VOL. 5
NO. 1

February 1953

The CLINICAL Chemist

HUGH J. McDONALD
Nominated for President
1953-1954

LT. COL. MONROE E. FREEMAN
Vice-Presidential Nominee
1953-1954

Official Publication
of
AMERICAN ASSOCIATION
of
CLINICAL CHEMISTS,
INC.

AACC NATIONAL ELECTION
CLINICAL CHEMISTRY PROGRAM
LOS ANGELES, CALIFORNIA
MARCH 16

THE CLINICAL Chemist

P.O. Box 123
Lenox Hill Station New York 21, N.Y.

VOL. 5, NO. 1 FEB. 1953

THE SECRETARY REPORTS

At this writing the Association is now entering the fifth year of its organization. We have available a great deal of data concerning the geographical distribution of our membership, and the training and experience of many clinical chemists. However, much pertinent data is not yet available to us. It would certainly be of interest to have statistical studies as to the number of hospitals and medical institutions that are now employing competent clinical chemists; the extent of the staffs of such laboratories as a function of the size and activities of the institutions; and the salary ranges of such positions. The compiling of these statistics would of course require a good deal of effort, cooperation, and expense.

Such a survey was carried out in the Department of Hospitals of the City of New York. The results of this survey after a year's study, were reported in great detail and submitted on October 16, 1950 to Commissioner Marcus D. Kogel by Dr. Warren M. Sperry, chairman of the committee. A covering letter stated in part, "For reasons which are discussed in detail in the report, we were led to the conclusion that the clinical chemical service in most of the New York City Hospitals is inadequately staffed, housed, and equipped. We are recommending detailed changes which, if adopted, will go far, in our opinion, to rectify the conditions which now exist..... We realize that the adoption of all of our recommendations would entail additional expenses, but we believe that the expenditure would be more than justified in terms of improved services to the patients of our hospitals."

As a result of the above survey, and with the cooperation of the Commissioner, the Department is being effectively improved as it pertains to clinical chemical services. Perhaps more such surveys would be indicated on a local, state, or national level to bring to the attention of hospital administrators the ways and means in which these important services could be improved.

Max M. Friedman, National Secretary

INVITATION

The Southern California Section, host to the AACC at the 123rd National Meeting of The American Chemical Society, extends the following invitation:

The members of the Southern California Section wish to extend a cordial welcome to all members of the American Association of Clinical Chemists to meet with them at a luncheon to be arranged for some convenient time during the 123rd National Meeting of the American Chemical Society, March 15 to 19, Los Angeles.

When you arrive in Los Angeles, do not forget to look up the time and place! Call our chairman, Dr. Richard J. Henry, at the Bio-Science Laboratories, CRestview 4-5106.

Announcements will be posted at the ACS Registration Centers, Galeria, Hotel Biltmore; Ballroom Floor, Hotel Statler.

1953 DIRECTORY

As a supplement to this issue of THE CLINICAL CHEMIST, every member of the AACC will receive a copy of the 1953 Directory. This directory has been compiled from the latest files of the Association and contains the names of the elected membership as of January 1, 1953, with their last known mailing address. The directory of the Association is one of its assets and the use as a mailing list for circularizing purposes is prohibited unless written permission for that purpose is first obtained from the National Secretary.

NOMINATING COMMITTEE ANNOUNCEMENT

The National Nominating Committee, elected to serve in 1952 proposed the following nominees for the National Executive Committee for voting by the membership of the AACC.

Dr. Hugh J. McDonald, Professor and Chairman of the Department of Biochemistry, Stritch School of Medicine Loyola University and present Vice-President of the AACC was nominated as President.

Lt. Col. Monroe E. Freeman, Chief of Department of Biochemistry, Army Medical Service Graduate School, and Chief of the Allied Science Section M.S.C. was proposed as Vice-President. Dr. Freeman was instrumental in the organization of the Washington Section of the AACC.

Dr. Max M. Friedman, Senior Chemist Queens General Hospital, N.Y. and Dr. Louis B. Dotti, Chemist to St. Luke's Hospital, N.Y. were nominated to retain their present positions as Secretary and Treasurer respectively.

The proposed members of the new National Executive Committee are, Drs. Albert E. Sobel, New York, Cecilia Riegel, Philadelphia, Joseph I. Routh, Iowa State University, Arthur Knudson, Albany Medical College, and Robert M. Hill, University of Colorado.

The above nominations were proposed by the 1952 Nominating Committee consisting of Harry Sobotka, Louis B. Dotti, Samuel Natelson, Joseph Benotti, Miriam Reiner, Warren Sperry and John G. Reinhold. Members have the opportunity to write in names of their own choosing in the space provided on the ballot.

The elected National Executive Committee will serve from July 1, 1953 to June 30, 1954.

EXECUTIVE COMMITTEE ELECTION

Members are urged to send in their ballots for the election of the National Executive committee. Ballots, together with appropriate envelopes were included with this issue of THE CLINICAL CHEMIST. The proposals of the Nominating Committee are indicated. Members may write in their own choice in the spaces provided. Seven names are required for the 1953 Nominating Committee. Ballots must be post marked on or before April 15, 1953 to be counted.

CLINICAL CHEMISTRY PROGRAM 123rd NATIONAL ACS MEETING

The program of the Division of Biological Chemistry, American Chemical Society, features one afternoon devoted to papers on clinical chemistry. The session will be held Monday afternoon, March 16, in the Renaissance Room, Hotel Biltmore, Los Angeles, Calif. Dr. Otto Schales will preside.

MONDAY AFTERNOON PROGRAM

2:00– 13.* OTTO SCHALES. Introductory Remarks.

2:05– 14. RICHARD J. HENRY. Review of Interlaboratory Accuracy Surveys of Clinical Chemical Analyses.

2:35– 15. EARL M. BILGER, LEONORA NEUFFER BILGER, AND EDWARD IZAWA. An Experimental Proposal of New Methods for the Determination of Barbiturates in Biological Fluids.

2:50– 16. BERNARD F. McKENZIE AND MARSCHELLE H. POWER. Determination of Barbiturates in Blood.

3:05– 17. HENRY TAUBER, WILTON E. VANNIER, EDWARD L. PETIT, AND HAROLD J. MAGNUSON. Serum Changes in Diseases as Found by Paper Chromatography.

3:20– 18. ALBERT L. CHANEY AND WILLIAM E. McKEE. The Determination of Urinary Estrone and Estradiol.

3:35– 19. ALBERT ZLATKIS, BENNIE ZAK, HAROLD H. BROWN, AND ALBERT J. BOYLE. A New and Rapid Method for the Determination of Free Serum Cholesterol.

3:50– 20. ALBERT L. CHANEY AND KENNETH D. JOHNSON. The Direct Micro-Titration of Serum Calcium.

4:05– 21. ALFRED D. WINER AND DWIGHT M. KUHNS. Determination of Serum and Urine Calcium by Flame Spectrophotometry using a Photomultiplier Tube.

4:20– 22. GEORGE R. KINSLEY AND ROSCOE R. SCHAFFERT. Effect of Organic Solvents on the Emission Spectra of Cations in Serum and Aqueous Solutions.

4:35– 23. BENNIE ZAK, ALBERT ZLATKIS, AND ALBERT J. BOYLE. The Quantitative Estimation of Serum Bilirubin with the Acid Iron Reagent.

4:50– 24. KENNETH D. JOHNSON AND HERBERT I. HARDER. A Rapid Titrimetric Method of the Estimation of Serum Lipase.

**Time and paper number*

Biographical Sketches of Proposed New Officers

PRESIDENT

HUGH J. MCDONALD. Born, Glen Nevis, Ontario, Canada, July 27, 1913; Queen's University, 1930-1932; B.Sc. in Chemistry (with highest honors), McGill University, 1935; M.S., Carnegie Institute of Technology, 1936; D.Sc., 1939. Major work for doctorate in physical chemistry, with minors in organic chemistry, physiological chemistry and physics.

Research fellow, teaching assistant and part time instructor, Carnegie, 1936-1939; instructor in chemistry, Illinois Institute of Technology, 1939-1941; Assistant Professor, 1941-1943; Associate Professor, 1943-1946; Professor, 1946-1948; Professor and Chairman, Department of Biochemistry, Stritch School of Medicine of Loyola University, Chicago, since 1948. Consultant, Argonne National Laboratory, since 1946. Manhattan Project, Columbia University, 1943. Awarded competitive scholarship, Royal Institution for Advancement of Learning, 1933-1934. Sigma Xi research award, 1944; research award, American Academy Arts and Sciences, 1945.

Fellow, A.A.A.S., 1946; Member, American Chemical Society; American Association Clinical Chemists (Chairman Committee on Education); Electrochemical Society; American Association University Professors; Sigma Xi; Phi Lumbda Upsilon; Alpha Chi Sigma, Chaos Club (Chicago).

Dr. McDonald is the present Vice-President of the AACC, and Chairman of the Committee on Education.

VICE-PRESIDENT

MONROE E. FREEMAN, Chief, Department of Biochemistry Army Medical Service Graduate School, also Chief, Allied Science Section, M.S.C., Office of the Surgeon General, Department of the Army.

Educated at the University of Minnesota, B.S., M.S., Ph.D. (1928-1931 in biochemistry.

Has served as instructor of chemistry at University of Arizona, 1929-30; Assistant Professor Biochemistry, University of Maine 1930-1936; and Professor of Chemistry at University of Massachusetts 1936-1948.

Entered Regular Army in 1948 at the Army Medical Service Graduate School. World War II service as chief of chemistry and toxicology section of the First Medical General Laboratory in the European Theatre of Operations.

Investigative interests in plant virus diseases, hemicelluloses, carbohydrates, clinical chemistry, lipoid hemolysins, hyaluronidase, bacterial antigens.

SECRETARY

MAX M. FRIEDMAN, Senior Chemist at Queens General Hospital, New York, Consultant Chemist at Lebanon Hospital. He was born in Austria on January 24, 1907 and completed his undergraduate work at the University of Alabama in 1930. After also studying at Columbia and New York University he was awarded his Doctorate by the Polytechnic Institute of Brooklyn in 1947. His main scientific interest is body water or, more specifically, extracellular fluids. His research for the past several years has been divided between body fluids and nucleic acid in normal and pathological tissues.

Dr. Friedman was the first President of the AACC and has served as National Secretary since 1950.

TREASURER

LOUIS BASIL DOTTI is Chemist at St. Luke's Hospital in New York City and Lecturer in Physiology and Biochemistry at the New York Medical College. He was born in New York City on August 13, 1903, and graduated from Columbia University in 1929. He also did his post-graduate work at Columbia, receiving his M.A. in 1931 and his Ph.D. in 1936. He has worked extensively on carbohydrate and calcium metabolism, digestive enzymes and liver function tests.

Dr. Dotti has been Treasurer of the AACC since 1948.

MEMBERS OF THE EXECUTIVE COMMITTEE

ALBERT E. SOBEL, Head of the Department of Biochemistry of the Jewish Hospital of Brooklyn is also Adjunct Professor of Chemistry at the Polytechnic Institute of Brooklyn. He was born in Luko, Hungary on September 24, 1906. He holds the degrees of Bachelor of Science (1930) and Chemical Engineer (1935) from Cooper Union. He was awarded a Masters degree from Columbia University in 1936 and received his doctorate from the Polytechnic Institute of Brooklyn in 1940. He is the author of 76 papers on micro methods, mineral metabolism, sterols, gastric ulcers and aqueous dispersion of fat-soluble vitamins.

Dr. Sobel is at present President of the AACC. His term expires June 30, 1953.

ARTHUR KNUDSON. Associate Dean and Professor of Biochemistry at Albany Medical College, Albany, N.Y. Dr. Knudson was born in Milwaukee, Wisc., August 13, 1889. He received his doctorate degree at Columbia University 1914 in biochemistry after attending Missouri and Wisconsin Universities. Post-doctorate work took him to Harvard and to Cambridge. He has been associated with Albany Medical College since 1914. He has held the chair in biochemistry since 1921. He was appointed Associate Dean in 1943.

Dr. Knudson is well known for his work on food and nutrition and was a member of the National Research Council 1943-1945 and did research for the Armed Forces in the last war. His interests center on the biochemistry of lipids; radiation; vitamin D; metabolism in leukemia; metabolism of cholesterol and cholesterol esters; chemical assay of digitalis and strophanthus series.

Dr. Knudson has returned from a year's leave, teaching in the medical schools of Bangkok, Thailand.

ROBERT M. HILL, Professor of Biochemistry University of Colorado, received his doctorate in biochemistry from Cambridge 1931 and Copenhagen 1932. Was formerly Asst. Professor of Biochemistry School of Medicine, Loyola University and Assoc. Professor Biochemistry, University of Colorado.

Dr. Hill served with the U.S. Navy and Public Health Service during World War II as a civilian consultant. His scientific interests concern sulphur oxidations, plasma proteins, body temperature control and metabolism of tumors.

CECILIA RIEGEL, Chemist to the Lankenau Hospital, Philadelphia, Pa., received her doctorate in medical science from the University of Pennsylvania in 1927. Dr. Riegel was on the faculty of Women's Medical College and the University of Pennsylvania Medical School in the Biochemistry Department. During World War II she served as a civilian with the Office of Science Research and Development.

Her investigative interests encompass the physiology of the gall bladder, blood substitutes, lactic acid metabolism and blood coagulation.

Dr. Riegel is Chairman of the Philadelphia Section of the AACC.

JOSEPH I. ROUTH, Professor of Biochemistry State University of Iowa, received his B.S. degree at Purdue University in 1933 and his M.S. and Ph.D. in Biochemistry at Michigan in 1937. He joined the University of Iowa faculty as an Instructor in Biochemistry in 1937 and was appointed Associate Professor in 1946.

Dr. Routh's scientific interests in Biochemistry feature investigations of biologically active sulphur compounds, keratins, body fluids, polysaccharides and properties of enterogastrone.

NEW PROCEDURE FOR AWARDS COMMITTEE

The 1953 Ernst Bischoff Award of the American Association of Clinical Chemists will be presented to a recipient during the fifth annual meetings of the Association to be held in Chicago, Illinois in September, 1953. The procedure for the award was determined by the Executive Committee at the Atlantic City meetings.

An award committee of three members, appointed annually, shall receive recommendations from the membership. Based on these recommendations, the committee shall submit three candidates to the honorary members of the Association. The award recipient shall be selected by the honorary members from these three candidates submitted by the award committee.

The award committee for 1953 will consist of Otto Schales, Ochsner Medical Clinic, New Orleans, La. as chairman; Joseph H. Roe, George Washington University, Washington, D.C.; and Fritz Bischoff, Santa Barbara Cottage Hospital, Santa Barbara, Calif.

Members of the Association are advised to consider this matter seriously, and submit their recommendations to the award committee. The prospectus should be as complete as possible, with biography of the scientific and professional attainments of the proposed candidate and a complete statement as to the reasons for the recommendation. The data should be submitted in triplicate to Dr. Otto Schales, 3503 Prytania Street, New Orleans, La. before March 31, 1953.

As is usual in these matters, all correspondence with the award committee will be confidential. The recipient of the Ernst Bischoff Award for 1953 will be announced on or before June 15, 1953.

PHILADELPHIA SECTION FEBRUARY 24 MEETING

Dr. Albert E. Sobel, President of the American Association of Clinical Chemists, Head of the Department of Biochemistry of the Jewish Hospital of Brooklyn, will present a lecture on "Quantitative Ultramicroanalysis in Clinical Laboratories" at the February 24, 1953 meeting of the Philadelphia Section. Dr. Sobel was one of the pioneers in the field of ultramicroanalysis in clinical biochemistry, and he is also well known for his research on mineral metabolism, sterols, gastric ulcers, and aqueous dispersion of fat-soluble vitamins.

REVIEW OF TECHNIQUES FOR PROTEIN BOUND IODINE

by

Albert L. Chaney

Albert L. Chaney Chemical Laboratory, Los Angeles, California

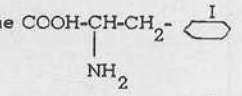
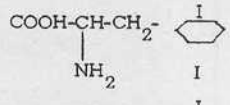
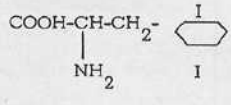
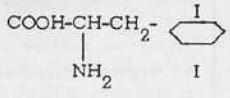
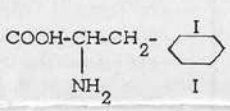
The determination of Protein Bound Iodine is an analytical problem of more than usual complexity, and at the same time it has reached a clinical importance that places it among the more frequently used tests, particularly in some localities.

As a result, a large variety of techniques have been described, particularly in the last few years, and it seems appropriate at this time to compare them and outline their mutual relationships.

Before discussion of analytical techniques, the present status of the biochemistry of iodine containing compounds will be summarized. At least eight different iodine containing compounds occur physiologically or are derived from physiological material.

The organic compounds may be all considered as iodinated derivatives of a single amino acid tyrosine, and are listed in the following table, together with their occurrence.

Table 1

1. Sodium or potassium iodide—Inorganic		Absorbed from foods and water.
2. Mono-iodo-tyrosine		Minor constituent of hydrolysis of thyroglobulin.
3. Di-iodo-tyrosine		Constituent of thyroglobulin.
4. Thyroxine		Active hormone and also constituent of thyroglobulin.
5. Thyroxine-glucuronidate—(Probable formula) A combination of thyroxine and glucuronic acid.		Occurs in bile as the excretion form of thyroxine.
6. Tri-iodo-thyronine		Present in serum (?) Constituent of thyroglobulin (?). Very active metabolically.
7. Di-iodo-thyronine		May not occur naturally. 4% as active as thyroxine.

8. Thyroglobulin—A high molecular weight protein (675,000) containing variable proportions of iodinated tyrosine as mono-iodo-tyrosine, di-iodo-tyrosine, thyroxine, and tri-iodo-thyronine.
Thyroglobulin occurs as the storage form of iodine in the thyroid gland.

The relationships of these various compounds may be briefly summarized as follows:

Inorganic iodide is selectively trapped or concentrated and retained in the thyroid gland, (Mechanism unknown). An oxidative enzyme system converts iodide to the free element state in which form it combines with the tyrosine component of the protein thyroglobulin to form the iodinated derivatives already described.

Under the influence of pituitary hormones (T.S.H.), thyroglobulin is enzymatically hydrolyzed and free thyroxine formed which is secreted into the blood stream for distribution to the tissues.

Excess thyroxine is concentrated in the liver, detoxified by conjugation with glucuronic acid and excreted in the bile.

It is now quite generally accepted that the principal forms in which iodine occurs in the blood stream are an active hormonal form, probably thyroxine, (and also tri-iodo-thyronine), and the inorganic salt form. The concentration of the hormone is an indicator of thyroid activity and of general metabolism, while the concentration of iodide reflects the balance between dietary intake, utilization by the thyroid gland, the metabolism of other iodine compounds, and urinary excretion.

It has been empirically found that when proteins of serum are precipitated the hormone is quite quantitatively co-precipitated, while the inorganic salt form remains in the filtrate. This separation is now quite generally adopted as a preliminary step.

For purposes of comparison, it is convenient to divide the complete analytical process into various stages and to see how these are combined in different published procedures.

Table 2 lists the principal steps and the more commonly used methods for each step.

It will be impossible in the space available to present an adequate historical review of iodine analytical techniques, even as applied to this limited field. However, it seems justified to present in outline form those features which are the basis of recent methods and to portray a sort of geneological relationship between them.

The period 1935-1940 represents a transition from obsolete to recent methods. Values published prior to that time were for whole blood, usually, and in addition the values seem in many cases to be too high as judged by our present information.

Accordingly, the outline will be devoted primarily to the period 1937 - 1952, with only brief reference to the contributions derived from earlier analysts. For those interested in earlier work, comprehensive review may be found in published references (1),(2).

In figure 1 the schematic relationship of the principal methods described during the period is shown on a chron-

ological basis.

The first column indicates the types of final analyses proposed and used, and the succeeding columns list the methods according to the way in which proteins, etc., are destroyed.

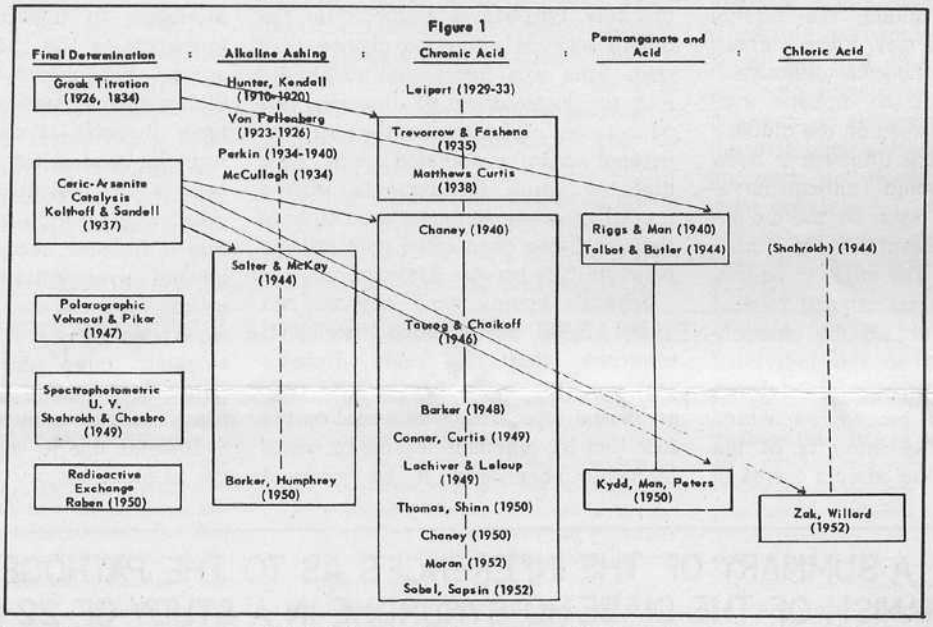
Those procedures which are enclosed together are in general similar in basic outline. The diagonal arrows indicate the groups of procedures using a particular type of quantitative determination.

The following bibliography gives references on the procedures outlined in Figure 1.

Table 2

I. Separation of Hormone and Inorganic Forms —	Protein Precipitation Solvent Extraction
II. Destruction of Protein — Acid Digestion or other interfering material	(a) Chromic Acid (b) Acid Permanganate (c) Chloric Acid
Alkaline Ashing	
III. Isolation of Iodine —	Distillation Solution and Filtration
IV. Quantitative Determination —	Titration Colorimetric Catalytic Spectrophotometric Radioactivity

Figure 1



Bibliography

1. Iodine Metabolism and Thyroid Function, A. W. Elmer, Oxford Medical Publications, 1938.
2. The Endocrine Function of Iodine, W. T. Salter, Harvard University Press, 1940.
3. Hunter, A., J. Biol. Chem. 7:321 (1910).
4. Kendall, E. C. and Richardson, F. S., J. Biol. Chem. *43*:161 (1920).
5. Fellenberg, T. Von, Mitt. Lebenson, Hyg. *14*: 161-240 (1923).
6. Groak, B., Biochem. Zeit. *175*:455-60, (1926).
7. Leipert, T., Biochem. Zeit. *261*:436 (1933).
8. Perkin, H. G., Brown, B. R., and Lang, J., Canad. Med. Ass. J. *31*:365 (1934).
9. McCullagh, D. R., J. Biol. Chem. *107*:35 (1934).
10. Trevorrow, V., and Fashena, G. J., J. Biol. Chem. *110*:29, (1935).
11. Kolthoff, I. M., Sandell, E. B., Microchim. Acta *1*:9, (1937).
12. Matthews, N. L., Curtis, G. M., and Brode, W. R., Ind. & Eng. Chem. (Anal. Ed.) *10*:612 (1938).
13. Chaney, A. L., Ind. & Eng. Chem. (Anal. Ed.), *12*:179 (1940).
14. Riggs, D. S., and Man, E. B., J. Biol. Chem. (*134*:193(1940), (*143*:363(1942).
15. Talbot, N. B., Butler, A. M., Saltzman, A. K., Rodriguez, J. Biol. Chem. *153*:479, (1944).
16. Shahrokh, B. K., J. Biol. Chem. *154*:517 (1944).
17. Salter, W. T., and McKay, E. A., Endocrin. *35*:380 (1944).
18. Taurog, A., and Chaikoff, I. L., J. Biol. Chem. *163*:313 (1946).
19. Vohnout, S., and Pikar, O., Casopisu lekaru Ceskych, *87*:1182 (1948).
20. Barker, S. B., J. Biol. Chem. *173*:715 (1948).
21. Connor, A. C., Curtis, G. M., et al., Surgery, *25*:510 (1949).
22. Lachiver, F., and Leloup, J., Bull. de la Soc. Chem. Biol. *31*:1128 (1949).
23. Shahrokh, B. K., and Chesbro, R. M., Anal. Chem. *21*:1003 (1949).
24. Custer, J. J., and Natelson, S., Anal. Chem. *21*:1005 (1949).
25. Kydd, D. M., Man, E. B., and Peters, J. P., J. Clin. Invest. *29*:1033 (1950).
26. Barker, S. B., and Humphrey, M. J. (J. Clin. Endo. *10*:1136 (1950), (J. Clin. Invest. *30*:55 (1951).
27. Raben, M. S., Anal. Chem. *22*:480 (1950).
28. Thomas, J. W., Shinn, L. A., et al, Anal. Chem. *22*:726 (1950).
29. Chaney, A. L., Anal. Chem. *22*:939 (1950).
30. Man, E. B., Kydd, D., and Peters, J. P., J. Clin. Invest. *30*:531-538 (1951).
31. Decker, J. W., and Hayden, H. S., Anal. Chem. *23*:798 (1951).
32. Harsha, W. N., Am. J. Med. Sci. *221*:626 (1951).
33. Lein, A., and Schwartz, N., Anal. Chem. *23*:1507 (1951).
34. Moran, J. J., Anal. Chem. *24*:378 (1952).
35. Zak, B., Willard, H. H., et al, Anal. Chem., *24*:1345 (1952).
36. Sobel, H., and Sapsin, S., Anal. Chem. *24*:1829 (1952).

STUDIES ON THE PATHOGENESIS OF THE DIABETIC SYNDROME

By

BRUNO W. VOLK, M.D. and SYDNEY S. LAZARUS, M.D.

Jewish Sanitarium and Hospital For Chronic Diseases

Diabetes is an error of metabolism characterized by hyperglycemia and usually glycosuria. Experimental diabetes was originally produced in dogs by removal of the pancreas, so that for a long time it was thought that human diabetes was basically a pancreatic disorder. More recent work has shown that the diabetic syndrome may not be based only on primary insulin deficiency, but that dysfunction of the anterior pituitary gland, the adrenal cortex or the liver may cause chronic impairment of carbohydrate tolerance.

The diagnosis of the diabetic syndrome is normally based on the glucose tolerance test which although it does detect hyperglycemia unresponsiveness, throws no light on the pathogenesis of the impairment of carbohydrate tolerance. The study to be discussed represents an attempt to find means of differentiating the possible cause of diabetes in the individual patient. For this purpose we employed certain laboratory procedures which might determine the integrity of the anterior pituitary, the adrenal cortex or the liver as to their functional relationship to carbohydrate metabolism.

In the normal individual the administration of glucose is accompanied by a significant decline of the absolute lymphocyte count. This phenomenon is a result of stimulation of the pituitary-adrenal axis. In applying this procedure to a group of 22 diabetic patients it was found that only 11 responded with a normal decline of the absolute lymphocyte count while the others showed either no change or a rise. This was interpreted to signify that the latter group of diabetics has a functional disturbance of the pituitary-adrenal axis associated with their diabetes while the patients with a normal response were assumed to have their diabetes associated with primary pancreatic or hepatic dysfunction.

Several years ago Forsham and Thorn used the glucose-phosphorus tolerance test to divide diabetic patients into an endocrine and non-endocrine type. This was based on the fact that for a normal decline of serum inorganic phosphorus to be observed after glucose administration a normal balance between the supply of insulin and its antagonists must be present within the body. The results of both these procedures, namely the change of the absolute lymphocyte count and of serum inorganic phosphorus after glucose administration were then studied in this same group of 22 diabetic persons in order to establish the pathogenetic factor of the diabetic syndrome in the individual patient. Inasmuch as the change of serum inorganic phosphorus would divide the diabetic syndrome into a non-endocrine type (hepatic dysfunction diabetes) and an endocrine type, while the change of the absolute lymphocyte count would divide this endocrine type into a diabetes secondary to pituitary-adrenal dysfunction and one due to primary pancreatic insufficiency, it was possible by this means to distinguish three groups of diabetic patients. In those patients which by these method were considered to have a diabetes due to hepatic dysfunction, the clinical history usually supported

A SUMMARY OF THE INFERENCES AS TO THE PATHOGENETIC MECHANISM OF THE DIABETIC SYNDROME IN A STUDY OF 22 PATIENTS *as indicated by the change of serum inorganic phosphorus and absolute lymphocyte count after glucose administration and the insulin sensitivity elicited by the modified glucose insulin tolerance test*

no. of patients	*change in serum inorganic phosphorus after glucose administration*	*change in absolute lymphocyte count after glucose administration*	*insulin sensitivity as determined by the modified glucose-insulin-tolerance test*	*probable mechanism*
4	non-significant variation from the fasting level	normal decline	normal	primary insulin deficiency
11	non-significant variation from the fasting level	non-significant variation from the fasting level or a moderate rise	usually diminished	pituitary-adrenal dysfunction
7	normal decline	normal decline	usually diminished	hepatic dysfunction

this inference; most of them had cirrhosis of the liver or gave histories of jaundice or gallbladder disease.

Theoretically a patient with diabetes due to overactivity of the insulin antagonists of the anterior lobe of the pituitary or of the adrenal cortex as well as many individuals with hepatic dysfunction would be insulin resistant, whereas patients with primary insulin deficiency diabetes should have normal insulin sensitivity. Therefore, the modified glucose insulin tolerance test which was previously introduced by the authors was utilized for the estimation of the insulin sensitivity of these same 22 patients. This procedure consists of the intravenous administration of 25 grams of glucose in 50% solution followed 30 minutes later by 0.1 unit of insulin/kilo/ body weight intravenously. A normal insulin sensitivity is indicated by a return of the blood sugar level to fasting within 75 minutes.

By this means the endocrine type of diabetes as indicated by the change in serum inorganic phosphorus was subdivided into a type due to overactivity of the insulin antagonists of the anterior pituitary or of the adrenal cortex and a type due to primary insulin deficiency. A comparison of the results thus obtained with those obtained by the change of the absolute lymphocyte count and the serum inorganic phosphorus after glucose showed a correlation as to pathogenesis in 85% of the cases.

In summary then, as seen from Table 1, the patients having a non-significant decline of the serum inorganic phosphorus combined with a normal decline of the absolute lymphocyte count and normal insulin sensitivity are considered to have a diabetes due to primary insulin deficiency. The individuals having a non-significant decline of the serum inorganic phosphorus associated with insulin resistance and a lack of a normal lymphocyte response probably have a diabetes due to dysfunction of the pituitary-adrenal axis. The pattern of the third group of patients, namely a normal decline of the serum inorganic phosphorus associated with a normal decline of the absolute lymphocyte count and in most cases an increased insulin resistance, would indicate a diabetes due to hepatic dysfunction.

Since attempts have repeatedly been made to treat diabetes with other substances besides insulin such as androgens or estrogens with the purpose of supressing anterior pituitary function or with regimens directed at compensating hepatic dysfunction and since in most reported series of cases a certain percentage were improved, it is felt that if by this means the etiologic factors of the diabetic syndrome could be properly established in the individual patients, a more rational approach to therapeutics would be made possible.

Delivered before the New York Section AACC at Symposium on Diabetes, December 9, 1952.

THE ROLE OF A MODERN CHEMISTRY DEPARTMENT IN A HOSPITAL

by

Albert E. Sobel

The role of the chemistry department in a hospital is a dynamic one. The advances are rapid, revolutionary, and cause improvements that are of great importance to the medical profession. Because of the kinetic nature of the field, one cannot follow traditional formulae, but must depend upon the originality, resourcefulness, and cooperation of the men who bring this newer knowledge to medicine. One can, however, utilize the classical principles of reliability and trustworthiness of the work accomplished as a guiding principle. While chemistry has a great deal to contribute, these contributions may be sterile from the medical point of view, unless the chemist seeks out the experience of the clinician. One of the great impeti in focusing the knowledge gained into fruitful fields of human value, originates from clinical experience. The two, clinical and chemical experience, are therefore mutually interdependent at present, and will continue to be more so in the future. In view of the above considerations, the following policy is advocated for a department of biochemistry in a hospital:

(1) The analyses should be done with such accuracy and understanding as to inspire full confidence on the part of the medical staff.

(2) New methods should be introduced and adapted to the growing needs of the hospital, anticipating demands whenever possible.

(3) The cooperation of the members of the laboratory and the clinical departments should be inspired by undertaking and cooperating in enterprises in which the other departments are interested.

(4) Independent chemical research which is of ultimate medical interest should be undertaken.

(5) An educational program in laboratory sciences should be fostered to make the clinical staff aware of the possibilities and limitations inherent in laboratory methods, and thus stimulate improved diagnosis, treatment, and investigative work.

In order to carry out suggestion (1) it is necessary that fresh and uncontaminated samples be obtained. To ascertain this, it is essential that the collection of blood samples be under the jurisdiction of the Biochemistry Department. One way of establishing this desideratum is to assign two junior and one senior intern to chemistry, who in return for this work receive training in the chemical approach to medicine with full opportunities for research. The other alternative is to assign a well trained technician whose sole duty would be the taking of blood samples. The first plan has the advantage from the hospital's point of view, inasmuch as when these men are given rotating internships following their period of training, they will emphasize the study of the chemical changes in a patient in a more intelligent fashion. Moreover, these men will be in a better position to undertake research later on. Those men who go directly into practice will be more valuable on hospital staffs.

Once it is known that the blood is free of chemical alteration, the chemist can then check his determinations by using the same criteria that are used in the establishment of a newly developed method, without fear that error in the taking of blood will invalidate his work. This consists of running first a known solution, then recovering added amounts of a known solution to the blood quantitatively, and finally running all determinations in duplicate.

To keep the chemist interested, the clinical significance of the values should be discussed regularly. Moreover, research on methods in their spare time should be encouraged, as this will exemplify the pitfalls of everyday work. However, since each individual needs special treatment, a uniform recipe cannot be prescribed in advance.

To organize the routine work, special slips should be made for chemistries, where the various types of determinations would be listed. The men requesting these determinations would check the type of determination necessary.

(continued on following page)

BOSTON SECTION

On November 20, 1952, the Boston Section held its second meeting of the 1952-53 season. Held at the Stearns Auditorium of the New England Medical Center, the featured speaker was Dr. Ralph Dorfman of the Worcester Foundation, whose subject was "The Metabolism of the Neutral Steroid Hormones."

As well as outlining the physiology of the major groups, the androgens, estrogens, and corticoids, the speaker also considered the methods for their determination. Urine, in general, is the specimen of choice, although blood, in spite of lower concentrations, may now by studied somewhat profitably by paper chromatography.

Analytically, the Zimmerman reaction (m-dinitrobenzene) appears to be highly specific for the 17-ketosteroids. A carbonyl group elsewhere, as on a sidechain, contributes only a negligible amount of color.

The Pettenkofer reaction has been used to determine dehydroiso-androsterone, as well as digitonin precipitation. Adrenal cortical hormones having an alpha keto group on the sidechain may be determined by copper reduction methods.

After the speaker, a business meeting was held which chiefly concerned itself with both expanding the section and insuring maximum attendance at meetings. The membership, having been advised of the matter beforehand, contributed many suggestions. The major proposal adopted creates a second meeting each month; this one will have no featured speaker but will rather concern itself with common daily analytical problems, discussed by a panel drawn from the membership itself.

The Boston Section held its fourth meeting of the current season on the evening of January 15, 1953, at the Stearns Auditorium of the New England Center Hospital. The speaker of the evening was Dr. L. B. Rogers, Associate Professor of Chemistry at the Massachusetts Institute of Technology. His subject was "Analytical Errors," which dealt chiefly with measurement instruments and their limitations.

Beginning with pH instruments, he stated that the meter-type has an accuracy of no greater than one scale division, and hence, in his opinion nothing is gained by estimating beyond. Further, lack in accuracy results with change in temperature of buffer solutions, and this is further complicated by the fact that different buffers may not respond similarly with identical temperature changes. He pointed out that pH values above 8.00 are affected by sodium error, unless the electrode is made of a lithium glass instead of a sodium glass. To illustrate this latter adverse effect, a solution whose pH may actually be 11.00, might read about pH 10.2. The magnitude of error rises with the pH.

Even in precision spectrophotometers, Professor Rogers declared, errors exist which are not always considered. Again there is the meter error which approximates one scale division if percent scale is used, although null-balance meters are better due to great sensitivity of the potentiometer. Also, the mechanical components may not constantly yield their greatest reproducibility, which, with fatiguing of the phototube, may amount to considerable discrepancy.

Galvanometers should be read for maximum accuracy between 20 and 60% transmission. The minimum error may be mathematically demonstrated to occur at 36% transmission. In the ultraviolet, because peaks are much sharper, slight mechanical defects of the wavelength setting may introduce enormous error. This can be appreciated when one considers that benzene

---

THE ROLE OF CHEMISTRY

It will become necessary to emphasize to the clinical staff the significance of the determinations, as well as their limitations, as otherwise a great deal of unnecessary work may be requested once the staff has full confidence in the laboratories. On the other hand, certain determinations which are important in the management of the patient may be overlooked.

A 24-hour emergency service, 7 days a week, should be organized in a modern hospital. In the long run, this will be best accomplished by a professional staff, rather than medical students or the intern staff.

Suggestion (2) will grow out of contact with recent developments. For example: it is definitely necessary that a new system of ultramicro chemistry be developed for studies on newborn children where the supply of blood is limited. Part of the problem has been already solved by the chemist, and only needs adaptation to medicine. Such techniques, once established should be incorporated into the usual routine practice. Another example is the significance that hormone and additional enzyme determinations may have in disease. There are many other such examples, of which the above two are representative.

Suggestion (3) should be the basic policy of the department. Close contact should be maintained with the pathologist, bacteriologist, serologist, hematologist, and especially with the clinician, since all of these groups are mutually interdependent. The best way of developing a cooperative spirit is to work with the men in the various departments, discuss the chemical phases of their problems, and vice-versa.

Suggestion (4) should be left to the judgment of the chemistry department. The work under this heading, however, should stimulate and improve the department of chemistry by fostering a grip of the fundamentals of the department.

Suggestion (5) should consist of

(a) Organized lectures on the fundamentals of clinical chemistry to the House Staff, to medical students when the hospital has connections, and also to the physician out in practice.

(b) In addition, regular participation in clinical departmental conferences should be undertaken to understand the medical point of view and to present the chemical thoughts that occur in explaining diseased conditions. Such activity will be an important spur to the chemist in directing his energies into constructive and fruitful channels as an investigator.

(c) Educational activities should also include inviting chemists who work in the fundamental aspects of the topics, to present recent developments which can provide the thoughts and techniques for further expansion of clinical chemistry and avoid the danger of the chemistry department becoming a poor imitation of a medical department.

(d) Seminars by members of the staff, oriented along the daily problems encountered, are also a desideratum.

It is this author's opinion, based on personal experience, that if the path outlined above is pursued, the recognition of chemistry as an integral, yet independent function of a hospital, is inevitable and only a matter of time.

for instance has several deep absorption bands within only 10 millimicrons.

In flame photometers of the filter type, error is introduced by what might be termed "light leakage". The passage of calcium along with sodium illustrates this. Again, the nature of the anion present may affect emission. In this regard, the emission of copper is affected if the chloride or nitrate ion is present. Even in the determination of sodium and potassium, the presence of one increases the spectral emission of the other.

PHILADELPHIA SECTION

The second meeting of the 1952-53 season of the Philadelphia Section, American Association of Clinical Chemists, was held at 7:45 P.M. on Tuesday, November 25, 1952 in Alumni Hall of the Hospital of the University of Pennsylvania. Prior to the meeting, there was an informal dinner in honor of the speaker at the Lido Restaurant.

The president, Dr. Cecilia Riegel, introduced Dr. James Walker, Jr., John and Mary R. Markle Fellow, Department of Surgical Research, University of Pennsylvania, Philadelphia, Pa., who spoke on "Fluid Balance."

After discussing the advantages and disadvantages of the various methods that have been proposed for the determination of blood volume in problems involving fluid balance, Dr. Walker considered in detail the Evans Blue dye procedure which he has used over a period of several years in carrying out determination in a very extensive series of normal individuals and of surgical patients both before and after treatment with blood, blood plasma, various blood plasma extenders, and crystalloid solutions. Numerous lantern slides were used in illustrating the conditions of fluid balance that are encountered clinically and the effectiveness of various means of treatment.

In discussing the technical details of the blood volume method, Dr. Walker pointed out the possible sources of error and the steps that he has taken to keep them at a minimum. Significant errors from turbidities are minimized by preventing heating of plasma specimens while they are being centrifuged. By using standards prepared from the subject's undyed plasma, he is able to eliminate rather large and erratic errors in total blood volume that would otherwise be obtained in about twenty percent of the patients studied. This is especially important in patients who have received plasma extenders which vary in the capacity they have for binding dye. He has not been able to explain erratic results that are obtained in a large number of jaundiced patients. Further details of Dr. Walker's blood volume technique and his experiences with its use in studying fluid balance are to be published.

After the lecture, Dr. Walker answered numerous questions related to his subject.

CALIFORNIA SECTION

William Werkheiser, Ph.D., Instructor in Biochemistry and Nutrition, University of Southern California Medical School, was guest speaker December 2, 1952 at the Veterans Administration Center, Los Angeles. Dr. Werkheiser, with his special aptitude and background in chromatography and associated instrumentation, reviewed the "Practical Applications of Paper Chromatography". He touched on many of the valuable variations in qualitative and quantitative paper chromatography with special emphasis on the apparatus he has employed for ionophoresis and electrophoresis on paper strips.

Clinton H. Thienes, M.D., Ph.D., Director of the Institute of Medical Research, Huntington Memorial Hospital, Pasadena, was guest speaker January 6, 1953 at the Los Angeles County Hospital. Dr. Thienes is the well-known authority in pharamcology and toxicology who headed the department at the University of Southern California for almost twenty years. During his discussion of "Poisons and the Clinical Chemist", he considered several important poisons, evaluated a number of texts on the subject, and gave rather detailed recommendations on the proper general procedure for collection and analysis of biopsy and autopsy material, supplemented by several personal anecdotes drawn from his long medical practice.

BOOK REVIEWS

A LABORATORY MANUAL OF PHYSIOLOGICAL CHEMISTRY, 7th Ed. by D. Wright Wilson, University of Pennsylvania, 293 pages $3.25 The Williams and Wilkens Co., Baltimore 2, Md. 1952

This laboratory manual can be more adequately described as a basic manual of clinical chemistry, and if the text is followed by lecture work, then Professor Wilson's university presents a rather good course.

The book is an excellent primer to stimulate student interest in clinical chemical procedures. Certain determinations have been revised for teaching purposes, but in these cases notations are made to show just where accuracy has been sacrificed.

About a third of the experiments concern themselves with basic experiments of biochemistry: carbohydrates, proteins and lipids, with demonstrations of paper chromatography technique and isolation and preparation of pure biological compounds. The rest of the volume describes experiments with gastric juice, blood and urine. Colorimetric determinations are arranged for the Klett photometer.

Here is a good laboratory manual for teaching basic clinical chemistry. With the shortage of technical help in our hospitals, one would be quite pleased to get a graduate who had performed all the experiments outlined in Dr. Wilson's manual.

CONDENSED REVIEW OF PHARMACY by George W. Furo. John Wiley & Sons, Inc., 440 Fourth Ave., N.Y. 16, N.Y. 1952.

In this Condensed Review of Pharmacy, the chemist working with pharmaceuticals, or seeking information concerning the properties and actions of various drugs might consult this book to good advantage. The book condenses, in tabular form, the U. S. Pharmacopolia and the National Formulary and presents pertinent information on such topics as solutions of the U. S. P., Materia Medica, animal and plant drugs, common names of official drugs and toxicology.

The sections on common names of Official Drugs and Biological Preparations showed to be of special interest to those working in a clinical laboratory. The section on toxicology is concise, and will prove valuable to an understanding of the basis of emergency treatment of poisoning.

IT'S STANDARD PROCEDURE to make STANDARD Your Source of Supply

STANDARD'S SPECIALS of the MONTH!

Keeping Pace with your Laboratory Needs!

From Raw to Pure Water

"DEEMINAC"

WITH JUST A SQUEEZE

MAKES PURE WATER INSTANTLY

Simple to operate. Fill the polyethylene bottle with ordinary tap water, plug-in the filter and squeeze the bottle.

Water processed by "Deeminac" is equal to triple distilled water.

"Deeminac's" filter is easy to replace. Just remove the old filter and replace it with a new one exactly as you would if you were filling the bottle.

The filter tells you when to replace. With use, a distinct brown-yellow band works its wty up the filter towards the spout. When the filter has completely changed color, it must be replaced.

"Deeminac" is economical. The smallest filter will purify 20 gallons of water.

The "Deeminac" filter is made of specially blended and processed ion exchange resins which grip and hold all ionized impurities huch as minerals and salts of calcium, sodium, iron, magnesium, as well as sulphates, chloride bicarbonate and silicate.

"DEEMINAC" comes in three handy sizes.

6 oz. bottle with 2 oz. filter
8 oz. bottle with 3 oz. filter
16 oz. bottle with 4 oz. filter

Cat. No.	Size	Ea. Complete
54459A—	6 oz.	$1.75
54459B—	8 oz.	2.25
54459C—	16 oz.	3.00

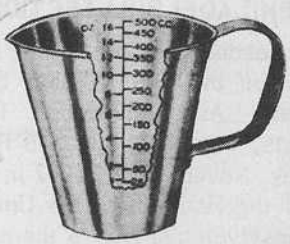
Cat. No.	Extra filters	Supplied 2 to a box
54459D—	2 oz. Filter only	$2.50 per box
54459E—	3 oz. Filter only	3.50 per box
54459F—	4 oz. Filter only	4.50 per box

New! Stainless Steel

BEAKERS

Graduated — Pourout Lip — Tapered Shape

- English and Metric graduations
- Rustproof and stainproof with most acids
- Fit inside each other to stock—save space
- Tapered style
- Drawn from heavy 18-8 stainless steel
- Graduations die-embossed for long life
- A handy graduate



SAVE MONEY—THEY ARE UNBREAKABLE

Cat. No.	Size	Each
24435A—	5 oz. (150 cc) without handle	$1.90
24435B—	8 oz. (250 cc) without handle	2.10
24435C—	16 oz. (500 cc)*	3.10
24435D—	24 oz. (750 cc)*	4.10
24435E—	32 oz. (1000 cc)*	4.50

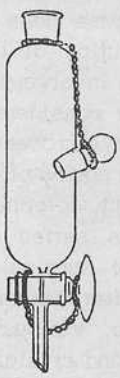
*Available with or without handle—specify when ordering

Save Your Glassware

USE STAINLESS STEEL LEASHES

The five sizes offered provide a range to fit practically every size and type of glassware

- Made of non-corrosive stainless steel
- Resistant to oils
- Long-lived, usually outliving the glassware to which it is attached
- Fits the glass snugly and holds tightly, yet permits glass to expand or contract under normal temperature changes
- Consists of two flexible stainless spring loops connected by a stainless steel chain
- Small spring loop is simply slipped over stopper or stopcock plug and the large loop is slipped over the neck of the vessel or shell of stopcock
- Also used to maintain tension on ground joints and wash bottles



Cat. No. 94550

DIMENSIONS

Size	Ex Small	Small	Med.	Large	Ex. Large
Length Overall	70	80	95	125	145
Diam. large loop	8	11	16	24	35
Diam. small loop	7	9	10	11	13
Chain length	45	48	57	75	75

MEASUREMENTS ARE GIVEN IN MM.

Extra Small	$1.35
Small	1.45
Medium	1.68
Large	1.90
Extra Large	2.10
Assorted	1.80

PRICE SHOWN IS THE PRICE PER DOZEN

STANDARD SCIENTIFIC SUPPLY CORP.

34 West 4th Street • New York 12, N. Y.

LABORATORY APPARATUS — REAGENTS AND CHEMICALS