Robert E. Shank Papers

Folder title:

American Association for Study of Liver Diseases, evening sessions, 1966.

Recommended citation for this document:

American Association for Study of Liver Diseases, evening sessions, 1966, Box 4, Folder 8, Robert E. Shank Papers, Bernard Becker Medical Library Archives, Washington University School of Medicine.

Identifier:

FC034-S01-B004-F08

(17)

METABOLIC STUDIES WITH PERFUSED CIRRHOTIC LIVER. Keith S. Henley, Roland Scholz, Joachim Grunst, Theodor Buecher, and Leslie U. Hendelman. (Department of Internal Medicine, Section of Gastroenterology, University of Michigan and Institute for Physiological Chemistry, University of Munich).

The livers of rats, made cirrhotic by dietary means, (Arch. Path. 70: 50, 1960) were perfused. To ensure uniform perfusion of the organ, the pressure in the hepatic vein was raised, and to eliminate the metabolic effects due to blood, a hemoglobin-free synthetic medium was used. (Biochem. Z. 341: 334, 1965). In the perfusate, the ratios of lactate to pyruvate (indicating the redox state of the extramitochondrial space), and of β-hydroxbutrate to acetoacetate (indicating the redox state of the mitochondria) were similar in all groups of animals, suggesting that perfusion was adequate. For a period of two hours from the start of the perfusion, the amount of glucose released, the rate of synthethis of urea, the rate of release of ammonia, and the rate of release of lactic dehydrogenase into the perfusing medium was similar in cirrhotic animals and controls. The rate of oxygen uptake by cirrhotic livers, (corrected for the presence of non-parenchymatous elements) was, however, less than in both male and female controls. Upon addition of 2:4 dinitrophenol to the perfusing medium the rate of oxygen uptake, as expected, increased. The magnitude of the increase was less in cirrhotic livers compared with the controls, but when expressed as a fraction of the baseline value it was similar in cirrhotic livers when compared with livers from animals of the same strain and sex. This suggests that the number of units capable of accepting molecular oxygen is less in the cirrhotic liver compared with the normal, but that, on an average, both are in a similar, controlled, state of respiratory activity. The response to 2:4 dinitrophenol was less marked in normal, male Sprague Dawley rats compared with normal female Wistar rats. (Supported, in part, by Research Career Development Award and Grant AM-07361 of the National Institute of Health).

(17)

METABOLIC STUDIES WITH PERFUSED CIRRHOTIC LIVER. Keith S. Henley, Roland Scholz, Joachim Grunst, Theodor Buecher, and Leslie U. Hendelman. (Department of Internal Medicine, Section of Gastroenterology, University of Michigan and Institute for Physiological Chemistry, University of Munich).

The livers of rats, made cirrhotic by dietary means, (Arch. Path. 70: 50, 1960) were perfused. To ensure uniform perfusion of the organ, the pressure in the hepatic vein was raised, and to eliminate the metabolic effects due to blood, a hemoglobin-free synthetic medium was used. (Biochem. Z. 341: 334, 1965). In the perfusate, the ratios of lactate to pyruvate (indicating the redox state of the extramitochondrial space), and of β-hydroxbutrate to acetoacetate (indicating the redox state of the mitochondria) were similar in all groups of animals, suggesting that perfusion was adequate. For a period of two hours from the start of the perfusion, the amount of glucose released, the rate of synthethis of urea, the rate of release of ammonia, and the rate of release of lactic dehydrogenase into the perfusing medium was similar in cirrhotic animals and controls. The rate of oxygen uptake by cirrhotic livers, (corrected for the presence of non-parenchymatous elements) was, however, less than in both male and female controls. Upon addition of 2:4 dinitrophenol to the perfusing medium the rate of oxygen uptake, as expected, increased. The magnitude of the increase was less in cirrhotic livers compared with the controls, but when expressed as a fraction of the baseline value it was similar in cirrhotic livers when compared with livers from animals of the same strain and sex. This suggests that the number of units capable of accepting molecular oxygen is less in the cirrhotic liver compared with the normal, but that, on an average, both are in a similar, controlled, state of respiratory activity. The response to 2:4 dinitrophenol was less marked in normal, male Sprague Dawley rats compared with normal female Wistar rats. (Supported, in part, by Research Career Development Award and Grant AM-07361 of the National Institute of Health).

(1)

-2-
SK.

October 10, 1966

Dr. Keith S. Henley
Associate Professor
Department of Internal Medicine
University of Michigan
Ann Arbor, Michigan

Dear Doctor Henley:

The abstract which you submitted for the meeting of the American Association for the Study of Liver Diseases in Chicago on November 3 has been selected for inclusion in the program of that evening. The paper will be listed as follows:

17. Metabolic studies with perfused cirrhotic liver.
K. S. Henley, R. Scholz, J. Grunst, T. Buecher and
L. U. Hendelman, Ann Arbor and Munich.

Five minutes are allotted for the presentation. Kindly inform us at an early date if the listing is incorrect or if someone other than the first named author is to present the paper.

Thank you for your interest. We look forward to an interesting and exciting meeting.

Very sincerely yours,

Robert E. Shank, M. D.

THE UNIVERSITY OF MICHIGAN

MEDICAL CENTER

ANN ARBOR, MICHIGAN

DEPARTMENT OF INTERNAL MEDICINE
Section of Gastroenterology
Gastroenterology Research Unit

September 28, 1966

Dr. Robert E. Shank, President, AASLD
Department of Preventive Medicine and Public Health
Washington University School of Medicine
660 South Euclid Avenue
St. Louis, Missouri

Dear Doctor Shank:

The enclosed abstract "Metabolic Studies with Perfused Cirrhotic Liver" is submitted for presentation at the forthcoming meeting of the American Society for the Study of Liver Diseases.

Yours sincerely,

Keith S. Henley, M.D.
Associate Professor
Department of Internal Medicine
University of Michigan Medical School

KSH/gb
enc.

THE
CHILDREN'S
HOSPITAL
OF
PHILADELPHIA
FOUNDED 1855

18th & BAINBRIDGE STREETS
PHILADELPHIA 19146

(18)

October 17, 1966

Dr. Robert E. Shank
Department of Preventive Medicine and Public Health
Washington University
660 South Euclid Avenue
St. Louis, Missouri 63110

Dear Dr. Shank:

Paper no. 18, "Serum amino acid concentrations in alcoholic hepatitis", of the AASLD meeting on November 3 will be presented by myself and not by the first author.

Sincerely yours,

Leah M. Lowenstein, M. D., D. Phil.

LML/ds

(18)

SERUM AMINO ACID CONCENTRATIONS IN ALCOHOLIC HEPATITIS. M. Ning, L. M. Lowenstein, and C. S. Davidson. Thorndike Memorial Laboratory, II and IV (Harvard) Medical Services, Boston City Hospital, and the Department of Medicine, Harvard Medical School, Boston, Massachusetts.

Alcoholic hepatitis is usually preceded by a period of heavy ethanol ingestion combined with inadequate food intake. Blood amino acid concentrations were studied in patients with this disease to determine the degree of protein malnutrition present. Blood was studied from 24 patients with acute alcoholic hepatitis during various phases of their illness. Analysis was made for total free amino acid concentration, the ratio of nonessential to essential amino acids using one-dimensional chromatography, and for the concentrations of the individual amino acids, termed the amino acid pattern, using automated amino acid analysis was carried out on the serum. Patients with other forms of liver disease were also studied for comparison. Patients with alcoholic hepatitis had a normal concentration of free amino acids; the values ranged between 2.5 and 3.95 mM. The ratio of nonessential to essential amino acids was elevated to a mean of 3.96 $\pm$ 1.08 (S.D.), as compared to the normal value of 2.51 $\pm$ 0.49. The values returned to normal in the 10 patients who improved and remained elevated in the patients who died. The ratio also correlated well with a low serum albumin concentration. An abnormal serum amino acid pattern was consistently demonstrated in the patients with alcoholic hepatitis. Low values of the branched-chain amino acids leucine, isoleucine, and valine with high values of glutamate were regularly found, a pattern similar to that in children with kwashiorkor. Patients with cirrhosis, without evidence of alcoholic hepatitis, had normal amino acid patterns. Patients with massive necrosis caused by viruses or drugs had great elevations of the total amino acid concentrations, and abnormal amino acid patterns as described by others. Subjects without liver disease showed either minor or no change in the amino acid patterns during alcohol infusions. The markedly abnormal amino acid pattern with no elevation of total concentration found in alcoholic hepatitis is similar to the changes observed in severe protein deficiency but has also been found after hepatectomy.

SERUM AMINO ACID CONCENTRATIONS IN ALCOHOLIC HEPATITIS. M. Ning, L. M. Lowenstein, and C. S. Davidson. Thorndike Memorial Laboratory, II and IV (Harvard) Medical Services, Boston City Hospital, and the Department of Medicine, Harvard Medical School, Boston, Massachusetts.

Alcoholic hepatitis is usually preceded by a period of heavy ethanol ingestion combined with inadequate food intake. Blood amino acid concentrations were studied in patients with this disease to determine the degree of protein malnutrition present. Blood was studied from 24 patients with acute alcoholic hepatitis during various phases of their illness. Analysis was made for total free amino acid concentration, the ratio of nonessential to essential amino acids using one-dimensional chromatography, and for the concentrations of the individual amino acids, termed the amino acid pattern, using automated amino acid analysis was carried out on the serum. Patients with other forms of liver disease were also studied for comparison. Patients with alcoholic hepatitis had a normal concentration of free amino acids; the values ranged between 2.5 and 3.95 mM. The ratio of nonessential to essential amino acids was elevated to a mean of 3.96 $\pm$ 1.08 (S.D.), as compared to the normal value of 2.51 $\pm$ 0.49. The values returned to normal in the 10 patients who improved and remained elevated in the patients who died. The ratio also correlated well with a low serum albumin concentration. An abnormal serum amino acid pattern was consistently demonstrated in the patients with alcoholic hepatitis. Low values of the branched-chain amino acids leucine, isoleucine, and valine with high values of glutamate were regularly found, a pattern similar to that in children with kwashiorkor. Patients with cirrhosis, without evidence of alcoholic hepatitis, had normal amino acid patterns. Patients with massive necrosis caused by viruses or drugs had great elevations of the total amino acid concentrations, and abnormal amino acid patterns as described by others. Subjects without liver disease showed either minor or no change in the amino acid patterns during alcohol infusions. The markedly abnormal amino acid pattern with no elevation of total concentration found in alcoholic hepatitis is similar to the changes observed in severe protein deficiency but has also been found after hepatectomy.

HARVARD MEDICAL SCHOOL — DEPARTMENT OF MEDICINE
BOSTON CITY HOSPITAL

HARVARD MEDICAL UNIT

THORNDIKE MEMORIAL LABORATORY AND
SECOND AND FOURTH MEDICAL SERVICES

818 HARRISON AVENUE
BOSTON, MASSACHUSETTS 02118
KENMORE 6-8600

September 28, 1966

Dr. Robert E. Shank, President
American Association for the Study of Liver Disease
Department of Preventive Medicine and Public Health
Washington University School of Medicine
660 South Euclid Avenue
St. Louis, Missouri 63110

Dear Dr. Shank:

Enclosed is an abstract entitled, "Serum Amino Acid Concentrations in Alcoholic Hepatitis," by Drs. Ning, Lowenstein, and Davidson for your consideration at the annual meeting of the American Association for the Study of Liver Diseases. Both Dr. Lowenstein and I are members.

Sincerely yours,

Charles S. Davidson, M.D.
Associate Director

CSD:sw
cc: Dr. Ning
Dr. Lowenstein
Enclosures: abstract form
3 double-spaced copies

October 10, 1966

Dr. Charles S. Davidson
Associate Director
Harvard Medical School
Department of Medicine
Boston City Hospital
818 Harrison Avenue
Boston, Massachusetts 02118

Dear Doctor Davidson:

The abstract which you submitted for the meeting of the American Association for the Study of Liver Diseases in Chicago on November 3 has been selected for inclusion in the program of that evening. The paper will be listed as follows:

18. Serum amino acid concentrations in alcoholic hepatitis.
M. Ning, L. M. Lowenstein and C. S. Davidson, Boston.

Five minutes are allotted for the presentation. Kindly inform us at an early date if the listing is incorrect or if someone other than the first named author is to present the paper.

Thank you for your interest. We look forward to an interesting and exciting meeting.

Very sincerely yours,

Robert E. Shank, M D.

PROTEIN CLOTTING FACTOR SYNTHESIS IN LIVER DISEASE. C Tamburro and C M Leevy. Department of Medicine, New Jersey College of Medicine and the East Orange Veterans Administration Hospital, East Orange, N.J.

Production of protein clotting factors in the isolated perfused rat liver is diminished by liver cell necrosis and increased by stimulation of DNA-dependent RNA protein synthesis. Applicability of these findings to human liver disease was investigated in a group of 14 patients with cirrhosis and vitamin K-resistant hypoprothrombinemia. Factors II, V, VII and X were determined before and after randomly selected periods of therapy (10 days) with a placebo or an androgenic-anabolic steroid (Anavar) previously demonstrated to increase nuclear RNA synthesis. Findings were related to histopathology; clearance of indocyanine green; in vitro incorporation of H^3T into DNA and H^3U into RNA; serum protein electrophoresis; and serum aminograms. Protein clotting factors remained unchanged during receipt of placebo therapy. Administration of anabolic steroids caused a significant increase in clotting factors in 11 patients and a reduction in 3. Of those exhibiting an improvement 8 had an increase in factor II and 6 in factor V without alteration of factors VII and X. An increase in nuclear RNA synthesis, with or without change in serum proteins or amino acids, was associated with an increase in factors II and V. Deterioration of hepatic reserve was characterized by a reduction in all protein clotting factors. Results confirm a relationship between hepatic nucleic acid and protein clotting factor synthesis in man, and demonstrate differences in occurrence of individual factor deficits in liver disease and their correction by drug-induced anabolism.

(19)

PROTEIN CLOTTING FACTOR SYNTHESIS IN LIVER DISEASE

Carlo Tamburro, M.D. and Carroll M. Leevy, M.D.

East Orange, N.J.

Production of protein clotting factors in the isolated perfused rat liver is diminished by liver cell necrosis and increased by stimulation of DNA dependent RNA protein synthesis. Applicability of these findings to human liver disease was investigated in a group of 14 patients with cirrhosis and vitamin K resistant hypoprothrombinemia. Factors II, V, VII and X were determined before and after randomly selected periods of therapy (10 days) with a placebo or an androgenic-anabolic steroid (Anavar) previously demonstrated to increase nuclear RNA synthesis. Findings were related to histopathology; clearance of indocyanine green; in vitro incorporation of H_3T into DNA and H_3U into RNA; serum protein electrophoresis; and serum aminograms.

Protein clotting factors remained unchanged during receipt of placebo therapy. Administration of anabolic steroids caused a significant increase in clotting factors in 11 patients and a reduction in 3. Of those exhibiting an improvement 8 had an increase in Factor II and 6 in Factor V without alteration of Factors VII and X. An increase in nuclear RNA synthesis, with or without change in serum proteins or amino acids was associated with an increase in Factors II and V. Deterioration

From the Division of Hepatic Metabolism and Nutrition, New Jersey College of Medicine, and the East Orange, N.J. Veterans Administration Hospital.

of hepatic reserve was characterized by a reduction in all protein clotting factors.

Results confirm a relationship between hepatic nucleic acid and protein clotting factor synthesis in man and demonstrate differences in occurrence of individual factor deficits in liver disease and their correction by drug-induced anabolism.

dr Shank —

This could be a very exciting paper. It all depends on how good their clotting factor assays are and how big the differences are.

Jack G.

(19)

PROTEIN CLOTTING FACTOR SYNTHESIS IN LIVER DISEASE. C Tamburro and C M Leevy. Department of Medicine, New Jersey College of Medicine and the East Orange Veterans Administration Hospital, East Orange, N.J.

Production of protein clotting factors in the isolated perfused rat liver is diminished by liver cell necrosis and increased by stimulation of DNA-dependent RNA protein synthesis. Applicability of these findings to human liver disease was investigated in a group of 14 patients with cirrhosis and vitamin K-resistant hypoprothrombinemia. Factors II, V, VII and X were determined before and after randomly selected periods of therapy (10 days) with a placebo or an androgenic-anabolic steroid (Anavar) previously demonstrated to increase nuclear RNA synthesis. Findings were related to histopathology; clearance of indocyanine green; *in vitro* incorporation of H^3T into DNA and H^3U into RNA; serum protein electrophoresis; and serum aminograms. Protein clotting factors remained unchanged during receipt of placebo therapy. Administration of anabolic steroids caused a significant increase in clotting factors in 11 patients and a reduction in 3. Of those exhibiting an improvement 8 had an increase in factor II and 6 in factor V without alteration of factors VII and X. An increase in nuclear RNA synthesis, with or without change in serum proteins or amino acids, was associated with an increase in factors II and V. Deterioration of hepatic reserve was characterized by a reduction in all protein clotting factors. Results confirm a relationship between hepatic nucleic acid and protein clotting factor synthesis in man, and demonstrate differences in occurrence of individual factor deficits in liver disease and their correction by drug-induced anabolism.

New Jersey College of Medicine and Dentistry

24 BALDWIN AVENUE JERSEY CITY, N. J. 07304

September 30, 1966

Dr. Robert Shank
Department of Medicine
Washington University
School of Medicine
St. Louis, Missouri

Dear Dr. Shank:

Enclosed is an abstract entitled "Protein Clotting Factor Synthesis in Liver Disease" which is being submitted for consideration for presentation at the Fall Meeting of the American Association for Study of Liver Disease. Dr. Tamburro is in his second year of postdoctoral research fellowship training.

I returned from the meetings in Kyoto today, and the appropriate abstract forms were locked up; they will be sent to you on Monday.

With best wishes,

Yours sincerely,

Carroll M. Leevy, M.D.
Professor and Director
Division of Hepatic Metabolism
and Nutrition

CML/jkp

Enclosure

October 10, 1966

Dr. Carroll M. Leevy
Professor and Director
Division of Hepatic Metabolism and Nutrition
New Jersey College of Medicine and Dentistry
24 Baldwin Avenue
Jersey City, New Jersey 07304

Dear Doctor Leevy:

The abstract which you submitted for the meeting of the American Association for the Study of Liver Diseases in Chicago on November 3 has been selected for inclusion in the program of that evening. The paper will be listed as follows:

19. Protein clotting factor synthesis in liver disease.
C. Tamburro and C. M. Leevy, East Orange.

Five minutes are allotted for the presentation. Kindly inform us at an early date if the listing is incorrect or if someone other than the first named author is to present the paper.

Thank you for your interest. We look forward to an interesting and exciting meeting.

Very sincerely yours,

Robert E. Shank, M. D.

(20)

HEPATIC ALBUMIN SYNHTESIS IN MAN. A.S. Tavill, Anne Craigie and V.M. Rosenoer. Department of Medicine, Royal Free Hospital, London, England.

The ^{14}C carbonate incorporation technique has been used to measure hepatic albumin synthesis in normal subjects and in patients with various diseases. The method has been validated on the basis of simultaneous ^{131}I albumin catabolic studies and repeated observations on the same individual. Reduced albumin synthesis was found in cirrhosis, in Budd-Chiari's syndrome, and in malnutrition. Elevated rates were found in one patient with hepatoma and one with protein losing enteropathy. Intravenous albumin infusion reduced albumin synthesis in one patient with steatorrhoea and normal liver function and surprisingly increased it in 3 of 4 patients with cirrhosis. The relation of these results to an albumin "feed-back" mechanism will be discussed.

Empire
This work was supported by the British/Cancer Campaign

(2) all in vol

HEPATIC ALBUMIN SYNHTESIS IN MAN. A.S. Tavill, Anne Craigie and V.M. Rosenoer. Department of Medicine, Royal Free Hospital, London, England.

The ^{14}C carbonate incorporation technique has been used to measure hepatic albumin synthesis in normal subjects and in patients with various diseases. The method has been validated on the basis of simultaneous ^{131}I albumin catabolic studies and repeated observations on the same individual. Reduced albumin synthesis was found in cirrhosis, in Budd-Chiari's syndrome, and in malnutrition. Elevated rates were found in one patient with hepatoma and one with protein losing enteropathy. Intravenous albumin infusion reduced albumin synthesis in one patient with steatorrhoea and normal liver function and surprisingly increased it in 3 of 4 patients with cirrhosis. The relation of these results to an albumin "feed-back" mechanism will be discussed.

This work was supported by the British Empire Cancer Campaign

October 10, 1966

Professor Sheila Sherloch
Department of Medicine
The Royal Free Hospital
Gray's Inn Road
London, W.C. 1, England

Dear Doctor Sherloch:

The program of the American Association for the Study of Liver Diseases has been selected. The abstract which you submitted entitled "Hepatic albumin synthesis in man," by A. S. Tavill, A. Craigie, and V. M Rosenoer has been included in the program. You advised us that Doctor Tavill would present the paper. Since we do not have his address, would you please advise him of this selection, informing him that five minutes will be allotted for the presentation. I would also appreciate it if you would provide me with his address at the earliest possible date.

With warm personal regards,

Sincerely,

Robert E. Shank, M. D.

(21)

PLASMA VOLUME MEASUREMENTS IN CIRRHOSIS. Fred L. Lieberman and T.B. Reynolds. Hepatic Service, John Wesley County Hospital and Department of Medicine, University of Southern California, Los Angeles, California.

The validity of the elevated values for plasma volume found in cirrhosis has been questioned because of possible leakage into the ascites and hepatic lymph of the tagged albumin used for measurement. Furthermore, the sodium retention and renal insufficiency accompanying ascites are features more compatible with a low plasma volume. We have measured the plasma volume in 110 patients with cirrhosis divided into groups of 62 without ascites and 48 with ascites. Measurements were made with both I^{131} tagged albumin and Cr^{51} tagged erythrocytes, and compared to a group of 24 control subjects, the mean plasma volume was elevated in both groups of cirrhotic patients by both methods of measurement. There was no statistical difference in the mean plasma volume between patients with and without ascites, nor between patients with uncomplicated ascites and a subgroup of 15 patients with ascites and functional renal failure. The amount of radioactivity in the ascites of ten patients was negligible in accounting for the elevated plasma volume. By measuring the rate of appearance of I^{131} albumin in the lymph of six patients undergoing thoracic duct drainage for the treatment of ascites, we were able to calculate the size of the thoracic duct lymph space. The quantity of radioactivity in this space was also negligible in accounting for the elevated plasma volume. We concluded that the plasma volume is truly elevated in patients with ascites and that this elevation is not an artifact due to leakage of the albumin tag from the plasma during mixing.

(21)

PLASMA VOLUME MEASUREMENTS IN CIRRHOSIS. Fred L. Lieberman and T.B. Reynolds. Hepatic Service, John Wesley County Hospital and Department of Medicine, University of Southern California, Los Angeles, California.

The validity of the elevated values for plasma volume found in cirrhosis has been questioned because of possible leakage into the ascites and hepatic lymph of the tagged albumin used for measurement. Furthermore, the sodium retention and renal insufficiency accompanying ascites are features more compatible with a low plasma volume. We have measured the plasma volume in 110 patients with cirrhosis divided into groups of 62 without ascites and 48 with ascites. Measurements were made with both I^{131} tagged albumin and Cr^{51} tagged erythrocytes, and compared to a group of 24 control subjects, the mean plasma volume was elevated in both groups of cirrhotic patients by both methods of measurement. There was no statistical difference in the mean plasma volume between patients with and without ascites, nor between patients with uncomplicated ascites and a subgroup of 15 patients with ascites and functional renal failure. The amount of radioactivity in the ascites of ten patients was negligible in accounting for the elevated plasma volume. By measuring the rate of appearance of I^{131} albumin in the lymph of six patients undergoing thoracic duct drainage for the treatment of ascites, we were able to calculate the size of the thoracic duct lymph space. The quantity of radioactivity in this space was also negligible in accounting for the elevated plasma volume. We concluded that the plasma volume is truly elevated in patients with ascites and that this elevation is not an artifact due to leakage of the albumin tag from the plasma during mixing.

(2)

(2)

Well done!

MMK.

CAPITOL 5-1511
CAPITOL 5-3131

UNIVERSITY OF SOUTHERN CALIFORNIA
SCHOOL OF MEDICINE
2025 ZONAL AVENUE
LOS ANGELES, CALIFORNIA 90033

DEPARTMENT OF MEDICINE

September 23, 1966

Robert E. Shank, M.D.
President, AASLD
Department of Preventive Medicine and Public Health
Washington University School of Medicine
600 South Euclid Avenue
St. Louis, Missouri 63110

Dear Doctor Shank:

Enclosed is the abstract we are submitting for the Association meeting of November 3, 1966 in Chicago. Our abstract is entitled "Plasma Volume Measurements in Cirrhosis", by Fred L. Lieberman,M.D. and Telfer B. Reynolds, M.D. Dr. Lieberman will present the paper if it is accepted for the program.

Sincerely yours,

Fred L. Lieberman

Fred L. Lieberman, M.D.
Instructor in Medicine

FLL:p

October 10, 1966

Dr. Fred L. Lieberman
Instructor in Medicine
University of Southern California
School of Medicine
2025 Zonal Avenue
Los Angeles, California 90033

Dear Doctor Lieberman:

The abstract which you submitted for the meeting of the American Association for the Study of Liver Diseases in Chicago on November 3 has been selected for inclusion in the program of that evening. The paper will be listed as follows:

21. Plasma volume measurements in cirrhosis.
F. L. Lieberman and T. B. Reynolds, Los Angeles

Five minutes are allotted for the presentation. Kindly inform us at an early date if the listing is incorrect or if someone other than the first named author is to present the paper.

Thank you for your interest. We look forward to an interesting and exciting meeting.

Very sincerely yours,

Robert E. Shank, M D.

(22)

October 20, 1966

Dr. George Margolis
Department of Pathology
Dartmouth Medical School
Hanover, New Hampshire 03755

Dear Dr. Margolis:

The Annual Meeting of the American Association for the Study of Liver Diseases will be held on Thursday, November 3, 1966, at the Hotel Sheraton-Chicago, 505 N. Michigan Avenue, Chicago, Illinois 60611.

Members and guests have been asked to use the rooms the hotel has reserved for the Association. Therefore if you make a reservation there, indicate that you will be attending the meeting.

The dinner will be held at 6:30 p.m. - price $6.00. Make check payable to the Association and send to;

Dr. Emanuel Rubin
Treasurer, AASLD
The Mount Sinai Hospital
Fifth Avenue and 100 Street
New York, N.Y. 10029

Sincerely yours,

Robert E. Shank, M. D.

(22)

DARTMOUTH MEDICAL SCHOOL
Department of Pathology
HANOVER · NEW HAMPSHIRE 03755

October 14, 1966

Dr. Robert E. Shank
Department of Preventive Medicine & Public Health
660 South Euclid Avenue
St. Louis, Missouri 63110

Dear Dr. Shank:

Thank you for your letter of October 10th notifying me of the acceptance of my paper for presentation at the meeting of the American Association for the Study of Liver Diseases. The indicated title and authorship are correct. I shall present the paper.

To date, I have no details regarding the locale of the meeting. Therefore, I would appreciate whatever information you can supply.

Sincerely,

George Margolis, M.D.

GM/pb

RAT VIRUS DISEASE, AN EXPERIMENTAL MODEL OF NEONATAL HEPATITIS.

G. Margolis and L. Kilham. Departments of Pathology and Microbiology, Dartmouth Medical School, Hanover, New Hampshire.

Rat virus (RV) manifests a unique virus-cell interaction. This small DNA-containing pantropic agent exhibits a selective affinity for cells with active DNA synthesis attending mitosis. Perinatal infections induce severe disturbances in development, determined by an attack, at critical phases of histogenesis, on tissues with deficient regenerative capacity. A salient sequel is the cerebellar hypoplasia resulting from destruction of the external germinal mantle during its intense postnatal growth phase. In the rat, the natural host of RV, the liver is a prime target, where a primary cycle of extraneural replication occurs and where postnatal susceptibility and viral activity persist longest. With maturation the liver becomes resistant, but receptivity is restored during regeneration after surgical or chemotoxic lesions. The spectrum of RV hepatitis includes: 1) an acute phase featured by intranuclear inclusions and necrosis of hepatocytes; 2) a subacute phase characterized by giant cell transformation with variable polyploidy, proliferation of intrinsic bile ducts, or a distorted adenomatoid pattern with large vascular lakes; and 3) post necrotic stromal collapse with nodular hyperplasia. This unique virus-cell interaction offers new insights into the pathogenesis of viral hepatitis, particularly of neonatal "giant cell" hepatitis.

(22)

RAT VIRUS DISEASE, AN EXPERIMENTAL MODEL OF NEONATAL HEPATITIS.

G. Margolis and L. Kilham. Departments of Pathology and Microbiology, Dartmouth Medical School, Hanover, New Hampshire.

Rat virus (RV) manifests a unique virus-cell interaction. This small DNA-containing pantropic agent exhibits a selective affinity for cells with active DNA synthesis attending mitosis. Perinatal infections induce severe disturbances in development, determined by an attack, at critical phases of histogenesis, on tissues with deficient regenerative capacity. A salient sequel is the cerebellar hypoplasia resulting from destruction of the external germinal mantle during its intense postnatal growth phase. In the rat, the natural host of RV, the liver is a prime target, where a primary cycle of extraneural replication occurs and where postnatal susceptibility and viral activity persist longest. With maturation the liver becomes resistant, but receptivity is restored during regeneration after surgical or chemotoxic lesions. The spectrum of RV hepatitis includes: 1) an acute phase featured by intranuclear inclusions and necrosis of hepatocytes; 2) a subacute phase characterized by giant cell transformation with variable polyploidy, proliferation of intrinsic bile ducts, or a distorted adenomatoid pattern with large vascular lakes; and 3) post necrotic stromal collapse with nodular hyperplasia. This unique virus-cell interaction offers new insights into the pathogenesis of viral hepatitis, particularly of neonatal "giant cell" hepatitis.

1. I like this paper
partly because I am
interested in neonatal
hepatitis. Some aspects of
this work would seem
to have quite important
implications (eg restoration
of integrity by regeneration
or toxic damage).
JMK

(3)

DARTMOUTH MEDICAL SCHOOL
Department of Pathology
HANOVER · NEW HAMPSHIRE 03755

September 28, 1966

Dr. Robert E. Shank, President
American Society for the Study of Liver Disease
Department of Preventive Medicine and Public Health
Washington University School of Medicine
St. Louis, Missouri 63110

Dear Dr. Shank:

Enclosed is an abstract of a paper offered for presentation at the fall meeting of your society. This paper is submitted at the behest of Dr. W. A. Tisdale, who has expressed a strong interest in our studies and is desirous of having this work presented before your society.

Sincerely,

George Margolis, M.D.
Professor of Pathology

GM/pb

CC: Dr. W. A. Tisdale

October 10, 1966

Dr. George Margolis
Professor of Pathology
Dartmouth Medical School
Hanover, New Hampshire 03755

Dear Doctor Margolis:

The abstract which you submitted for the meeting of the American Association for the Study of Liver Diseases in Chicago on November 3 has been selected for inclusion in the program of that evening. The paper will be listed as follows:

22. Rat virus disease, an experimental model of neonatal hepatitis.
G. Margolis and L. Kilham, Hanover, New Hampshire.

Five minutes are allotted for the presentation. Kindly inform us at an early date if the listing is incorrect or if someone other than the first named author is to present the paper.

Thank you for your interest. We look forward to an interesting and exciting meeting.

Very sincerely yours,

Robert E. Shank, M. D.

LIVER DYSFUNCTION WITH MESTRANOL BUT NOT WITH NORETHYNODREL IN A PATIENT WITH ENOVID® INDUCED JAUNDICE

Ernest Urban, Barry W. Frank and Fred Kern, Jr.

Department of Medicine, Division of Gastroenterology
University of Colorado Medical Center
Denver, Colorado

A twenty year old woman had two attacks of pruritis and jaundice in association with Enovid therapy. Since both the estrogen and progesterone components of Enovid are 17α alkyl substituted steroids a study was designed to determine whether she was sensitive to both. A year after the jaundice, her liver function tests including 45 minute bromsulphalein retention and intravenous cholangiogram were normal. The estrogen component, Mestranol, 0.16 mg/day, was given and serial measurements of liver function were made. Pruritis was noted on the fifth day and the drug discontinued. She did not become jaundiced but pruritis persisted for twenty days. The bromsulphalein retention increased to a maximum of 36% and the serum alkaline phosphatase increased from 1.8 to 4.5 Bessey Lowry units and both remained abnormal for 30 and 60 days respectively. Serum bilirubin and SGOT concentration remained normal. A constant intravenous infusion of bromsulphalein seventeen days after the cessation of Mestranol showed a decrease in maximum hepatic transport rate to 28% of normal and a threefold rise above normal in the relative storage capacity of bromsulphalein in the liver. Plasma bile salts were markedly elevated during the pruritis. Liver biopsy twenty-four hours after cessation of Mestranol showed a few fine canalicular bile plugs and was otherwise normal by light and electron microscopy. Five months later the patient was challenged with the progesterone component, Norethynodrel, 10 mg daily for 14 days. There were no abnormal clinical findings and the results of serial laboratory studies of liver function were normal. It was concluded that the 17α alkyl substituted radical was not responsible for the hepatic dysfunction. The demonstration in our patient that estrogen and not progesterone impairs BSP metabolism is consistent with the recent observation that natural estrogens and not progesterone impair BSP metabolism in the rat (Gallagher, T. F., Mueller, M. N. and Kappas, A., Trans. Assoc. Amer. Phys. 78:187, 1965).

23

LIVER DYSFUNCTION WITH MESTRANOL BUT NOT WITH NORETHYNODREL IN A PATIENT WITH ENOVID® INDUCED JAUNDICE

Ernest Urban, Barry W. Frank and Fred Kern, Jr.

Department of Medicine, Division of Gastroenterology
University of Colorado Medical Center
Denver, Colorado

A twenty year old woman had two attacks of pruritis and jaundice in association with Enovid therapy. Since both the estrogen and progesterone components of Enovid are 17α alkyl substituted steroids a study was designed to determine whether she was sensitive to both. A year after the jaundice, her liver function tests including 45 minute bromsulphalein retention and intravenous cholangiogram were normal. The estrogen component, Mestranol, 0.16 mg/day, was given and serial measurements of liver function were made. Pruritis was noted on the fifth day and the drug discontinued. She did not become jaundiced but pruritis persisted for twenty days. The bromsulphalein retention increased to a maximum of 36% and the serum alkaline phosphatase increased from 1.8 to 4.5 Bessey Lowry units and both remained abnormal for 30 and 60 days respectively. Serum bilirubin and SGOT concentration remained normal. A constant intravenous infusion of bromsulphalein seventeen days after the cessation of Mestranol showed a decrease in maximum hepatic transport rate to 28% of normal and a threefold rise above normal in the relative storage capacity of bromsulphalein in the liver. Plasma bile salts were markedly elevated during the pruritis. Liver biopsy twenty-four hours after cessation of Mestranol showed a few fine canalicular bile plugs and was otherwise normal by light and electron microscopy. Five months later the patient was challenged with the progesterone component, Norethynodrel, 10 mg daily for 14 days. There were no abnormal clinical findings and the results of serial laboratory studies of liver function were normal. It was concluded that the 17α alkyl substituted radical was not responsible for the hepatic dysfunction. The demonstration in our patient that estrogen and not progesterone impairs BSP metabolism is consistent with the recent observation that natural estrogens and not progesterone impair BSP metabolism in the rat (Gallagher, T. F., Mueller, M. N. and Kappas, A., Trans. Assoc. Amer. Phys. 78:187, 1965).

2+ interesting especially since it is contradictory to other observations MMMK

UNIVERSITY OF COLORADO
MEDICAL CENTER
4200 EAST NINTH AVENUE
DENVER, COLORADO 80220

COLORADO GENERAL HOSPITAL
COLORADO PSYCHOPATHIC HOSPITAL
CHILDREN'S DIAGNOSTIC CENTER
SCHOOL OF MEDICINE
SCHOOL OF NURSING

September 27, 1966

Dr. Robert E. Shank, President, AASLD
Department of Preventive Medicine and Public Health
Washington University School of Medicine
660 South Euclid Avenue
St. Louis, Missouri, 63110

Dear Doctor Shank:

Enclosed are two abstracts, "Exchange Transfusion in the Treatment of Acute Hepatic Necrosis" and "Liver Dysfunction with Mestranol But Not with Norethynodrel in a Patient with Enovid® Induced Jaundice", submitted for your consideration for the program of the American Association for the Study of Liver Diseases.

Sincerely yours,

Fred Kern, Jr., M. D.
Professor of Medicine
Head, Division of Gastroenterology

FK:ll
Enclosures

October 10, 1966

Dr. Fred Kern, Jr.
Professor of Medicine
Head, Division of Gastroenterology
University of Colorado
Medical Center
4200 East Ninth Avenue
Denver, Colorado 80220

Dear Doctor Kern:

The abstract which you submitted for the meeting of the American Association for the Study of Liver Diseases in Chicago on November 3 has been selected for inclusion in the program of that evening. The paper will be listed as follows:

23. Liver dysfunction with mestranol but not with norethynodrel in a patient with enovid induced jaundice.
E. Urban, B. W. Frank, and F. Kern, Jr., Denver.

Five minutes are allotted for the presentation. Kindly inform us at an early date if the listing is incorrect or if someone other than the first named author is to present the paper.

Thank you for your interest. We look forward to an interesting and exciting meeting.

Very sincerely yours,

Robert E. Shank, M. D.

FINE STRUCTURAL CHANGES IN THE LIVER IN PATIENTS RECEIVING NICOTINIC ACID FOR HYPERCHOLESTEREMIA. A. H. Baggenstoss, N. A. Christensen, K. G. Berge, W. P. Baldus, and R. E. Spiekerman. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Sixty-seven patients with hypercholesteremia (plasma cholesterol, 250 mg/100 ml or more) have been treated with nicotinic acid in doses of 1.5 to 6 gm/day for periods of 1 month to 9 1/2 years. Jaundice developed in three patients during treatment. Needle biopsy of liver in two of these revealed a form of hepatitis characterized by cholestasis, focal and individual cell necrosis of both acidophilic and lytic types, and mild inflammation of the portal tracts. All three patients recovered promptly when treatment was discontinued. However, because of these findings, hepatic needle biopsies have been performed recently in eight additional patients who have received continuous treatment with nicotinic acid for periods of 1 5/6 to 8 1/2 years. Seven patients have been on continuous treatment for more than 3 years. At the time of the biopsies, the plasma cholesterol values ranged from 181 to 293 mg/100 ml. Blood sugar was above normal (> 90 mg/100 ml) in three cases and uric acid was above normal (> 6 mg/100 ml) in two cases. The values for SGOT, alkaline phosphatase, sulfobromophthalein retention, and serum bilirubin were normal in all eight cases. Histologic examination revealed normal liver or only minor histologic alterations. Electron microscopic studies disclosed dilatation of the endoplasmic reticulum with formation of numerous vesicles and sacs of various sizes and shapes. These were largely smooth-surfaced, but many still had a few particles attached and numerous ribosomes were observed in the ground substance. The mitochondria revealed unusual shapes and markedly elongated and giant forms. In three cases, crystalloids were observed in the mitochondrial matrix. These appeared to be closely related to either the cristae or to the internal mitochondrial membrane. Other organelles, glycogen, and lipid appeared to be normal. The alterations are interpreted as evidence of focal cytoplasmic degradation of endoplasmic reticulum and mitochondria, which, in most instances, has not reached a degree of severity to interfere seriously with cell function or give rise to clinical or laboratory evidence of hepatic dysfunction.

(24)

FINE STRUCTURAL CHANGES IN THE LIVER IN PATIENTS RECEIVING NICOTINIC ACID FOR HYPERCHOLESTEREMIA. A. H. Baggenstoss, N. A. Christensen, K. G. Berge, W. P. Baldus, and R. E. Spiekerman. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Sixty-seven patients with hypercholesteremia (plasma cholesterol, 250 mg/100 ml or more) have been treated with nicotinic acid in doses of 1.5 to 6 gm/day for periods of 1 month to 9 1/2 years. Jaundice developed in three patients during treatment. Needle biopsy of liver in two of these revealed a form of hepatitis characterized by cholestasis, focal and individual cell necrosis of both acidophilic and lytic types, and mild inflammation of the portal tracts. All three patients recovered promptly when treatment was discontinued. However, because of these findings, hepatic needle biopsies have been performed recently in eight additional patients who have received continuous treatment with nicotinic acid for periods of 1 5/6 to 8 1/2 years. Seven patients have been on continuous treatment for more than 3 years. At the time of the biopsies, the plasma cholesterol values ranged from 181 to 293 mg/100 ml. Blood sugar was above normal (> 90 mg/100 ml) in three cases and uric acid was above normal (> 6 mg/100 ml) in two cases. The values for SGOT, alkaline phosphatase, sulfobromophthalein retention, and serum bilirubin were normal in all eight cases. Histologic examination revealed normal liver or only minor histologic alterations. Electron microscopic studies disclosed dilatation of the endoplasmic reticulum with formation of numerous vesicles and sacs of various sizes and shapes. These were largely smooth-surfaced, but many still had a few particles attached and numerous ribosomes were observed in the ground substance. The mitochondria revealed unusual shapes and markedly elongated and giant forms. In three cases, crystalloids were observed in the mitochondrial matrix. These appeared to be closely related to either the cristae or to the internal mitochondrial membrane. Other organelles, glycogen, and lipid appeared to be normal. The alterations are interpreted as evidence of focal cytoplasmic degradation of endoplasmic reticulum and mitochondria, which, in most instances, has not reached a degree of severity to interfere seriously with cell function or give rise to clinical or laboratory evidence of hepatic dysfunction.

2-3
Really quite an interesting series of observations. JMP

(3) and J. Gastroent

MAYO CLINIC
ROCHESTER, MINNESOTA
55901

SECTION OF EXPERIMENTAL
AND ANATOMIC PATHOLOGY
A.H. BAGGENSTOSS, M.D.
G.P. SAYRE, M.D.
R.C. BAHN, M.D.
A.L. BROWN, M.D.
J.L. TITUS, M.D.
K.E. HOLLEY, M.D.
H. OKAZAKI, M.D.
J. LUDWIG, M.D.

TELEPHONE 282-2511
AREA CODE 507

September 23, 1966

Robert E. Shank, M.D.
Department of Preventive Medicine and Public Health
Washington University School of Medicine
660 South Euclid Avenue
St. Louis, Missouri 63110

Dear Doctor Shank:

The enclosed abstract entitled "Fine Structural Changes in the Liver in Patients Receiving Nicotinic Acid for Hypercholesteremia" is submitted for your consideration in the program of the meeting of the American Association for Study of Liver Disease on November 3. I plan to present the findings. Dr. William Baldus is a member of the Association, but Drs. Christensen, Berge, and Spiekerman are not members.

Sincerely,

A H Baggenstoss

A. H. Baggenstoss, M.D.

AHB:cjk

October 10, 1966

Dr. A. H. Baggenstoss
Mayo Clinic
Rochester, Minnesota 55901

Dear Doctor Baggenstoss:

The abstract which you submitted for the meeting of the American Association for the Study of Liver Diseases in Chicago on November 3 has been selected for inclusion in the program of that evening. The paper will be listed as follows:

24. Fine structural changes in the liver in patients receiving nicotinic acid for hypercholesteremia. A. H. Baggenstoss, N. A. Christensen, K. G. Berge, W. P. Baldus, and R. E. Spiekerman, Rochester, Minn.

Five minutes are allotted for the presentation. Kindly inform us at an early date if the listing is incorrect of if someone other than the first named author is to present the paper.

Thank you for your interest. We llok forward to an interesting and exciting meeting.

Very sincerely yours,

Robert E. Shank, M. D.

(25)

ELECTRON MICROSCOPIC CHANGES IN DILANTIN HEPATITIS. A.M. Hoyumpa, O.J. Kim, W.T. Scott and L. Schiff. Departments of Internal Medicine and Pathology, University of Cincinnati College of Medicine, Cincinnati, Ohio.

Hepatitis is a rare but serious complication of Dilantin therapy and knowledge of the morphologic changes in the liver is meager. Ultramicroscopic changes have not been described. A chance to study liver tissue was presented by a fourteen year-old boy who received Dilantin. After three weeks of treatment he developed exfoliative dermatitis, fever, chills, and generalized lymphadenopathy followed shortly by jaundice, hepatomegaly and splenomegaly accompanied by lymphocytosis and eosinophilia. A needle specimen of the liver examined under light microscopy showed changes consistent with drug-induced hepatitis with dense eosinophilic infiltration and acidophilic bodies. On electron microscopy the bile canaliculi were dilated and the microvilli flattened or absent. Giant mitochondria with crystalline inclusions were demonstrated. The Kupffer cells had enlarged, elongated and more numerous cytoplasmic processes. In the dilated sinusoids there were a few necrotic cells with coarsely granular cytoplasmic masses and swollen, distorted, smooth endoplasmic reticulum corresponding to the acidophilic bodies noted on light microscopy. Since these ultramicroscopic features are found in various liver disorders, they must be considered non-specific. It is hoped that studies of similar cases will help determine the constancy of these changes and perhaps throw additional light on the hypersensitivity type of drug-induced hepatitis.

ELECTRON MICROSCOPIC CHANGES IN DILANTIN HEPATITIS. A.M. Hoyumpa, O.J. Kim, W.T. Scott and L. Schiff. Departments of Internal Medicine and Pathology, University of Cincinnati College of Medicine, Cincinnati, Ohio.

Hepatitis is a rare but serious complication of Dilantin therapy and knowledge of the morphologic changes in the liver is meager. Ultramicroscopic changes have not been described. A chance to study liver tissue was presented by a fourteen year-old boy who received Dilantin. After three weeks of treatment he developed exfoliative dermatitis, fever, chills, and generalized lymphadenopathy followed shortly by jaundice, hepatomegaly and splenomegaly accompanied by lymphocytosis and eosinophilia. A needle specimen of the liver examined under light microscopy showed changes consistent with drug-induced hepatitis with dense eosinophilic infiltration and acidophilic bodies. On electron microscopy the bile canaliculi were dilated and the microvilli flattened or absent. Giant mitochondria with crystalline inclusions were demonstrated. The Kupffer cells had enlarged, elongated and more numerous cytoplasmic processes. In the dilated sinusoids there were a few necrotic cells with coarsely granular cytoplasmic masses and swollen, distorted, smooth endoplasmic reticulum corresponding to the acidophilic bodies noted on light microscopy. Since these ultramicroscopic features are found in various liver disorders, they must be considered non-specific. It is hoped that studies of similar cases will help determine the constancy of these changes and perhaps throw additional light on the hypersensitivity type of drug-induced hepatitis.

2.

How clearly established is it that this (or any) "toxic hepatitis" is due to "hypersensitivity" (may be best term) or do authors mean "idiosyncratic"?

UNIVERSITY OF CINCINNATI
COLLEGE OF MEDICINE

ADDRESS:
DEPARTMENT OF INTERNAL MEDICINE
CINCINNATI GENERAL HOSPITAL
CINCINNATI 29, OHIO

Gastric Laboratory
September 28, 1966

Dr. Robert E. Shank, President, AASLD
Department of Preventive Medicine and Public Health
Washington University School of Medicine
660 South Euclid Avenue
St. Louis, Missouri 63110

Dear Bob:

I am enclosing an abstract on a case of Dilantin hepatitis for presentation at the coming meeting of the American Association for the Study of Liver Disease.

Very sincerely yours,

Leon Schiff

Leon Schiff, M.D.
Professor of Medicine

LS:eb

Encl.

October 10, 1966

Dr. Leon Schiff
Professor of Medicine
University of Cincinnati
College of Medicine
Department of Internal Medicine
Cincinnati General Hospital
Cincinnati 29, Ohio

Dear Doctor Schiff:

The abstract which you submitted for consideration for the program of the American Association for the Study of Liver Diseases in Chicago on November 3, 1966, has been selected for presentation if time permits in the evening session. We shall make every effort to save time for your paper. Presentation will be limited to five minutes. The listing will be as follows:

25. Electron microscopic changes in dilantin hepatitis.
A. M. Hoyumpa, O. J. Kim, W. T. Scott, and L. Schiff, Cincinnati.

Please inform us if the listing is incorrect of if other than the first named author is to present the paper. We shall be grateful for your cooperation and look forward to an interesting program.

Very sincerely yours,

Robert E. Shank, M. D.

* 26

THE UMBILICAL VEIN AS AN APPROACH TO THE PORTAL CIRCULATION

R. E. KESSLER, M. D. and D. S. ZIMMON, M. D. The Surgical and Medical Services, Veterans Administration Hospital, New York, N. Y.

The umbilical vein passes from the umbilicus by way of the round ligament to the porta hepatis and enters the portal vein at or near its bifurcation. Dilatation and catheterization of this structure permits direct access to the portal venous system.

Umbilical vein catheterization has been evaluated in terms of simplicity, safety, and clinical application in fifty consecutive cases. Thirty catheterizations were performed under general and twenty under local anesthesia. There were six technical failures (12%). Only one of the last twenty-five attempts was unsuccessful. Two minor and one major complications were encountered.

This technic provides a method for accurately measuring portal pressure and visualizing the portal vein by angiography without the hazards or high technical failure rate of splenic puncture and despite splenic vein obstruction or prior splenectomy. Since injected dye enters the liver directly, excellent hepatograms cen be obtained. Mass lesions as small as 0.5 cm. in diameter can be outlined and the hepatic veins can be visualized.

Umbilical vein catheterization is a safe and useful method for entering the portal venous system offering a number of unique advantages for pressure measurement and angiography.

(2)
Mk

VETERANS ADMINISTRATION
HOSPITAL
FIRST AVENUE AT EAST 24TH STREET
NEW YORK, NEW YORK 10010

YOUR FILE REFERENCE:

September 20, 1966

IN REPLY REFER TO:

Robert E. Shank, M.D.
Department of Preventive Medicine and
Public Health
Washington University School of Medicine
St. Louis, Missouri 63110

Dear Dr. Shank:

Enclosed you will find abstract entitled "Oxygen Binding of Hemoglobin as an Estimate of Hepatic Function" which is submitted for consideration for presentation at the meeting of the American Society for Study of Liver Diseases, November 3, 1966.

Sincerely,

David S. Zimmon

DAVID S. ZIMMON, M.D.
Chief, Gastroenterology Section
Medical Service

DSZ:dnb

Show veteran's full name and VA file number on all correspondence. If VA number is unknown, show service number.

October 10, 1966

Dr. David S. Zimmon
Chief, Gastroenterology Section
Medical Service
Veterans Administration Hospital
First Avenue at East 24th Street
New York, New York 10010

Dear Doctor Zimmon:

The abstract which you submitted for consideration for the program of the American Association for the Study of Liver Diseases in Chicago on November 3, 1966, has been selected for presentation if time permits in the evening session. We shall make every effort to save time for your paper. Presentation will be limited to five minutes. The listing will be as follows:

26. The umbilical vein as an approach to the portal circulation.
R. E. Kessler and D. S. Zimmon, New York.

Please inform us if the listing is incorrect or if other than the first named author is to present the paper. We shall be grateful for your cooperation and look forward to an interesting program.

Very sincerely yours,

Robert E. Shank, M. D.