serum fibrin split products?

Dr. STIEHM: We have not as yet had extensive experience correlating urine fibrin split products with biopsy evidence of deposited fibrinogen. We have found poor correlation between serum levels of fibrin split products and immunofluorescent evidence of a fibrinogen.

6 *Functional Asplenia in Sickle Cell Anemia—A Reversible Defect.* ALLEN D. SCHWARTZ, HOWARD A. PEARSON, JOSEPH H. ZELSON, RICHARD P. SPENCER and SORRELL L. WOLFSON. Depts. of Ped. and Nucl. Med., Yale Univ. Sch. of Med., New Haven, Conn.

LOUIS K. DIAMOND (University of California Medical Center, San Francisco): Shortly after hearing of this work of Dr. SCHWARTZ and Dr. PEARSON, we had the opportunity to study two children in one family with severe sickel cell anemia. The younger, a 12-year-old girl, had a spleen that was easily palpable two to three finger breadths below the costal margin. The older boy, 16 years of age, had an even larger spleen at an age when it is usually fibrosed and not palpable. He had had more than 30 admissions in the first 10 years of his life, several of them with pneumonia, one of them with pneumococcal pneumonia and septicemia.