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The Department of Medicine

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In the admirable account of the Department of Anatomy which Robert Terry recently published in the Quarterly, he was able to trace the history of an ideal, to discuss progress over a period of years and to record the splendid results that may be attained by the continuous pursuit of a well conceived program. It would be desirable to apply a similar method to the discussion of the Department of Medicine. Unfortunately, however, a historical sketch of its many ramifications would require much more space than the editor has allowed and would preclude any adequate presentation of present activities. The following remarks, therefore, concern the department as it is today, with little mention of the past and with only occasional comments on the general direction of its development and its needs for change or expansion.

Scope and Purposes

The responsibilities of a modern department of medicine are numerous and exacting. At Washington University, as elsewhere, it is assigned the task of instruction in history taking, physical diagnosis, clinical microscopy and other methods of case study. It must devote much attention to the anatomical, physiological and chemical basis of symptoms. It must arrange to offer adequate instruction in the natural history of all important general and organic diseases. It must establish and maintain standards for case study which will serve as guides to the student in future practice, whether this be in medicine, pediatrics, obstetrics or surgery. On the department of medicine also falls the responsibility of maintaining laboratories

where valid microscopic, chemical, bacteriological, immunological, metabolic and electrocardiographic tests may be performed and interpreted. It must offer adequate instruction in the rapidly developing field of therapeutics. It must arrange to care for a relatively large number of both ambulant and bed-fast patients. It shares with other clinical departments the responsibility of stressing social and psychological aspects of disease. Finally, and this of course applies to all departments of a medical school, it must conduct its teaching in such a manner that students will not be content with obvious and established facts but will be constantly stimulated to investigate and to advance the knowledge of medicine. This is only a partial list.

Staff. To conduct such a department requires a large staff. At present the department of medicine has on its rolls 84 physicians who participate actively in teaching, clinical work or research. Of these, only 10 are strictly full time and this list includes four members of the resident staff at Barnes Hospital and two who are classified as research fellows. As in the past, the department depends for the greatest part of its important work upon men who are more or less actively engaged in the practice of medicine. A few of these who spend relatively large amounts of time in the service receive stipends or subsidies from the department. Some of the most valuable and significant clinical teaching is undertaken without any remuneration. For the interest, loyalty and service of this devoted group the writer of this summary statement wishes again to express his gratitude and appreciation.

Seventeen years ago, as now, the nucleus of the department consisted of Albert Taussig, Warren Elmer, William Olmsted, Drew Luten, Joseph Larimore, Walter Baumgarten, Jerome Cook, Llewellyn Sale, Louis Hempelmann, Walter Fischel, Frank Gorham, Charles Eyer mann, Arthur Strauss, Samuel Grant and Alfred Goldman. Since that time, a very few men have been imported from other medical centers. For the most part the staff has grown by accretion, each year adding its quota of residents and house officers until at present it constitutes in ability, accomplishments and interests a group of which any university might well be proud. That it is insufficient to fulfil the possibilities of development in the Depart-

ment of Medicine can be regarded as no criticism of the quality and attainments of the individual members. It is only an indication of the tremendous complexity and extent of the teaching and clinical responsibilities in a modern medical department.

Clinical Services

The activities of the Department of Medicine are chiefly concentrated in Barnes Hospital and in the Washington University Clinics. In addition it has clinical responsibility for a medical service at City Hospital and a large share of responsibility for the care of patients at the Homer G. Phillips Hospital. It has access to the tuberculosis service at Koch Hospital and to the St. Louis City Isolation Hospital.

Barnes Hospital. The service at Barnes Hospital consists of about 80 beds. The Jacob Porter Tirrill Metabolism Ward, which houses 14 patients, is conducted as a somewhat separate service. With its adjoining special diet kitchen and chemical laboratory it offers admirable facilities for the treatment of diabetics and of others who require carefully regulated diets or metabolic investigation. The new colored ward in the basement of the medical wing will provide greatly improved arrangements for the care of a selected group of negro patients.

During the school year Dr. Barr and Dr. Alexander act as senior physicians on the general ward services. Routine daily rounds are covered at various times during the year by a group consisting of Drs. Grant, Goldman, Bulger, Kountz, Moore, Myers, Hageman, Duden and Bromberg. The metabolism ward and laboratory are under the direction of Dr. Cyril MacBryde. This service has been closely integrated with the diabetic and endocrine clinics in the Outpatient Department and during the last two years with a large metabolic clinic at the St. Louis City Hospital. Recently its work has been greatly strengthened by the participation of two research fellows, Dr. Harry Mantz, now in the military service, and by Dr. Dante Castrodale. The dietetic work is under the competent supervision of Miss Marjorie Jorgensen.

Washington University Clinics. In the Outpatient Department medical patients are received both morning and afternoon. The morning session is conducted as a teaching clinic for senior students and is in active charge of Dr. Robert

Elliott. The afternoon clinic for routine care and admission is conducted by Dr. Joseph Edwards and Dr. Malcolm Cook.

A long continued effort has been made to support and develop special clinics where large groups of patients suffering from the same or closely related maladies may be assembled for study. While these special clinics have had as their primary purpose the provision of elective courses for senior students and of educational opportunities for internes and residents, they also provide valuable nuclei for postgraduate teaching in the medical subspecialties.

The development of each clinic requires a considerable personnel and sustained active interest over a period of years. The number of patients must be sufficient to allow for clinical variation and to provide extensive experience for undergraduate and postgraduate groups. The staff must be large enough to permit thorough and even leisurely study of each clinical problem and thus to provide an interest which will attract successive groups of students.

(a) *Clinic for Cardiovascular Diseases.* The Cardiac Clinic adjoins the Heart Station. For years it has been maintained through the loyal and devoted services of Dr. Arthur Strauss and Dr. Hiram Liggett. Dr. Drew Lutten has spent much time in the consideration of difficult clinical problems; the interest of Dr. Kountz and Dr. Jensen have been important factors in its development. Recently the work has been much strengthened by the efforts of Dr. Edward Massie and Dr. John Smith. During the past few years Dr. Julius Jensen has done much to encourage clinical study of cardiac cases both in the wards and the outpatient department of the St. Louis City Hospital and has been able to integrate these activities with the studies of other members of the cardiac group.

Closely associated is the work of Dr. Kountz and Dr. John Smith on peripheral vascular diseases, an enterprise which has been greatly aided by the "cold room" constructed by Dr. Lawrence in the Clinic Building.

(b) *Chest Clinic.* The Chest Clinic conducted for many years by Dr. Singer and later maintained and developed by Dr. Alfred Goldman is now under the active supervision of Dr. Dan Myers, with the help of Dr. David Skilling and Dr. L. C. Miller. At present its activities are closely integrated with the Medi-

cal-Surgical Chest Service at Barnes Hospital. Dr. Myers has also found time to establish contacts with both of the City Hospitals and to keep in touch with the activities of Dr. Kettelkamp and Dr. Murphy at the Koch Hospital. Although the staff of the Chest Service is still insufficient, it offers even in its present form excellent opportunities for clinical investigation and teaching.

(c) *Allergy Clinic.* For twenty-five years Dr. Charles Eyer-
mann has been conducting and developing insofar as facilities permitted an outpatient department for the study of allergic states. Close contact has been preserved with the ward service and with the studies which Dr. Alexander and others have conducted on the wards. Quite independently Dr. Malone Stroud has developed a large service at the Barnard Free Skin and Cancer Hospital for the study of contact dermatitis and other allergic states. Recently there has been a successful attempt to correlate the medical and otolaryngological work and to establish a more unified group for the clinical study of allergy. For the past year the entire program has been greatly strengthened by the addition to the staff of Dr. Stanley F. Hampton. No mention of the allergy group can be complete without reference to the excellent work of Miss Mary Johnson in the preparation of antigens, in routine testing as well as in investigation.

(d) *Diabetic and Endocrine Clinics.* These clinics maintained for many years through the interest and initiative of Dr. William Olmsted have been continued by Dr. Harold Bulger and Dr. Cyril MacBryde. They are closely integrated with the work of the Jacob Porter Tirrill Metabolism Ward and also with the Dietetic Clinic which has been so effectively developed by Miss Ruth Kahn.

(e) *Gastro-Intestinal Clinic.* For many years the Department of Medicine has maintained a fellow in gastroenterology who has had the opportunity of working with Dr. Joseph Larimore in the Mallinckrodt Institute in the morning and in the gastrointestinal outpatient department in the afternoon. This plan has provided for expert training of a number of young men, many of whom have left St. Louis. It has finally resulted in the assembly of a group for the study of gastrointestinal diseases in the outpatient departments. At present this con-

sists of Dr. Bruce Kenamore, in charge, Dr. John Horner, Dr. Robert Kelley, Dr. Harold Scheff and Dr. Alfred Fleishman. Even with this staff it has not been possible to devote sufficient attention to development of outpatient services in the City Hospitals, although an encouraging start has been made.

(f) *Venereal Clinic*. On three evenings each week a clinic is held for the treatment of venereal diseases. Formerly conducted by the dermatological staff, it is now a joint enterprise in which internists, dermatologists, neurologists, urologists and obstetricians participate. This is one of the few clinics which is now ready for use in postgraduate teaching. At present Dr. Louis Aitken is in charge of the general clinic, Dr. Lee D. Cady of neurosyphilis, and Dr. Rogers Deakin of urology and of the management of gonorrhea.

City Hospital. The Department of Medicine has clinical responsibility for one-third of the medical service at City Hospital. The word is under the directorship of Dr. Thomas Findley. Dr. Julius Jensen acts as Director of the Clinics and is responsible over a considerable part of the year for the care of patients in the wards. Rounds are also made by Dr. Charles Eyer mann, Dr. Frank Gorham, Dr. Marshall Seibel, Dr. Sim Beam, Dr. Cecil Charles and others. Development at City Hospital has been delayed by many factors but chiefly because the staff in the medical department has not been sufficiently numerous to cover several large clinical services. The gradual increase in the number of available consultants offers hope of subsequent progress.

Homer G. Phillips Hospital affords a magnificent opportunity for clinical service and for teaching. Under the present arrangements the care of approximately 180 patients, including those available in two tuberculosis wards, are under the supervision of the Department of Medicine. The opportunities for clinic development are almost unlimited. Dr. Leo Gottlieb is director of this service and has established many improvements in the past two years. The staff which can be assigned to him is totally insufficient. Dr. Harold Scheff has been particularly helpful. Dr. Barrett Taussig, Dr. John Seddon, Dr. John Smith and Dr. Raymond Holden have aided in the clinical care of patients. Dr. Myers has supervised the tuberculosis wards, Dr. Carl Moore has been available for consultations in

hematology, and Dr. Bromberg has consulted in difficult problems in syphilis. The cooperation of the administration of the hospital has been in every way satisfactory.

Teaching

The instruction of the Department begins with the second trimester of the sophomore year and continues until the student graduates.

In the first course of Introductory Medicine, cases are presented for observation of physical signs but particularly for the purpose of demonstrating how fundamental knowledge of anatomy, physiology and chemistry may be utilized in the study of management of disease. Emphasis is placed on the analysis and understanding of symptoms. There is a conscious effort to avoid discussion of the classification and the natural history of disease. During the latter half of this course, psychological factors of disease are presented concurrently by Dr. Whitehorn.

The teaching of Introductory Medicine is integrated closely with the instruction in Physical Diagnosis. This is conducted by Dr. Dan Myers whose extensive knowledge of the lungs and heart and whose sound methods of teaching make this course one of the most valid and at the same time one of the most appreciated in the entire medical curriculum. Section work in Physical Diagnosis at the bedside was supervised this year by Dr. Oliver Abel, Dr. William Becke, Dr. Joseph Edwards, Dr. Truman Drake, Dr. David Skilling, Dr. Lee Harrison, Dr. Sim Beam, Dr. Edward Cannady, Dr. John Smith, Dr. Harold Friedman and Dr. Keith Wilson.

Clinical Microscopy is taught during the third trimester of the second year by Dr. Carl Moore with the very able assistance of Dr. Harry Agress, Dr. Henry Allen, Dr. Hiram Tsuchiya and Miss Olga Bierbaum. Dr. Moore's extensive training and experience, his investigative approach and his clarity of presentation contribute to the popularity of this course.

The instruction of the second year is so arranged as to equip the student with those techniques which are essential to case study.

In the third year, there are two major courses. The first

formerly conducted by Dr. Samuel Grant and Dr. Alfred Goldman consists now of a series of lectures and demonstrations in which about twenty-five members of the department participate. The intention is to acquaint the student with the natural history of the most important medical diseases. It is a systematic review of our heritage of medical knowledge.

The second course is a clerkship of eleven weeks which at present is conducted at the Homer G. Phillips Hospital. Each week a student is asked to study three or more patients. A tutor is assigned to a group of eight students and spends two hours each morning with them. This is fairly satisfactory but would be much better if each tutor could have a smaller group and longer contact during the working day. Even with the present arrangement, there is opportunity for the establishment of close relationships between students and instructors.

Dr. Barrett Taussig is in active charge of this clinical clerkship and has received able support from Dr. John Seddon, Dr. John Smith, Dr. Keith Wilson, Dr. Raymond Holden and Dr. Truman Drake. This is one of the very important courses since it should establish the habit of obtaining accurate, discriminating clinical histories and of performing thorough physical examination and exact clinical microscopy.

During the period of the clerkship clinics are held four times each week at Homer G. Phillips Hospital. Twenty-five of the best teachers of the department participate in this instruction and during the course of a trimester discuss subjects with which they are best acquainted. Juniors also attend the Saturday amphitheatre clinic.

During the senior year only eight weeks are now assigned for medical clinical clerkships. For one month of this time the entire day is spent in the wards of Barnes Hospital. Both medical and neurological cases are assigned for complete study and report. Ward rounds and frequent informal conferences are held by Dr. Barr and Dr. Alexander and by members of the neurological department. Special rounds are conducted each week at Isolation Hospital by Dr. Carl Harford.

The clinical clerkships in the Washington University Clinics are designed to acquaint the student with the problems of early illness and preventive medicine. The groups are divided between the general medicine clinic, under Dr. Robert Elliott,

the chest clinic under Dr. Dan Myers and the heart clinic under Dr. Edward Massie. This course is given its greatest value by the devoted service of a number of experienced consultants who have included Dr. Albert Taussig, Dr. Harry Alexander, Dr. Walter Baumgarten, Dr. Llewellyn Sale, Dr. Jerome Cook, Dr. Louis Hempelmann, Dr. Walter Fischel, Dr. Frank Gorham, Dr. Harold Bulger, Dr. William Kountz and Dr. Alfred Goldman. By the time the senior students take this clerkship, they are in a position to appreciate and to profit by the instruction of such teachers.

Amphitheatre Clinics are conducted each Saturday during the year by Dr. Taussig, Dr. Alexander or Dr. Barr.

The formal teaching of therapeutics is now entirely concentrated in a 33 hour course held each Thursday morning during the senior year. About twenty-five members of the department participate in this course. Although much incidental instruction or treatment is given during other courses in the third and fourth year, the time allowance for this important subject is entirely inadequate and reflects the meagre armamentarium of the past rather than the abundant resources of today.

Investigative Activities

Research in the Department has been delayed and curtailed by the multiplicity of more urgent clinical and teaching duties and also in part by the paucity of funds residual after the needs of routine laboratories, teaching and clinical activities had been met. Investigation to be valid requires uninterrupted time, contemplation and extensive provision for trial and error. Except under extraordinary circumstances important research is not accomplished in interstices of time or by those who devote most of their attention to other activities. Investigation is expensive. Each separate enterprise will usually require a considerable subsidy for adequate equipment and expert assistance. In spite of difficulties however, the department has been able to start several investigative projects which should with good fortune develop steadily during the next few years.

Hematological Laboratory. Note should first be made of the laboratory for the study of diseases of the blood which in its organization and support offers an example of what may be

required in the development of other investigative projects. This enterprise is under the direction of Dr. Carl Moore who has the invaluable assistance of Miss Olga Bierbaum and Miss Virginia Minnich. The laboratory has in the three years of its existence become a mecca for the resident and interne staff and for many of the senior students. Besides being a most satisfactory stimulus to more thorough study of clinical problems, the laboratory has been able to undertake a relatively large research program. This has included investigation of the site of absorption of iron from the gastrointestinal tract and of the effect of ascorbic acid, bile salts and hydrochloric acid on iron metabolism; a beginning of a study on the nutritive factors controlling the function of bone marrow; a study of vascular abnormalities in purpura and observations on the experimental transmission of leukosarcoma. Collaborators in these projects have included many members of the resident and interne staff. Next year Dr. William Arrowsmith, now resident in medicine, will receive a research fellowship from the American College of Physicians which will enable him to spend a year with Dr. Moore. Funds for a second fellowship have also been established. Preliminary observations have already been made upon the fate of radioactive iron in the body. This work will be continued and will be correlated with the distribution of iron as determined by the micronincineration method of Dr. Gordon Scott.

The Jacob Porter Tirrill Metabolism Ward and Laboratory. This station is now under the active direction of Dr. Cyril MacBryde. The studies which he started some years ago upon insulin sensitivity and insulin resistance are being continued and extended. With Dr. Dante Castrodale, Miss Olga Bierbaum and Dr. Helwig of the Department of Pathology he has made during the past two years a clinical and experimental investigation of the toxic properties of stilbestrol and of other natural and synthetic estrogens. With Dr. Harry Mantz, he has been studying the clinical effects of histone insulin and other new forms of insulin under a grant from the Ely Lilly Company. With Dr. Barr he has accumulated a large number of as yet unpublished observations on Cushing's syndrome and the adrenogenital syndrome. The developments in the metabolism laboratory during the past few years have been

encouraging and should be a source of satisfaction to the generous donor of the Jacob Porter Tirrill Metabolism Ward.

Investigation in Renal Physiology. Dr. Thomas Findley has been responsible for the receipt of a generous subsidy from the Smith, Kline and French Laboratories which has enabled him to pursue studies of importance at the St. Louis City Hospital and in the laboratories of the Department. With Dr. Harvey Lester White, he has made extensive observations on the factors concerned with renal excretion. He has studied these and other factors in the clinical state of diabetes insipidus. With Dr. Joseph Edwards and Dr. Louis Julianelle he has been actively conducting a most interesting study on the immunological identification of renin. Entirely aside from their fundamental significance, Dr. Findley's investigations are of especial importance in the development of the Department since they may represent a nucleus of research activities at the St. Louis City Hospital.

Laboratory for the Study of Cardiovascular Diseases. For many years, Dr. William Kountz has pursued a clinical and experimental study of cardiac and vascular disease. His training with Dr. Anrep of Cairo enabled him to make many valuable observations upon the revived human heart. His interests have been wide and have included contributions to the better understanding of emphysema, of electrocardiographic interpretation and peripheral vascular disease. During the past three years he has been studying with Dr. John Smith and Dr. Arthur Gilson of the Department of Physiology the heart action by means of a new instrument called the vibrocardiograph. This is a form of cathode ray oscillograph which makes possible an accurate recording of vibration waves which have not been previously recognized. This is pioneer work which promises to have clinical as well as academic significance. Dr. Kountz has also been interested in establishing at the St. Louis Infirmary a station for the study of cardiovascular disease in senescence. This latter enterprise is in its infancy but deserves interest and much greater financial support.

Allergy Laboratory. Ever since Dr. Harry Alexander came to St. Louis he has pursued persistently and continuously investigations upon the nature and management of hypersensitive states. With Dr. Kountz he has made fundamental ob-

ervation upon the pathogenesis and treatment of emphysema. His contributions are well known and have given him a well deserved prominence in the field of allergy. At present he is chiefly occupied with observations upon the effects of histamine in clinical and experimental states.

For many years, Dr. Charles Eyermann has conducted important studies in clinical allergy. Particularly worthy of note are his contributions to the understanding of gastro-intestinal forms of hypersensitization but his interests have been by no means confined to this field. Dr. Eyermann's methods in the clinical study of the patient are an inspiration to all who have had the opportunity of observing them.

Dr. Stanley F. Hampton and Miss Mary Johnson are now engaged in an investigation which promises to facilitate significantly the preparation of antigens for allergic testing. He is also pursuing with Dr. Olmsted the study of the treatment of gastro-intestinal allergy.

Gastro-intestinal Diseases. Perhaps there are relatively few even in our own institution who appreciate the importance of the studies of the function of the gastro-intestinal tract which have been conducted by Dr. Joseph Larimore over a period of the past twenty-five years. Taken together they constitute a unique experience. It is hoped that they will soon be available to all when Dr. Larimore's book on the gastro-intestinal tract, now in preparation, is finally published.

Dr. Olmsted's Investigations. In the midst of a busy practice, Dr. William Olmsted has always found time to conduct clinical investigation. Each year, for a quarter of a century he has been able to make some significant contribution to medical knowledge. His work has received relatively little financial support and has been conducted for the most part with the aid of student assistants, many of whom have been inspired by him to continued efforts in investigative medicine. His studies of the absorption of carbohydrates in the intestinal tract have brought him an international reputation in this field. At present he is occupied with Dr. Sidney Wright and Mr. Tom Callahan of the senior class upon a study of the excretion of ascorbic acid. He is also conducting with Dr. Hampton and Dr. Carl Harford an investigation of the use of completely synthetic diets in disease.

Other Investigations. Among other research activities of the Department of Medicine may be mentioned Dr. Harold Bulger's studies on methods for the determination of uric acid which have just now been completed with the able assistance of Miss Helen Johns; Dr. Barr's studies with Jean Fischer Bennett on the determination of tissue lipases; the investigations of Dr. Leon Bromberg and Dr. Malcolm Cooke in fever therapy; Dr. Paul Hageman's investigation of sulfonamide compounds undertaken last year with Dean Shaffer; Dr. Carl Harford's recent studies of the effect of sulfaguanidine on the intestinal flora; the development by Dr. Bruce Kenamore of an instrument by which biopsies may be obtained during gastroscopy; Dr. Myer's study of the localization of pulmonary suppurations and Dr. Massie's observations on the effects of the sulfocyanates in hypertension.

Several accomplishments are worthy of special note. For many years Dr. Luten has conducted careful studies on the clinical action of digitalis. His classically written book on this subject has exerted throughout the country a profound influence upon the use of a most important drug.

Dr. Julius Jensen for many years has been attending physician to the St. Louis Maternity Hospital. His monograph on the "Heart in Pregnancy" has brought to him an international reputation as an authority on this subject.

During the past three years Dr. Lawrence Thompson with the help of Dr. Joseph Edwards, Dr. Luther Terry and Dr. John Seddon has conducted a study on the treatment of pneumonia. These observations undertaken in both City Hospital and Barnes Hospital have not only constituted a valuable scientific contribution but have also encouraged more careful clinical observation of pneumonia in all hospitals of the group.

Of the research activities of the Department of Medicine only one, Dr. Moore's hematology laboratory, is so organized and supported as to assure continuous progress and development. Other laboratories and investigations have been forced to conduct activities with insufficient funds and often with inadequate technical assistance. At present, the prospect of a greater productivity is encouraging. This can be greatly accelerated, however, by provision of funds for specific re-

search projects which the budget of the Department and of the Medical School is as yet unable to undertake.

In concluding this summary statement, the author wishes to express to every member of the department his heartfelt thanks and his deep appreciation of the loyalty and constant spirit of cooperation which have permitted the department of medicine to attain its present state of development. Progress in a very extensive and complicated enterprise has been possible only through the combined efforts of many workers. Although the past accomplishments of the Department of Medicine have not been inconsiderable, it must be realized by all that they constitute only a beginning and that the possibilities of future development are immensely greater than anything that has been achieved. With the continued enthusiasm and cooperation of so able a staff, the future of the Department of Medicine should be bright.

The Reticulo-Endothelial System: Its Physiology and Pathology*

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Immunity, as currently conceived in the light of the factual evidence accumulated over the past fifty years, consists in the effective interaction of at least two essential components, the one cellular, the other humoral. With the development of vital dyes by Ehrlich,¹ and the demonstration by Goldmann² of their selective segregation in large phagocytic cells throughout the connective tissues, the foundation was laid for studying the protective role of specialized mammalian cells in the disposition of foreign particulate material, both animate³ and inanimate.⁴ The recent chemical synthesis of azo dye antigens⁵ has now provided histo-immunologists with a crucial link in the chain of objective evidence⁶ required to identify this same system of phagocytic cells as the most probable source of circulating, humoral, immune, antibody globulins.⁷ The really tremendous significance of these cellular constituents to mammalian health and survival, therefore, has been gradually but certainly established. Conversely, the physiologic conservational phagocytic activity of this system of cells may become excessive for one or another of the normal circulating elements, resulting in a variety of constitutional pathologic states, which will be analyzed briefly later.

I. Morphologic and Physiologic Considerations

Aschoff and Kiyono⁸ in 1913 very well indicated, and at the same time effectively arbitrated, the two chief divergent hypotheses in the conception and creation of the term "reticulo-endothelial system." By this designation it was implied that the definitive phagocytes of blood and tissues, other than the "microphages" (neutrophilic granulocytes) of Metchnikoff,⁹ could be derived either from connective tissue reticu-

* From the Department of Medicine, College of Medicine, Ohio State University, Columbus, Ohio. Condensed from lecture presented by Dr. Chas. A. Doan at Washington University School of Medicine on March 12th.

lum or from specialized endothelial cells, or from both, depending upon location and circumstance, and, perhaps, definition. At the present time only minor modifications or elaborations of this broad functional generalization may be said to have resulted from the intensive and diversified clinical and experimental investigations carried forward during the intervening years.

In the most primitive connective tissues at least three morphologic types of cells may always be differentiated: fat, cells, endothelial cells, and reticulum cells.

a. Role of the Fat Cell

The lipoblast, forerunner of the widely distributed fat cells of the tissues, arises from undifferentiated perivascular, mesenchymal cells related to the reticulum and entirely distinct from fibroblasts (Maximow, Mallory, Friedrich, Wassermann).

Wells¹⁰ has recently emphasized again the necessity of including adipose tissue within the reticulo-endothelial concept in harmony with the glandlike histologic character of the unfatted fat organs, and in conformity with the evidence that many cells distended with fat are still entirely capable of carrying on other functions. Dogliotti¹¹ has shown that both brown and white fat tissue cells may store vital dyes like other reticulo-endothelial derivatives, which process is especially well seen in the depleted fat cells; and Bremer¹² has demonstrated in the thin cytoplasmic ring in the periphery of fat-distended cells, granules of vital dyes suggesting participation by fat tissue in antibody formation. As might be anticipated, the opposite interpretation of such objective observations has been advanced, Chun Chang¹³ believing his experimentally altered omental and marrow fat cells in the rabbit to be nothing more or less than macrophages with a predominant fat content. He cites the finding of phagocytized hemosiderin and entire granulocytes in such fat-laden cells as circumstantial evidence of a macrophage origin for all fat cells. Certain it is that monocyte and lipid-stimulated epithelioid cells of blood and tissues frequently show a special type of progressive fatty metamorphosis, resulting in ultimate cell rupture in tuberculosis associated with caseation.¹⁴ Hausberger¹⁵ has reported the ability of the

interscapular fat organs to form fat from carbohydrate by way of glycogen deposit in the fat cells. Schoenheimer's studies¹⁶ with fat marked with heavy hydrogen showed immediate deposition of most of the food fat in specific adipose tissue, rather than direct metabolic utilization. The capacity of depleted fat cells to take up water, thus becoming extremely hydropic, has been noted in our own studies of experimental marrow hypoplasia in pigeons,¹⁷ and observations by Wassermann¹⁸ of hydrosis of distended fat cells led him to suggest that adipose tissue may play an important role in water metabolism. The truth probably lies somewhere between the extremes of the positions taken by the various investigators; viz., that lipoblasts are more or less differentiated cells of the connective tissues, predominantly equipped to efficiently store and promptly release essential fatty substances in the normal metabolic economy of the mammalian body, and on occasion, under special circumstances, such cells may take in small amounts of other substances; the true macrophage, conversely, participates, if at all, in fat phagocytosis only incidental to fat necrosis and to other pathologic disturbances involving fat metabolism, as for example the xanthomatoses.

b. Tissue Macrophage

The large highly phagocytic macrophage found in the parenchyma of spleen and bone marrow and scattered throughout the diffuse connective tissues is rarely seen in the circulating blood due to its size and sluggish motility. Such cells divide, giving rise to new, potentially phagocytic units on demand, their ultimate, fixed tissue origin being difficult to determine, being possibly reticulum (Chart 1). They phagocytize large particles of debris, digest whole red and white blood cells, selectively segregate vital dyes, and show intravacuolar reactions to neutral red, with a pH range from 6.8 to 8. Anchored in the sinuses of the liver and presumably deriving from the lining endothelium are functionally and morphologically similar units, the so-called Kupffer cells. In lymph nodes subject to drainage from areas of necrosis or hemorrhage, the sinus endothelium hypertrophies, becomes highly phagocytic, and individual cells may even detach themselves, becoming free and rounded phagocytes.

c. The Monocyte

On the other hand, always to be found in the circulating blood physiologically are the potentially phagocytic monocytes (large mononuclear or transitional cells of Ehrlich), which when stained supravivally with neutral red, reveal a more or less definite rosette pattern of small preformed segregation vacuoles, with constant pH.¹⁹ Their number in the blood is usually a direct reflection of their quantitative, extravascular representation in organs and tissues of the body, and they participate more or less actively in the cellular reaction to a variety of stimuli.²⁰ These blood monocytes appear to arise in the intervascular tissue spaces in association with undifferentiated, fixed reticulum cell hyperplasia, and must undergo a period of development with the elaboration of characteristic mitochondria and specific vacuoles before motility or functional maturity are attained. However, under stress, when engorged with whole blood cells or excessive nonspecific debris, the definitive phagocytes in a given inflammatory area frequently become indistinguishable morphologically in terms of their endothelial or reticular cell origin. The term "macrophage" (big eater) correctly and accurately describes such cells irrespective of their remote derivation.

d. Interrelationships of the Phagocytic Cells of Mammalian Tissues

Starting, therefore, ultimately either from specialized fixed endothelium or from fixed reticulum cells with primitive mesenchymal potencies, certain free phagocytic cells arise, showing more or less differentiating criteria with respect to cell size, morphology, staining reaction, degree of motility, intravacuolar pH, segregation capacity, and selectivity. Under various pathologic conditions and during *in vitro* cultivation, these differences may be either accentuated or minimized. Such firmly established and well-documented observations have resulted in two principal divergent interpretations; first, that all morphologic variations reflect simply different phases in the life cycle and/or stage of functional activity of one cell strain; second, that environmental circumstances more or less modify or efface the original identifying criteria of cells with phagocytic potencies arising from two or more sources.

The evidence adduced to date from tissue culture has tended largely to support the first conception. In the earlier studies the survival in vitro of living blood or tissue cells was associated almost invariably with extreme vacuolization, much of which was degenerative. With improvements in technique, more particularly the determination of essential nutritional elements and optimum gas concentrations for explanted cells, and with adequate provision for elimination of catabolic products, conditions were rendered more nearly physiologic and interpretations have been correspondingly more readily transferable to in vivo phenomena. During recent years in this laboratory, Houghton²¹ has directed in vitro culture studies toward the better understanding of this problem of the interrelationship of blood and tissue phagocytic cells. The monocyte of the normal blood would seem from these observations to have very considerable powers of survival, multiplication, and adaptation to functional requirements, more certainly than can be demonstrated for circulating lymphocyte, or for any of the granulocytic series of cells. Under these conditions definitive "macrophages" appear, which are indistinguishable from the tissue macrophages and which quite obviously have been derived from the circulating blood monocytes.

Ebert and Florey²² modified the Sandison-Clark chamber technique for the in vivo study of the extravascular development of the monocyte in the rabbit's ear. Tissue cells were marked with vital new red, pontamine sky blue, or trypan blue. With the aid of carbon injections, circulating ink-containing "monocytes" were observed to emigrate into the organizing clot on the growing edge of an injured tissue area. However, "though it was thus made certain that the blood monocyte was capable of developing extravascularly into a cell indistinguishable from that frequently called a histiocyte, it was not quite clear that *all* the macrophages present at the developing edge originated from monocytes. It is conceivable that some were due to the mobilization and division of pre-existing tissue histiocytes." While supravital preparations of rabbits' blood stained with neutral red were reported to have been made, no study of the tissue cells under similar conditions is recorded by these investigators. My co-workers and I^{14, 19} have shown that acid diazo dyes in dosages comparable to those used by

Ebert and Florey, while prominently identifying the so-called macrophages or histiocytes already in the tissues, are only rarely, if at all, demonstrable within the monocytic derivatives, if the latter are defined and identified by the rosette of vacuoles, revealed by superimposing vital neutral red upon the living tissues in question. Ebert and Florey interpret their data as supporting the monocytic origin of the tissue histiocyte, but in all fairness, a critical review of their evidence is hardly more convincing or conclusive in that direction than many previous studies. Of genuine interest, from the functional standpoint, however, are their observations suggesting that macrophage-ingested erythrocytes may be completely broken down within two hours, and that these same tissue macrophages, containing ingested vaseline, survived, and remained relatively stationary in position and condition within their rabbit ear "chambers" over an eleven-month period.

From fixed endothelium and from fixed reticulum—either directly, or via the lipoblast-fat cell route, or through the monoblast-monocyte-epithelioid maturational development—may be derived definitive units, which become increasingly difficult to recognize in terms of their origin, as maximum, heterogeneous, nonspecific, phagocytic activity obscures all other cytoplasmic criteria. Under physiologic conditions there can be no doubt as to their individual identity and more or less selective functions: the tissue-distributed macrophages of spleen and bone marrow always contain senile red blood cells in their role of conserver of iron to the body, and an occasional identifiable white cell; the Kupffer cells of the liver and the mesenteric lymph node endothelium contain debris salvaged from blood and lymph streams in the normal course of keeping the blood stream free of bacteria and of partially broken down proteins from the gastrointestinal tract; the monocyte retains its rosette of vacuoles, and is fastidious in its selection of only small particulate debris in contradistinction to the tissue clasmatocyte or macrophage; and the fat cells clearly limit their activities to the storage of lipoids. True, however, to the universal biologic principles of a common responsibility for community survival when external danger threatens, any or all of these physiologically distinctive units may, under pathologic conditions, become mobilized in a common cause invol-

ing the utilization of a common potential phagocytic capacity, and, to a greater or lesser degree, each may be able to contribute to the humoral antibody globulins so essential to adequate cellular defenses. In this connection, Sabin⁶ has pointed out that even the fibroblast may be seen to take up minute amounts of vital dyes or dye antigens when excessive quantities are forced upon the tissues, and that they may contribute their share to the circulating humoral antibodies.

Just as these various cells function more or less selectively in response to specific physiologic demands, thereby assuming certain distinguishing morphologic characteristics, it seems reasonable to assume that under differing pathologic requirements one or other of these units might be able to assume the major role of defense, to be secondarily aided from other areas, if and whenever necessary. Such has been demonstrated to be the case. In tuberculosis the monocyte-epithelioid response appears to be primary;¹⁴ in kala-azar the macrophagic ingestion of *Leishmania donovani* bodies leaves the monocytes of the hamsters relatively unaffected.²³ As further studies of pathologic reactions are analyzed on the basis of these cellular concepts, the examples will doubtless be multiplied.

II. Pathologic Considerations

A. Congenital Hemolytic Jaundice.—Directly related to the well-established physiologic phagocytic function of the reticulo-endothelial system for senile, or damaged, or imperfect blood cells would seem to be certain constitutional pathologic states in which an excessive destruction of these same elements is at least one factor contributing to the clinical symptom syndromes. Normal erythrophagocytosis, occurring in the macrophages of spleen, liver, and bone marrow in varying degree in different species, is followed promptly by red blood cell disintegration and by a splitting of the hemoglobin molecule into globin and hematin. The latter is further broken down into (1) the iron-free pigment *hematoidin*, which becomes the bilirubin of the plasma in hemolytic jaundice, or is secreted by the hepatic parenchymal cells as bile; and (2) *hemosiderin*, in which form iron remains stored until needed for hemoglobin resynthesis in the bone marrow. Mann and his associates²⁴ have demonstrated conclusively that the macrophages of spleen

and bone marrow, not the stellate cells of the liver, are normally the principal sources of bilirubin, and Kanner²⁵ has reported, and we can confirm, that no histologic alteration in the Kupffer cells of the liver occurs in hemogenous icterus. Upon these observations may be based the modern approach to the pathologic physiology of human congenital hemolytic icterus. A dominantly inherited constitutional tendency to excessive hemolysis, upon which many environmental factors (pregnancy, trauma, minor infections) may play disastrously, has been clearly established.²⁶ The more active phases of this disease are invariably associated with a directly proportionate degree of splenomegaly, in which excessive parenchymal erythrocyte segregation and phagocytosis may readily be demonstrated. Moreover, splenectomy, when successfully accomplished, and if it includes the removal of all accessory splenic tissue—even though the operation be performed during an acute hemoclastic crisis²⁷—invariably results in an immediate, complete, and usually permanent remission. Any significance, other than diagnostic, of defective, spherocytic erythrocytogenesis in congenital hemolytic icterus remains unsettled. Haden²⁸ believes spherocytosis to be the congenital prerequisite to increased erythrocyte fragility, while Dame-shek²⁹ interprets spherocytosis as the end result of hemolysin activity upon mature red blood cells without any inherent marrow defect. The fact that splenectomy is followed by a return not only of red blood cells, but also frequently of thrombocytes and granulocytes, to more nearly normal, highly stable, equilibria, at least suggests that any marrow contribution to this clinical syndrome is dependent upon a more fundamental splenic dysfunction. Farrar, Burnett, and Steigman³⁰ report a patient with hemolysin anemia with hepatic degeneration who responded dramatically to emergency splenectomy although excessive erythrophagocytosis by splenic macrophages was not apparent. An hemolysin was demonstrated in the blood serum before, but not after, removal of the spleen. Thus, at least two possible mechanisms of red blood cell destruction must be attributed to the spleen in hemolytic states; the one, direct phagocytosis by reticulo-endothelial cells, the other, indirect hemolysin elaboration, probably by the same cells.

B. Thrombocytopenic Purpura.—Reference has been made

to the frequency with which a mild thrombocytopenia and granulocytopenia are found secondary to primary splenic anemia.²⁷ Either of the former disequilibria may become primary in certain individuals and dominate the clinical and laboratory pictures. There is one type of thrombocytopenic purpura directly related to a normal-sized but pathologic spleen, and dependent upon, either selective abnormal macrophagic destruction of platelets³¹ or splenic inhibition of marrow megakaryocytic functional efficiency,³² or "thrombocytopen"³³ derived from the spleen. In these patients, successful splenectomy is followed by a prompt and maintained return of platelets to the circulation without any recognizable change in number and histologic integrity of marrow megakaryocytes before and after surgery.³⁴ The reticulo-endothelial phagocytes in these spleens probably play a more or less important role in the peripheral destruction of the important platelet elements.

C. Primary Splenic Granulocytopenia.—Recently a primary granulocytopenic syndrome, with marrow myeloid hyperplasia, splenomegaly without hepatic pathology, and a negative history for drug or bacterial idiosyncrasies, has been described from this clinic.³⁵ Hemolytic erythrocytopenia and/or thrombocytopenia have been either incidental or nonexistent. The clinical manifestations have ranged from acute, through subacute, to chronic, and in each instance splenectomy has resulted in complete recovery. Careful supravital surveys have confirmed in every instance a tremendous excess of highly phagocytic macrophages in the splenic parenchyma, with whole intact granulocytes representing the principal engulfed material; the organs, fixed and sectioned, using ordinary techniques, lost much of the dramatic demonstration of selective phagocytosis seen in the fresh tissues.

The evidence just presented, viewed in its entirety and in its interlocking and overlapping details, would certainly seem to justify the belief that the physiologic function of reticulo-endothelial phagocytosis by the normal spleen may become pathologically accentuated, either as an inherited or as an acquired trait; and that any or all of the elements arising in the marrow physiologically may be individually or collectively preyed upon to the extent or degree of producing symptoms characteristic of each critical deficit point, respectively.

III. Relationship of the Reticulo-Endothelial System to Humoral Immunity

In addition to the observations of selective phagocytic activity on the part of the reticulo-endothelial cells, a great many investigations have been undertaken in the attempt to demonstrate a direct relationship between this cellular system and humoral immunity. Reticulo-endothelial cell blockade with carbon particles or various vital dyes, or extirpation of the spleen, or both, have preceded the administration of a variety of antigens, with the variation in antibody titers, subsequently developed, used to measure the specific sensitivity of the tissue response. Most of the evidence thus accumulated has seemed to indicate the existence of an intimate relationship between the integrity of the reticulo-endothelial system and antibody formation.

When foreign erythrocytes are injected into an animal for the first time, they are promptly removed and destroyed by intracellular phagocytosis; when red blood cells from the same source are again injected after a suitable interval, intravascular, extracellular hemolysis occurs through the action of circulating hemolysins. That the cellular elements originally responsible for the elimination of the foreign red blood cells by phagocytosis should be the most likely source of the newly developed hemolysins is a reasonable assumption. In support of this hypothesis is the almost complete agreement that hemolysin production is interfered with to a greater or lesser degree by reticulo-endothelial blockade.³⁶

Of even greater interest in this general area have been the recent cooperative investigations of chemist, immunologist, and cytologist, each utilizing the latest technical approaches to the problem in his own domain. In 1930 Heidelberger and Kendall⁵ synthesized a dark red dye protein, R-salt-azo benzidine-azo-egg albumen, with marked antigenic properties, that showed highly selective phagocytosis by cells of the reticulo-endothelial system.

Preparing a more highly purified antibody than had previously been available, Heidelberger and his associates,⁷ using the ultracentrifuge and determining electrophoretic mobilities, found the molecular weights and electrical phenomena of antibodies to be those characteristic of proteins. This was in con-

formity with the previously observed invariable association of antibodies with the globulin fractions in serum. Sabin,³⁷ it will be remembered, pointed out in her early study of the chick blastoderm, among other things, the liquefaction of some of the angioblastic cells differentiating from the primitive mesenchyme to form the first protein-containing blood plasma. Ranvier³⁸ had noted the "shedding of exoplasm" by certain of the larger connective tissue cells in the frog, which led him to designate these elements as clasmatocytes. Supravital preparations of living cells from blood, lymph nodes, spleen, omentum, or peritoneal fluid regularly confirm the fragmentation of cytoplasm. This phenomenon is especially prominent in young lymphocytes, monocytes, and clasmatocytes or macrophages. These observations suggest the mesothelial origin of some, if not all, of the serum proteins; and the increase in fibrinogen and globulin following large doses of India ink and saccharated iron oxide has been explained on the basis of a stimulation of the tissue phagocytes. Recently Sabin⁶ took the alum precipitate of Heidelberger's dye protein, whose readily visible purplish-red particles had been proved to be of superior antigenic potency,⁷ and followed its physical disposition via various avenues of injection in rabbits. When given intravenously, the resulting antibody titer was higher than when the antigen was introduced by the intradermal, subcutaneous, or intraperitoneal routes, with phagocytosis by local macrophages and by the lymphatic endothelium and free macrophages of the regional lymph nodes only.

The details of this study make fascinating reading, but the evidence as finally interpreted seemed to justify the following conception: the phagocytic endothelium, both vascular and lymphatic, as well as the free macrophages of the tissues everywhere, are constantly phagocytizing foreign materials which may be divided into two general groups, antigens and nonantigens. These substances are first segregated into the vacuolar organs of digestion of the cell and prepared for diffusion into the cytoplasmic zone of synthesis; the normal food substances ingested are utilized in the formation of normal globulin, but foreign antigenic proteins increase and modify this synthesis of globulin, so that with the shedding of parts of the surface films of such cells, both normal and antibody globulins are

carried into the blood plasma. This conforms with the observation of a concomitant increase in both under such circumstances. These cells, during the period in which the modified globulin remains within the cytoplasm, react differently from the normal cell in the presence of additional original antigen, thus relating "sensitization" and "immunization" to different phases of the same mechanism.

The variation in species and individual response to various antigenic substances is readily explained by Sabin's observations. Two distinct steps are necessary for the development of antibodies: first, the phagocytosis and intravacuolar preparation of the antigen for introduction into the cytoplasm proper; and, second, the synthesis of new and modified globulins. Both these phases require time, which would naturally vary with the quantity of antigen available, its relative ease of degradation, and its ability to modify normal globulin synthesis. Furthermore, the units which comprise this phagocytic defense system of the mammalian organism are as diversified in origin and definitive type, and probably, therefore, in functional specificity and efficiency, as are the several units of a modern arm — granulocytes, monocytes, clasmatocytes, endothelial phagocytes, specialized as in the Kupffer cell and nonspecialized as in the lining cells of the lymph sinuses; and it is probable that each responds differently, quantitatively if not qualitatively, to different antigens and under different environmental circumstances. The various chemotherapeutic agents either assist or prevent clinical recovery in infectious diseases to the extent that they aid or hinder this important cellular mechanism of the body in its phagocytic and antibody-forming functions plus any direct effect they may have on pathogenic bacteria.

These recent studies of Dr. Sabin and her chemical and immunologic collaborators mark an enormous advance in our understanding of the essential mechanism of natural and acquired immunity, yet represent but a logical consummation and final unique demonstration of an hypothesis supported by the gradually accumulated experience of many years.

Summary

In summary, the following points may be accepted as a tentative working basis for present therapeutic applications, and for further exploratory excursions into this absorbing and important phase of medicine: (1) the reticulo-endothelial system represents a functional unit arising from mesenchymal derivatives possessing a common phagocytic capacity; (2) certain morphologic variations associated with a variety of physiologic functional requirements may be recognized; (3) under pathologic conditions and in tissue culture such morphologic criteria may become either accentuated or diminished; (4) when highly stimulated, all phagocytic cells, regardless of the ease of differential identification under physiologic conditions, tend to assume a common appearance and may be designated by the common descriptive term, macrophage; (5) while originally protective and conservational in functional objectives in the normal body economy, these phagocytic scavengers of the mammalian tissues may assume an excessive selective destructive affinity for any of the normal blood elements, thus precipitating a variety of characteristic clinical syndromes; (6) the spleen is usually the site of the greatest destructive activity, and when the appropriate diagnostic tests have localized the major pathology to this organ, splenectomy is indicated as the rational therapeutic procedure; (7) conclusive evidence of the active participation of the reticulo-endothelial cells in humoral antibody production would now seem to have been obtained; (8) this reaction has both favorable (protective antibodies) and unfavorable (hemolysin production) implications for mammalian survival; (9) a constantly increasing accumulation of carefully controlled factual information is providing an ever broader and more substantial foundation for a more effective manipulation of this important defense unit in the interest of individual health.

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The Electron Microscope*

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The assumption of DeBroglie, quickly confirmed by Thompson and many others, that matter in motion should have wave-like characteristics opened a new field in physics. From this conception has grown electron optics, as typified by electron microscopes, electron diffraction and practical television. The promise which one of these, the electron microscope, holds for biologists and chemists is our immediate concern.

Early workers in the field of electron optics were quick to realize that a very close analogy exists between the behavior of light rays and electron beams. When light rays are passed through quartz or glass lenses they can be focussed. When an electron beam is caused to traverse a magnetic or electrostatic field it can be brought to focus in much the same manner as light. The principles governing image formation, object and image distance in the simple lens apply equally well to both systems.

To illustrate let us take the resolving power of an optical system, that is, the ability to separate a pair of points in the object space, is among other quantities directly dependent upon the wave-length of the light used. It can be demonstrated that the resolving power of an objective is directly proportional to the wave-length of light employed and varies inversely with the numerical aperture of the lens. For light the maximum value obtainable in practise is about 0.1 microns (1-10,000th mm.). To achieve this it becomes necessary to use ultra violet light of 2550 Å wave-length as a source and quartz condensers and objectives. Since 2550 Å is about half the wave-length of ordinary light the limit of resolution is about doubled. By way of illustration: the highest magnification obtainable with ordinary light, an apochromatic objective of 1.4 numerical aperture and a 20 times compensating ocular is 2,000. But the loss of definition (resolution) is such that

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little is gained by working at higher magnifications than 1,200. In contrast to this magnifications of 3,200 with excellent resolution can be obtained by ultraviolet light and quartz lenses.

We see from the foregoing figures that with ordinary light and a good optical system two objects about 0.25 of a micron apart can be separated and visualized as two points. With ultraviolet light of appropriate wave-length the resolution can readily be stepped down to 0.1 of a micron. Since resolving power is directly proportional to the wave-length it follows that the shorter the wave-length the greater the resolving power of the system. An electron which has been accelerated by falling through a potential drop of V volts has an equivalent wave-length of

$$1.2 \times 10^{-7} \text{ cm.} \quad \sqrt{\frac{1}{V}}$$

Thus if $V=1$ volt the wave-length would be 1.2×10^{-7} centimeters. This value if substituted in the resolving power equation would result in a resolving power of about 1-10,000,000th centimeters. The attainment of such extremes is problematical because of the space charge on the electron but figures lower than .03 of a micron have been reported with magnifications of 30 or more thousand diameters. The theoretical possibility of magnification is in the neighborhood of 100,000.

When the resolutions obtainable with light microscopes and those using electrons are compared it is found that they are as follows:

Ordinary light	0.25 of a micron
Ultra-violet	0.1 of a micron
Electron microscope	0.001 of a micron

Principles of Electron Microscope

The principles behind the operation of the electron microscope are old although their application is new. The function of a magnifying lens is to change the direction of the rays originating at a given point in an object so they will be reunited at a single locus in the image. The case of the glass lens and rays of light is familiar to all. To illustrate the focussing action of a magnetic field upon electrons let us consider a U-shaped magnet in the plane of the printed page,

open end toward the top of the page and between the poles perpendicular to the plane of the page a flexible wire connected to a battery. When current is sent through the wire in one direction the wire will move toward the bottom of the page and upon reversal of current the wire will move in the opposite direction. This motion of the wire is due to the field of the magnet interacting with the magnetic field of the wire in which the current is flowing. Now let us put the magnet around an evacuated tube of non-magnetic material, brass for example, and replace the wire by an accelerated beam of electrons directed down the axis of the tube perpendicular to the lines of force of the magnet. This stream of electrons can be considered as a current and will be deviated from its path in the same way that the wire was moved. Such is the underlying principle of the magnetic lens.

The shape or direction the lines of force of the field of the lens is distorted by the proper form of the coil winding and its iron sheath so that electrons leaving from a given point in the object but in different directions, will, after passing through the field of the lens, be reunited at one locus in the image.

The focal length of a lens in the form of a flat circular coil depends in part upon the current flowing through the coil. This makes it possible to have a fixed object-image distance and a movable lens of varying power. Analogous to a glass lens which has a focal power dependent upon the wave-length of the light, so does the focal length of the magnetic lens vary with the wave-length of the electrons.

The first electron microscope to be used for biological investigations in this country was designed and built in the Anatomical Laboratories of Washington University. Work was started on this apparatus early in 1935¹ and a usable instrument was in operation routinely in the fall of the same year. The microscope was designed to aid in studies of the localization of mineral salts in cells and tissues carried on in this laboratory since 1930. Our problem was one which required a simple instrument of relatively low magnifying capacity. With this in mind a simple, yet flexible, microscope was constructed and has been used to localize accurately magnesium and calcium in cells, cell organelles and tissue fluids.

Since we were interested in localizing minerals in cells and tissues we started work with the following ideas in mind. That each mineral or its salt has some temperature at which it will give off electrons copiously by thermionic emission; That these temperatures of emission varied sufficiently from mineral to mineral to enable one to begin by heating at low temperature and completely exhaust the emission at that point, increase the temperature and exhaust emission until by a succession of such procedures there could be obtained a composite picture of the whole. With magnetic lenses and appropriate arrangements these emitted electrons could be focussed and a picture obtained of their source.

Unfortunately the procedure was in reality not quite so simple. We soon discovered that the amount of mineral present in thin sections of tissue did not give strong enough emission to photograph readily. This difficulty was overcome by coating the cathode with barium and strontium carbonate. This increased the emission, by activation, by nearly 1000 per cent. However, the electron emission turned out to be not from any salt which happened to be present in our tissue sections but from calcium and magnesium alone. We were able to demonstrate this by a long series of experiments with individual salts, mixtures of them and combinations with substances the consistency of tissues (Scott and Packer²).

It has been appreciated for some time that gentle and careful ashing of sections of biological tissues gives a remarkably faithful picture of the topographic distribution of minerals in such materials. Cells and their parts can be recognized with little difficulty. If material is prepared by a modification of the Altmann-Gersh frozen dehydration method there is little chance of any perceptible shift in the cellular location of the inorganic constituents. Since most of the inorganic elements in tissues, particularly Na, K, Ca and Mg, are excited to thermionic emission of electrons at more or less specific temperatures, it was expected that one would be able to differentiate between these various elements and localize them in cells and tissues. With this information at hand it seemed advisable to ash sections *in vacuo* on the surface of a barium and strontium coated cathode in the electron microscope (Scott and Packer³).

After many experiments, both with apparatus and methods, it has been possible to secure pictures in which cellular structure in smooth and striated muscle, gastric mucous membrane, nerve and in other tissues can be made out. So far the emission pictures obtained have been due to magnesium and calcium only. It has been possible to localize these elements definitely in the contraction bands of frozen and dehydrated skeletal muscle. Epithelial cells of the mucous membrane of the stomach and intestinal tract show extensive concentration of magnesium and calcium in the free borders of the cells.

In striated muscle, either cardiac or skeletal, the electron microscope shows in many preparations the sharp localization of Ca and Mg in the contraction nodes of the muscle fibers. These nodes or contraction waves are brought about by the rapid freezing technique employed. At the edges of the tissue section are many fibers however which are frozen before they have had time to contract and in such cells, the dark and light bands are readily visible in stained sections. When thin slices of the tissue are examined by the electron microscope method we employ, the Ca and Mg are found to be localized in the dark bands (anisotropic) of the muscle cells (Scott and Packer^{4, 5}).

Another fact, that should be pointed out in this connection, is the peculiar distribution of these elements, Ca and Mg, in the tissue. At this time it has not been possible to demonstrate either Ca or Mg in the tissue spaces of smooth or striated muscle. This is true despite the extreme sensitivity of the method (about 1×10^{-12} grams per kilo wet weight of muscle). This indicates that Ca and Mg are essentially elements found within the cells of tissues. Certainly both substances must be in the tissue fluids at times, perhaps constantly, but the quantity is extremely small in relation to the amount present in the cell (Scott⁶).

Recently it has been possible to demonstrate that there is at least one cell type surrounded by tissue fluid containing a relatively large amount of Ca and Mg. Mammalian and certain amphibian sympathetic ganglion cells are bathed in tissue fluids which do possess much Ca and Mg. Nuclear, nucleolar and Nissi substance in ganglion cells contain considerable Ca and Mg and the surrounding cytoplasm relatively less. In sharp contrast to this picture is the condition in nerve fibers

attached to or going to the ganglion cells. The whole of the Ca and Mg is found in the nerve fiber little or none being visible in the tissue space surrounding the fibers. In myelinated nerve fibers these salts are found in the myelin sheath with a dense concentration at its periphery (Scott⁷).

It is with some regret that one is forced to admit that so far in the application of the method it has not been possible to localize K and Na. Also the method seems to be limited, at least in our hands to the cations. Experiments are under way which are designed to test the possibilities of localizing the anions.

Another type of electron microscope, that designed for high magnification work, has been very recently put on the market by an American firm. Pictures obtained by its use have been displayed very prominently in the public press. Until just a month or so ago the results achieved seemed to be confined to publicity blurbs. Now, however, there is evidence that useful work is being done with this instrument (Morton and Anderson⁸). As a general rule its operation is limited to high magnification photographs of various substances, chemicals, crystals, viruses, bacteria, etc. These pictures are surprisingly clear and sharp even at 30 or so thousand initial magnification. Photographs of greater magnification, upwards of 50 thousand are usually obtained by enlarging, optically, the initial pictures. This procedure is, of course, justifiable as long as the object being examined is greater than the grain size of the film.

The future uses of the instrument are difficult to predict, however, the main range of usefulness should be in investigating the size range between the optically visible (the light microscope) and the object of molecular dimensions. There is an accumulating body of evidence that many physiological and biochemical phenomena are conditioned by submicroscopic molecular aggregates. In other words similar molecules act better or possibly even may be made reactive by performing in unison. Present methods for investigating molecular size and arrangement are excellent and are being actively exploited. The high magnification electron microscope can confidently be expected to reinforce and supplement them.

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The "New" Saint Louis City Hospital

AVERY P. ROWLETTE, M.D.

The City Hospital was one of the first teaching hospitals available to members of the medical profession of Saint Louis, and during the early part of this century afforded the only post-graduate center for medical graduates. The construction of teaching hospitals by the two Universities, plus the inadequacy of space and equipment, had led to the practical abandonment of City Hospital for undergraduate teaching.

Because undergraduate teaching of medicine affords a good visiting staff and stimulates the housestaff to a higher type of medical practice, we have fostered in every way the utilization of the hospital for this purpose.

This program has been aided by an economic change in the community; first, by the demand for private hospital beds by patients with group hospital insurance, thereby transferring many ward patients from free or part-pay to private service unsuitable for teaching purposes; and secondly, by a decrease in funds available to the University Hospitals for both inpatient and outpatient care from shrinking Community Chests and endowments, which further decreased both types of material available for undergraduate teaching.

Thus the stage was set for undergraduate teaching at the City Hospital, with its unlimited clinical material. We expect to again occupy a place in the scheme of medical education in the Community. We have attempted to supply the facilities to make this possible in our current program.

The Snodgras Laboratory has been completely reorganized by Drs. Sam H. Gray and Paul A. Wheeler. All new equipment and furnishings have been installed, and additional personnel has been added, until today it is considered one of the outstanding clinical laboratories in Saint Louis.

In order that the housestaff might be on a "straight" service basis rather than a "rotating" basis, it was necessary to add ten positions as Resident Physician and eleven as Assistant Resident Physician. Approved post-graduate training is now offered on all of the specialities of medicine.

The rotation of the Visiting Staff between City Hospital and the Colored City Hospital has been discontinued, allowing a permanent Staff at the City Hospital.

Additions to or reconstruction of the City Hospital was long overdue. The last buildings were erected in 1909 and at that time they were thought to be adequate until 1920. In 1935,



The New General Hospital Building, St. Louis City Hospital

nearly fifteen years later, for the first time, it was possible to continue the program and modernize the institution. This was made possible because the city officials eagerly accepted assistance from Public Works Administration, and the citizens voted to sell bonds to furnish the City's share of the cost.

The worst blight of all was the obsolete mental observation ward building which was virtually an antiquated type of prison. Hence, this was the first defect to be remedied. The Malcolm A. Bliss Psychopathic Hospital, constructed to the north of the old group, afforded a modern two hundred bed psychopathic unit. This was opened in 1939. This and other contemplated additions created the necessity for a Power House, Laundry, and Service Buildings. These three units have been constructed and are in operation. The new Service

Building includes separate dining facilities for the lay personnel, physicians, graduate nurses, student nurses, Resident Staff, and the Faculty of the School of Nursing. This arrangement decreased the size of the units served, and has greatly improved the service.

The Out-Patient Department occupied one floor of an out-moded building with totally inadequate space for the thousand patients which were handled daily. This building was virtually rebuilt into a completely modern four floor clinic building with the latest equipment. It was opened in November, 1939. Facilities and space for undergraduate and post-graduate teaching were included, which will be shared equally by both Washington and St. Louis University Schools of Medicine.

A new thirteen story general hospital building, which is nearing completion, was planned to consolidate the overhead facilities of the institution and to remedy the worst defects in the rest of the hospital. It was necessary to demolish three of the Buildings fronting on Carroll Street to allow space for its erection. This new building includes; first floor, Receiving Room and Internes' Recreation Room; second, X-ray Department, Cystoscopy and Deep Therapy; third, Surgical Pavilion with six major and four minor operating rooms; fourth, Ophthalmology and Otolaryngology; fifth, Urology; sixth, Gynecology; seventh, Obstetrics; eighth, Delivery Pavilion with six Delivery Rooms and quarters for undergraduate students from both Schools; ninth, Infants pediatrics; tenth, Older children, pediatrics; eleventh, Male Fractures; twelfth, Female Fractures; thirteenth, Prison, Occupational Therapy, Physiotherapy and several research laboratories. One pent-house provides a large room for experimental animals. Another provides entry to a Roof Pavilion covered with canvas for the enjoyment by patients of the open air and sun. The building will provide a total of five hundred beds. All the equipment is of the latest design and the best of manufacture, and will include a built in bi-plane fluoroscope for foreign body localization.

This new building will be the central receiving unit for all patients, and is conveniently connected with the three front buildings by direct corridor on the first and second floors. The old buildings which will be occupied by Medicine, Surgery,

Neurology, and Metabolism, will be completely rebuilt inside when the new building is occupied. Eventually in the old east and west ward buildings, each unit of the visiting staff on the major services of Internal Medicine and General Surgery, will occupy one floor. Plans call for the construction of several two bed wards and one ten bed ward in each wing.



The Malcolm A. Bliss Psychopathic Institute

When completed each ward of the hospital will have an adequate clinical laboratory, examination and treatment room, sterilization room, and classroom. The latter will be equipped with blackboard, x-ray viewboxes, cloak room, and lavatory. For larger assemblies there will be one auditorium of three hundred capacity, one of one hundred-fifty capacity, and one of seventy-five capacity. In addition, adequate locker space for students is provided for storing both clothing and microscopes. All facilities will be shared equally by Washington and Saint Louis University Schools of Medicine.

The entire program will cost in the neighborhood of \$4,000,000.00 and will be completed about January, 1943. We expect to occupy the new general hospital building in June, 1941. When completed Saint Louis City Hospital will be a modern

medical center with the latest diagnostic and therapeutic equipment, with extensive facilities for teaching undergraduates and post-graduates as well as for important clinical and experimental investigation.

General Hospital No. 21 and the Annual Military Ball

L. C. BOEMER, M.D., P-G '28*

An excellent representation of the staff members assigned to General Hospital No. 21, the affiliated unit of Washington University School of Medicine, were present at the 1941 Military Ball with their guests.

The Army and Navy Council, an association of the Services in the vicinity of St. Louis, having for its motif, "The Good of the Service," had over 700 in attendance.

At a beautifully decorated table for thirty, the 21st General Hospital functioned socially as never before, headed by Mrs. Lee D. Cady and Colonel Cady.

This year's annual ball was held Saturday evening, March 1st. The dinner and center of activities were in the Gold Room of Hotel Jefferson with dancing in the Ivory Room adjoining. Hal Havird's Orchestra provided the music. One of the outstanding features of the Ball was the Color Ceremony, when the Regimental Colors were brought in by a contingent of the Navy at 9:00 P. M. and again later when the colors were removed about midnight.

A most important contact in the interest of national defense is the fact that reserve officers of the St. Louis area at this Ball again meet with officers of the regular army.

The representation of General Hospital No. 70, the affiliated unit of St. Louis University, School of Medicine, was graciously headed by Mrs. A. M. Tripodi and Colonel Tripodi.

Other units of the U. S. Army Organized Reserve represented were the 53rd General Hospital, 4th Evacuation Hospital, 67th Evacuation Hospital, 70th Evacuation Hospital, 4th

* Secretary, General Hospital No. 21.

Surgical Hospital, 327th Medical Regiment, 25th Vet. Evacuation Hospital, 15th Medical Supply Depot, Headquarters 3rd Military Area, Headquarters 102nd Division, Headquarters 203rd Infantry Brigade, 406th Infantry, 407th Infantry, 45th Field Artillery, Headquarters 17th Field Artillery Brigade, 380th Field Artillery, 327th Engineers, Headquarters 41st Coast Artillery Brigade, 359th Engineers (G.S.), 45th Engineers (G.S.), 459th Engineers Battalion, 87th Engineers Battalion, 41st Coast Artillery Brigade Headquarters, 527th Coast Artillery (A.A.), 41st Coast Artillery Brigade, 79th Field Artillery, 321st Cavalry Regiment, 427th Quartermaster Regiment, 307th Signal Battalion, 425th Chemical Company, and 18th Quartermaster Squadron.

The U. S. Naval Reserve units represented were Headquarters 6th Area, 7th Battalion, Navel Reserve Aviation Base, Section 6 Naval Communication Reserves, Unit 2 Naval Communication Reserves, and Naval Reserve Flight Selection Board.

The Reserve Officers Training Corps of Washington University, Washington University, School of Medicine, St. Louis University, School of Medicine, Christian Brothers College, and Western Military Academy were represented.

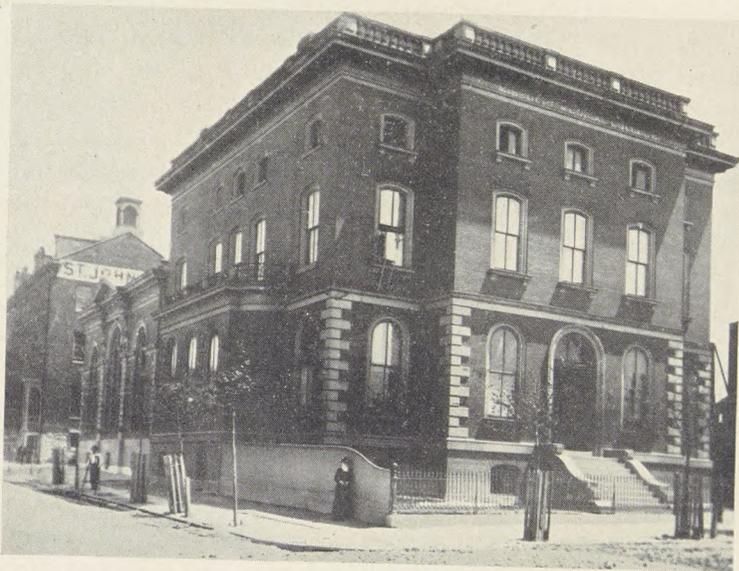
Jefferson Barracks units included Headquarters Missouri District CCC, 27th Air Squadron, Medical Detachment, Quartermaster Detachment, and 28th Air Squadron.

The National Guard of Missouri, composed of 138th Infantry, Battery A 128th Field Artillery, 35th Division Aviation, and First Missouri Infantry had its representation as did also the Army Air Corps at Scott Field, St. Louis Ordnance Procurement District, Div. Eng. U. S. Army Upper Miss. Valley Division, Div. Eng. U. S. Army St. Louis, Mo., U. S. Veterans Hospital No. 92, U. S. Marine Hospital No. 18, U. S. Marine Corps Reserves, St. Louis Medical Depot United States Army, St. Louis Quartermaster Procurement Planning District, Quartermaster, St. Louis, U. S. Army Recruiting, U. S. Navy Recruiting, and Army Finance Office.

The early high degree of organization of General Hospital No. 21, due to the efforts of its director, Colonel Lee D. Cady and the cooperation of the staff, accounted for its commendable representation at this outstanding social military event.

Report of the Committee to Mark the Grave of Dr. Joseph Nash McDowell

Since the publication of the proposal to mark the grave of the Founder of the Missouri Medical College, which appeared in the January number of the Quarterly and in the daily press,



The Missouri Medical College Building, erected on the north-east corner of Lucas Avenue and Twenty-second Street in 1873. It was razed some years ago. Photograph in the collection of Dr. Harold Bulger

we have received no word from any relatives of Dr. McDowell. The Bellefontaine Cemetery Association has no record of any heirs or descendants of Dr. McDowell. The last burial in the lot was Dr. Drake McDowell, January 8, 1882. The Bellefontaine Association will grant the erection of an appropriate granite monument if relatives or descendants of Dr. McDowell cannot be located.

It has been ascertained that a sum of approximately four hundred dollars will be needed for the project, of which two hundred would be expended to endow the McDowell lot for perpetual care by the Bellefontaine Cemetery Association and

two hundred would be used for making and erecting the monument.

The committee has decided to proceed with the plan and submits to the Alumni of the Missouri Medical College the proposal to subscribe the amount above named. The present year is happily an appropriate time to commemorate the Founder, for it completes the centenary of the graduation of the first class of the School established by McDowell, a school which has served with such distinction in the training of physicians and in the progress of medical education in the West.

The committee believes that every alumnus of the Old School (There are now 370 living) would want to subscribe. It is the plan to have the total amount, four hundred dollars, received by July 1, 1941, in order that the marker can be made and erected on the McDowell lot not later than next October. If for any reason the plan fails of accomplishment within the present year, all subscriptions will be returned. Checks should be made payable to The Dr. Joseph Nash McDowell Memorial Fund and communications addressed to R. J. Terry, Washington University School of Medicine, St. Louis, Missouri.

Robert E. Schlueter

M. George Gorin

John Zahorsky

Robert J. Terry

MAKE YOUR RESERVATIONS NOW FOR THE
ALUMNI BANQUET, MAY 31

DEPARTMENTAL CONFERENCES

Pathology

ACUTE OSTEOMYELITIS AND STAPHYLOCOCCUS SEPTICEMIA

History No. R251: A 7 months old girl was irritable for two days prior to admission to the St. Louis Children's Hospital. It had been noted that she had a tender right thigh, and on the day before admission she experienced a convulsion followed by coma and cyanosis. At the time of hospital entry, physical examination revealed signs of a generalized infection of the upper respiratory tract and a swollen, hot, tender right thigh that was apparently painful on motion. Following the institution of sulfathiazol treatment, a generalized rash consisting of hard, indurated, deep, maculopapules appeared. The drug was then discontinued; however, on the following day, the skin lesions became typical of those due to a Staphylococcal septicemia and a blood culture was reported positive for *Staphylococcus albus*, hemolyticus. Antistaphylococcus serum and blood were administered intravenously. The right thigh was incised and several hundred cc. of thin, cloudy pus spurted from beneath the periosteum of the right femur. A hole for drainage of the marrow cavity of that bone was made. Repeated blood cultures were positive for *Staphylococcus albus* and the same organism was grown from the pus obtained at operation. The infant died on the fourth day of hospitalization.

Autopsy Washington University No. 9041: Many small abscesses, 2 mm. in diameter, were noted in the skin. Slightly larger abscesses were found in both lungs, usually subpleural in position, and in the cortices of the kidneys. A single abscess was present beneath the parietal pleura on the left side and another in the myocardium of the left ventricle. In addition to the discrete abscesses, the lungs contained areas of hemorrhage and bronchopneumonia. The cancellous bone of the right femur was soft, dark red, and partially necrotic. Microscopically large masses of bacteria were seen in all the lesions.

This is an example of an overwhelming infection with a

virulent *Staphylococcus albus hemolyticus*. The portal of entry of the organism is not entirely clear, but may have been the respiratory tract. The lesion in the bone marrow cavity was probably the source from which many bacteria were distributed throughout the body producing a pyemia.

HEMACHROMATOSIS AND ACUTE INTERSTITIAL PANCREATITIS

History No. 85563: A 50 year old engineer first entered Barnes Hospital on November 1, 1940. He complained of painless jaundice and pruritus. Two weeks prior to his admission to the hospital he had had an attack of dull aching pain in the right upper quadrant of the abdomen. In 1931, he had had jaundice unaccompanied by pain which lasted 9 months, and two years later he began to have attacks of epigastric pain. In 1935, he went to the Mayo Clinic. He refused exploratory laparotomy at this time. The dermatologists made a diagnosis of hemachromatosis which was confirmed by skin biopsy. His urine was sugar-free, but he had an abnormal sugar tolerance curve.

At the time of his first admission to Barnes Hospital his jaundice was marked and his liver was palpable, although not tender. The gall-bladder was not visualized in a cholecystogram following intravenous administration of the dye. Diagnosis was made of toxic hepatitis. He was readmitted for further study on November 27, 1940, at which time he was still icteric but had no pain. The hippuric acid test of liver function was 21.9% of normal. X-ray studies of the gastrointestinal tract were indeterminate. At no time did his urine contain sugar. The patient again refused exploratory laparotomy and was discharged from the hospital. His jaundice diminished during the following weeks but recurred on January 19, 1941. Three days later he had severe epigastric pain and the following day had a chill followed by an elevation of temperature to 102°. On January 24 he was given morphine to control the abdominal pain and was sent to Barnes Hospital. On arrival at the hospital he was in coma and in spite of supportive therapy died 6 hours later.

Washington University Autopsy No. 9032: There was 750 cc. of clear yellowish brown fluid in the peritoneal cavity. The

liver weighed 1400 grams, and was greenish brown in color. The capsular surface had the characteristic nodular appearance of cirrhosis and on the cut surface there were fine interlacing bands of gray fibrous tissue. The gallbladder contained no stones and was normal, as were the extrahepatic bile ducts. The pancreas was enlarged. The cut surface was golden brown. There were 2 cysts in the tail of the pancreas which were filled with clear fluid. Perinpancreatic lymph nodes were dark brown in color. There were esophageal varices, and minute subperitoneal hemorrhages over the small intestines. The lungs showed edema and congestion.

The microscopic architecture of the liver was distorted by broad interlacing bands of fibrous tissue surrounding and extending between the portal spaces. There were numerous proliferating bile ducts. In some of the distorted lobules the liver cells were shrunken and there was a slight infiltration of lymphocytes and a few polymorphonuclear leukocytes. Numerous refractile granules of gold brown pigment, which stained blue with potassium ferrocyanide, were seen in the liver cells, in the connective tissue, and in the epithelium of the small bile ducts. Occasional granules of hemofuscin were demonstrated by fuchsin stain in the connective tissue and in the bile duct epithelium. There was a moderate increase in interstitial fibrous tissue in the pancreas, and iron containing pigment was found in the epithelium of ducts, acini, and islands, and in the connective tissue. In the interstitial tissue there was a moderate infiltration of polymorphonuclear leukocytes both inter- and intralobular. A similar acute inflammation was observed beneath the peritoneum over the stomach. Brown pigment was found in the peripancreatic and periaortic lymph nodes, in the mucosa of the stomach, in the adrenal gland, and in the acini of the prostate. In the skin there was an increase in the melanin pigment in the basal layers of the epidermis. Occasional cells in the epidermis and about small blood cells in the dermis contained iron pigment, and hemofuscin was demonstrated in the epithelium of sweat glands.

This is clearly an instance of hemachromatosis with the characteristic distribution of both the iron containing pigment, hemosiderin, and the iron free pigment, hemofuscin. The occurrence of hemofuscin in the epithelium of small bile ducts

and in the epithelium of sweat glands of the skin is well demonstrated in this case, and likewise the increase of melanin which has frequently been shown to account in large part for the bronzing of the skin in this disease. Diabetes was not present although an abnormal glucose tolerance curve was obtained. Since 22 per cent of 235 cases of hemachromatosis collected from the literature by Sheldon showed absence of glycosuria, its absence in this patient is not inconsistent with that diagnosis. The history of repeated attacks of jaundice, fever and abdominal pain together with the anatomical finding of focal areas of acute inflammation and degeneration of parenchymal cells in the liver in addition to the chronic changes of cirrhosis is evidence of recurring acute hepatitis, a condition not characteristic of the disease hemachromatosis. This history of severe abdominal pain prior to death is consistent with the autopsy finding of acute interstitial pancreatitis. A recent report by Cantarow and Bucher* describes a similar terminal event in a case of hemachromatosis. The relationship of the acute pancreatitis to this disease was not evident in either their case or in the present one.

GENERALIZED SARCOIDOSIS OF BOECK

History No. 5716. A 40 year old married colored woman entered Barnes Hospital, February 27, 1941 complaining of asthma, loss of 45 lbs. of weight, anorexia and afternoon fever for four months. For one month, she had had swelling of her ankles.

In past years, she had had "ragweed hay fever" associated with asthma every fall. These attacks usually lasted two to three weeks. However, in the fall of 1940, the asthma continued for four months and became so severe that she came to the out-patient clinic for relief. She was given digitalis in the medical clinic because of her dyspnea and dependent edema.

The physical examination revealed a thin negro woman whose breathing was asthmatic in type. Over the occiput and the right side of the neck the skin was elevated, scarred, indurated, shiny and more deeply pigmented than the surround-

* Cantarow, A. and Bucher, Carl J. Archives of Internal Medicine. Vo. 67, 333, 1941.

ing skin. Over the nose there was a butterfly shaped lesion of the same character. Laryngoscopic examination showed that the right vocal cord was in the cadaveric position, and did not move with phonation or respiration. The lymph nodes were generally enlarged. Auscultation of the chest revealed wheezing breath sounds. The percussion note was dull over the right middle lobe, and part of the right lower lobe. The breath sounds were diminished while tactile fremitus and whispered voice sounds were intensified in these areas. The blood pressure was 164/70. There was a soft systolic murmur over the cardiac apex. Edema of the ankles was present.

The Kahn reaction was negative on two occasions previous to this admission to the hospital. The urine was normal. The red blood cell count was 3,560,000 and the white blood cell count, 4,800. A roentogram of the chest showed wide hilar shadows bilaterally, more marked on the right. A bronchogram following instillation of lipiodol showed concentric narrowing of the right main bronchus and its large branches, and of the left main bronchus. Bronchoscopic examination on February 28, 1941 revealed a thickened carina, and bright red, thickened, "plaque-like" mucosa. The bronchial lumens were constricted just beyond the orifice of each of the main bronchi. The patient went into shock and died three hours following the bronchoscopic examination.

Post Mortem No. 9078: The mediastinum was infiltrated with firm white fibrous tissue which enclosed the trachea and main bronchi, the arch of the aorta, and the pulmonary artery in one solid mass. This tissue infiltrated the hilar structures of each lung, compressing the bronchi and large vessels. It extended into the wall of the auricles from the root of the aorta. The lungs contained numerous small firm greyish white nodules of similar tissue from 1 to 10 millimeters in diameter. The liver and spleen also contained a few such nodules. Nearly all the lymph nodes were greatly enlarged and firm, and on section were seen to be composed of white rubbery tissue. The right recurrent laryngeal nerve was compressed between two such nodes. Section of the thick skin of the occiput showed minute white nodules in the dermis. Microscopically the tissue reaction in the mediastinum, lungs, lymph nodes, liver, spleen, heart, and skin was of the same character. This process in-

volved the mucosa of the bronchi. Although the bronchial and tracheal mucosa was intact grossly, microscopically there were seen superficial ulcerations of the mucosa in a number of the small bronchi. The lesions, wherever seen, consisted of tubercle-like nodules, which resembled in certain respects the tissue reaction produced by the tubercle bacillus, together with a marked proliferation of connective tissue. With the Ziehl-Neelsen stain no acid-fast bacilli were found in the lesions.

In the sections from this case the characteristic tissue reaction long recognized as peculiar to the disease known as Boeck's sarcoid is well illustrated. This consists of nodules of epithelioid cells often sharply outlined. One or more giant cells with many nuclei arranged peripherally are present in many of these nodules. The cytoplasm of both the epithelioid cells and the multinucleated giant cells appear rarefied and vacuolated more frequently than in the typically tubercle. In contrast to the tubercle the nodular tissue reaction in this disease may contain small blood vessels or the nodule may be formed about a medium sized vessel. The tendency for the early and extensive formation of hyaline connective tissue is conspicuous. One frequently sees nodules which appear to be of recent origin surrounded by masses of dense hyaline tissue. Typical caseation necrosis is not found, although some of the nodules show a sort of coarse fibrillary material which appears to be degenerated connective tissue. Not only the microscopic tissue reaction but the gross distribution of the lesions in this case corresponds to that seen in other instances of generalized sarcoid. The involvement of the skin, lymph nodes, and tissue about the large bronchi and pulmonary vessels has been repeatedly observed. The characteristic cystic defects seen in roentograms of the bones of the fingers and toes were not demonstrated in this case. The etiology of the disease is unknown. Although the tubercle bacillus has been considered by some to be the etiological agent, satisfactory proof for this has not been offered. Many attempts to demonstrate this organism by animal inoculation have been unsuccessful except when there was a coexistent tuberculosis. In this instance three guinea pigs and three rats were inoculated with fresh material taken at autopsy. They developed no lesions. The absence of demonstrable tubercle bacilli taken together

with the unusual character of the tissue reaction speaks strongly against the idea that this is a type of tuberculosis.

CHRONIC ULCERATIVE COLITIS

History No. 87223: A 56 year old white woman was admitted to Barnes Hospital, January 1, 1941, following a profuse rectal hemorrhage. The present illness began one year before entry, when the patient first had bloody diarrhea. The diarrhea continued and was accompanied by nausea, vomiting, and fever. During a previous hospital admission, in Tennessee in July, 1940, the Flexner type of dysentery bacillus was cultured from the stools. Polyvalent dysentery serum was given and a moderate improvement in the symptoms resulted. Subsequently, there was exacerbation of all symptoms and the patient was admitted to a hospital in Cleveland, Ohio, on which occasion no pathogenic organisms were recovered from the stools. Therapy at that time included blood transfusions and the administration of neoprontosil. There was slight temporary improvement but many of the symptoms continued. Shortly before admission to Barnes Hospital a severe rectal hemorrhage occurred.

Physical examination revealed an extremely weak and pale woman. The blood pressure was 75/50 millimeters of mercury, the pulse was rapid and the respirations were deep and rapid. The abdomen was moderately distended and diffusely tender. The hemoglobin content of the blood and the red blood cell count were markedly decreased. There was a shift to the left in the Schilling differential count of the white blood cells. The urine was normal. Repeated stool cultures were negative for pathogenic organisms. Treatment consisted of blood transfusions and the administration of bismuth subcarbonate and sulphanilamide. The patient died one week after admission.

Post Mortem No. 9046: The mucosa of the colon showed extensive, elongated areas of deep ulceration which tended to be situated over the taenial bands. The hepatic flexure and the sigmoid portion of the colon were most severely affected. The rectum was uninvolved. The portal vein, and its branches in the left lobe of the liver contained an infected thrombus. Throughout the liver were many abscesses varying from 1 to 30 millimeters in diameter. Microscopically, the chronic ulcers

in many areas had completely destroyed the muscular coat of the colon, but had not eroded the peritoneal surface of the intestine. The abscesses in the liver were definitely associated with the radicals of the portal vein. The colon bacillus was cultured from these abscesses.

Discussion: The course of the disease in this instance was that usually associated with chronic ulcerative colitis. In 10% to 20% of the cases the stools during the initial attack contain pathogenic organisms of the dysentery type. Chronic ulcers along the taenial bands are the characteristic pathological findings but the rectum also is usually involved. Acute purulent pylephlebitis is an infrequent complication of this disease. However, two similar cases of chronic ulcerative colitis complicated by acute purulent pylephlebitis have come to autopsy in this laboratory in the last two years.

Surgery

Mr. Geo. C., aged 64, a yardman employed at Barnes Hospital, came to the emergency room on November 25, 1940, complaining of severe pain in his epigastric region, nausea and vomiting, of ten hours duration. The attack began at 3 a. m. that morning with severe pain in the mid upper abdomen, waking him up from sleep, and followed in about half an hour by nausea and vomiting. The pain was cramp-like in character and was more severe at certain times, but was continuous in that it never completely left. During the hours before admission he vomited five times and, on arrival at the emergency room, felt very weak and was still in severe discomfort.

Four months prior to his admission he had had a similar attack to the present one beginning at 3 a. m. in the morning also, accompanied by nausea and vomiting but relieved after a few hours following ingestion of epsom salts. Two milder attacks had occurred in the interim, one occurring at night, the other following the noonday meal. The last one was one month ago.

The patient stated that he had never been sick in his life until four months ago. He had had no severe illnesses of any kind, had had one carbuncle operated upon and one laceration of his arm sewed up. Systemic review revealed nothing of

consequence except that he was susceptible to frequent head colds. He gave no history of any familial disease. His mother died of apoplexy, his father of old age.

Physical examination upon admission showed an acutely ill, obese, slightly cyanotic man of about 60, who was rolling about on the examining table because of his severe pain. Temperature was 36, pulse 100, respirations 30, skin cold and moist, pulse of fairly good quality. Pupils were round and regular and reacted to light; sclerae showed slight icterus. There was a mild discharge from the nose without obstruction. His few remaining teeth were carious. Tongue was coated. Chest was clear. Heart sounds were regular and no murmurs were heard. The blood pressure was 174/100. The abdomen was obese, rounded and did not move with respiration. Percussion revealed dullness and some flatness in the left flank, but no shifting dullness. The maximum point of tenderness was found to be in the exact mid-epigastrium. There was lesser tenderness in the left upper quadrant. There was no tenderness in the right upper quadrant, and no masses were felt. Rebound tenderness was definite. Examination of the genitalia was negative; the prostate was found to be slightly enlarged, the reflexes were physiological. His white blood count on admission was 20,400, his red count 5.4 million with 105 per cent hemoglobin. The hematocrit reading was 51 per cent red blood cell volume. The impressions in the emergency room were: perforated ulcer, acute pancreatitis, cholecystitis. Because of the typical history pointing to a pancreatic disorder, blood was drawn for an amylase determination and found to be 1995 units, establishing the diagnosis. The lipase at this time was 2,305 cubic millimeters CO₂ per cc. The urine showed a trace of albumin. Blood sugar was 212 mg. per cent. Because the patient was not in shock of any severe degree, it was decided to treat him conservatively and he was given sedation, intravenous glucose and intravenous amino acids for the first three days. His temperature reached a high of 38.2° C. on the third day, and on the following day he developed a diarrhea which was quite severe and resulted in considerable dehydration, which accounts for his high non-protein nitrogen level as indicated below. This diarrhea was unaccompanied by mucus or blood, but did contain large quantities of fat.

From November 25 to November 30 his red blood count ranged from 5.4 on admission to 6.2, the white blood count falling at first to 9,000, then rising again to 17,000 on the 30th. The amylase determinations for these five days were 1995, 891, 298, 180, 180 and 30 units. Blood sugar from an initial determination of 212 dropped to 156, then 181 and up to 231, back to 189 mg. per cent. On December 1, six days after admission, his fasting level was 157. The 10:30 A. M. determination following breakfast was 234. Non-protein nitrogen was normal except for the fourth day when it rose to 59, probably due to dehydration. Plasma proteins were 6.7 grams per 100 cc. on November 27, 8 gms. on November 28, and 6.5 gms. on November 29. Following cessation of the diarrhea the patient's convalescence was not interrupted. The fullness and discomfort in his abdomen gradually subsided, his appetite increased, and his strength returned. On December 10 an intravenous cholecystogram was obtained which showed only slight visualization of the gallbladder and revealed many small stones. He was discharged from the hospital feeling well and requested to return after a month.

During the interim he had one attack of vague discomfort in his upper abdomen with nausea, but no vomiting and no actual pain, this attack lasting only a few hours. On admission on January 7, 1941, he felt well and was deemed in proper condition for a cholecystectomy. On January 8 the abdomen was opened and exploration of the pancreatic region revealed a nodular indurated organ about which, in the mesentery, were many small hard yellowish nodules, typical of a previous fat necrosis. One of these nodules was taken for biopsy, also a piece from the tail of the pancreas. This specimen was obtained by blunt dissection because of the difficulty of exposure, this procedure being possible because of the extreme friability of the gland. The gallbladder was found to be full of stones and was removed in the usual manner. Direct visualization and palpation of the common duct revealed no abnormalities and actual exploration of this duct was not carried out.

On the third postoperative day, after a very slight chill, the patient's temperature rose to 39, he began to cough up thick, tenacious bloody sputum, and developed signs of consolidation in the right lower lung field. Type nine pneumococcus was

cultured from the sputum. The patient was advised to cough vigorously, and this he did very effectively. Sulfathiazol was given in large doses and three days later the patient's temperature was normal and remained so. However, during one of his coughing spells, he felt a sharp pain in his wound and there followed some bloody discharge, which inspection revealed to be due to a disruption beneath the skin. He was treated conservatively for several days, then a secondary closure was done on January 19. His recovery from this was complicated only by a low grade infection of the wound. The urine throughout this infection was negative, the fasting blood sugar was 171 and 130 on two determinations.

When seen on follow-up examination in March, the patient was perfectly well and had almost regained his strength. He had developed no postoperative hernia; a few granulations still remained.

Urology

The diagnosis and treatment of carcinoma of the prostate is not easy. The diagnosis may be obvious in the elderly male with a large, irregular and stony hard prostate but the patient can be offered little other than palliative treatment for his malignancy. The same physical characteristics which identify the prostate as cancerous also indicate the extension of the process beyond the confines of the gland and may limit hope from remedial surgery or irradiation therapy. This individual, if obstructed, may be temporarily relieved of his obstruction by the transurethral removal of obstructive gland tissue in his prostatic urethra. Deep X-ray therapy within the limits of soft tissue tolerance will usually relieve the pain in the back and legs produced by metastases in the pelvic bones and lower spine. Urinary antiseptics to combat infection, local bladder instillations and judicious sedation represent other palliative treatments.

In the patient presented here today, the cancerous prostate is not so large, hard or irregular and is a somewhat different problem. The physical evidences on rectal palpation are suggestive but not unmistakable. Cystoscopic visualization of the extension of the malignant process into the urethra or bladder might remove any doubt as to the character of the lesion but

such extension by a necrotic tumor mass does not present itself in this patient. There is no history of vague pain in the back or legs to suggest a diagnosis of malignancy. Occasionally, X-ray evidence of bone metastases will remove any uncertainty about the diagnosis.

The insertion of trocar-like prostatic biopsy forceps, such as have been devised by Lowsley or Hoffman, directly into the prostate through the perineum offers one means of securing tissue for pathological examination.

On the other hand, it may be necessary to fall back upon a transurethral resection of the prostate in order to obtain biopsy specimens to confirm an impression left by rectal palpation. This was our procedure in this case. Such biopsy specimens should be obtained if the suspicion of malignancy is strong even though there be no suggestion of mechanical obstruction. Usually there is some obstruction with which to justify the need for resection entirely aside from the consideration of biopsy. Even the transurethral removal of several specimens from the prostate for biopsy may fail to solve the problem, however, since such specimens are taken rather superficially whereas the malignant process may be confined to the more distant subcapsular portions of the gland.

There are those who believe that cancer of the prostate arises in the surgical capsule and that this is an additional reason for radical perineal removal of the gland and the adjacent structures if some cases are to be cured. It is with this in mind that the Department has recently installed a Hugh Young perineal table so that the results of a more radical approach to malignant prostates can be studied. Certainly, suprapubic enucleation of the malignant gland is very unsatisfactory and apt to be attended with a stormy post-operative course. The implantation of radium needles has never been attended with consistently good results. It has been our feeling in the past that transurethral resection of malignant prostates and irradiation of metastases was a sound method of handling these patients. It will be interesting to see if more radical measures improve our results.

The apparently benign prostate in which malignancy is not suspected until the gland is sectioned after enucleation or resection is not uncommon.

Finally, it should be kept in mind that the pathological diagnosis of carcinoma of the prostate is in itself not always easy, both as to differentiation of malignant changes from benign changes and because of the chance that a malignancy may be missed unless a large number of sections are examined.

News of the School

Dr. R. J. Terry to Retire

Announcement has been made that Dr. R. J. Terry will retire in June as the head of the Department of Anatomy in the School of Medicine. He will be succeeded by Dr. Edmund V. Cowdry, professor of cytology, whose department will be combined with the anatomy division.

In his long teaching career, Dr. Terry has instructed about 3000 medical students in anatomy. Born in St. Louis, he attended Cornell University and obtained his medical degree from the old Missouri Medical College in 1895.

During the war, he was dean of the Officers' School of Oral and Plastic Surgery at Washington University. He has served as president of the American Association of Physical Anthropology and of the St. Louis Academy of Science. From 1921 to 1927, he was a member of the National Research Council. He has written papers and textbooks on human and comparative anatomy, anthropology and wild life conservation. He is associate editor of the American Journal of Physical Anthropology.

Three years ago, alumni of the medical school presented a portrait of Dr. Terry to the school and set up a fund in his name to be used for research in anatomy.

Dr. Cowdry, sent by the Rockefeller Foundation to South Africa on the invitation of the Government there in 1924, discovered an organism causing a disease known as heart water, found in sheep, goats and cattle. In 1930 he discovered the life cycle of the East Coast fever parasite.

After teaching anatomy at the University of Chicago and Johns Hopkins University from 1909 to 1917, he became professor of anatomy at Peking (China) Union Medical College, operated by the Rockefeller Foundation. He remained there four years. Then from 1921 to 1928, he was an associate of the Foundation, working most of the time in New York.

He was a member of scientific expeditions to Alaska, Russia, Japan, South China, Tunis and Kenya Colony. Since 1928 he has been on the Washington University faculty as professor of cytology, the study of cell anatomy. He has served on com-

missions studying yellow fever, infantile paralysis and leprosy. In 1939 he was appointed Director of Research at Barnard Free Skin and Cancer Hospital, St. Louis.

Southern California Medical and Dental Alumni Form Chapter

L. CLIFFORD MCAMIS, JR., D.D.S. '38

Medical and dental alumni in Southern California have organized to get together periodically and reminisce once again of the good times they had while attending Washington University. Their first meeting was held at the University Club in San Diego. Paul U. Hartman, M.D., '35, was elected president, and L. Clifford Amis, Jr., D.D.S., '38, secretary-treasurer.

Following an excellent dinner, everyone contributed anecdotes of their experiences at Washington. Dr. Vernon G. Clarke, the senior alumnus attending the gathering, graduated from the Missouri Medical College in 1896, and he gave a very interesting summary of the history of the old school. He also gave some thumb nail sketches of his class mates which proved very interesting inasmuch as the younger men present recalled them as their professors.

This group hopes to serve as a nucleus of a larger alumni chapter for all those now living in Southern California. The next meeting has been planned for April 26th and will again be held in San Diego. All those who are interested should contact Dr. Clifford McAmis, 625 Broadway, San Diego, Calif.

Those present at the first meeting were: Paul U. Hartman, M.D., '35, L. Clifford McAmis, D.D.S., '38, Vernon G. Clarke, M.D., '96, James I. Knott, M.D., '25, Tim V. Richey, M.D. '38, John D. McCausland, M.D., '37, E. H. Christopher, M.D., '25, Frank H. Robinson, M.D., '35, W. H. Geistweit, M.D., '19, Robert Sayre Smylie, M.D., '24, Thomas F. Wier, M.D., '10, Paul C. Sheldon, M.D., '35, Philip K. Allen, M.D., '27, M. J. Kotler, M.D., '28, George E. Zukovich, M.D., '33, W. W. Belford, M.D., '25, Edward A. Blondin, M.D., '19.

Dr. Evarts A. Graham Elected to Swedish Society

Dr. Evarts A. Graham, Professor of Surgery at Washington University Medical School, has been elected to the Royal Society of Sciences of Upsala, Sweden. The Society, founded in 1710, elected five members. Dr. Graham was the only Amer-

ican chosen. Election to the Society is based on scientific merit in the members chosen field. Dr. Graham has been responsible for many of the advances in chest surgery which have taken place in the last two decades. He was the first in medical history to remove successfully an entire lung. He has received honorary degrees from Yale and Princeton Universities and the University of Pennsylvania.

In 1939 Dr. Graham was elected president of the American College of Surgeons and a lectureship was established at Washington University the same year. Last June Dr. Graham was made head of a national defense surgical committee.

Society of University Surgeons

The third annual meeting of the Society of University Surgeons was held at the Washington University Medical School and Barnes Hospital on Friday and Saturday, February 13 and 14, 1941. This organization is composed of men under forty-five years of age who have completed their residency in the surgical departments of Cornell, Columbia, Yale, Harvard, University of Rochester, University of Cincinnati, University of Illinois, Vanderbilt, University of Chicago or Washington University and are still actively engaged in a university hospital on the teaching staff of the Department of surgery.

Dr. Evarts Graham presented a dry clinic on Friday morning illustrating the advances in chest surgery. The remainder of the morning program was devoted to presentations of original work by members of the organization.

The Society was the guest of the Board of Trustees of Barnes Hospital at a luncheon with Mr. Frank C. Rand, Chairman of the Board of Trustees, as the presiding officer.

The principal speaker at the evening dinner meeting at the Chase Hotel was Dr. Warren H. Cole, President of the Society, a Washington University alumnus, class of 1920, former resident in surgery at Barnes Hospital and now Professor of Surgery at the University of Illinois.

The Saturday morning program was devoted to the remainder of the scientific papers by the membership, all of which will appear in the Journal of Surgery, its official organ.

Dr. Frank Glenn, Associate Professor of Surgery at Cornell,

and Washington University alumnus, Class of '27, was elected President of the Society.

Fifty-three members attended the session out of the membership of some fifty-nine and the University Hospitals of the University of Virginia, Duke University, University of Minnesota were declared eligible for membership in the organization. Its honorary guests included Dr. Mont Reid, Professor of Surgery at the University of Cincinnati, Dr. Dallas Phemister, Professor of Surgery at the University of Chicago, Dr. Alfred Blalock, Professor of Surgery at Johns Hopkins University and Dr. Evarts A. Graham, Professor of Surgery, Washington University School of Medicine.

Alumni Banquet to Be Held May 31

The annual banquet of the Washington University Medical School Alumni Association will be held May 31, 1941.

Place: Jefferson Hotel. Time: 7:00 P. M.

No formal speeches are planned. Make reservations through the Alumni Office.

Barnard Free Skin and Cancer Hospital Lecture

The second Barnard Free Skin and Cancer Hospital Lecture was held at the St. Louis Medical Society, November 19, 1940. Carl Voegtlin, Ph.D., Chief of the National Cancer Institute, National Institute of Health, U. S. Public Health Service, Bethesda, Maryland, gave the lecture on "Possibilities of Improved Therapy for Cancer Patients."

Medical Library

Dr. Hardy A. Kemp, dean of the University of Vermont College of Medicine, was a welcome visitor in the library, February 21st. He was especially interested in the Beaumont collection of manuscripts.

Dr. Alfred O. Adams of the class of 1924, who is now in Spokane, Washington, paid a visit to the library in February.

Some twenty years ago there were three young men in the laboratories of Washington University School of Medicine, all imbued with the idea of research: Edgar Allen, Charles Danforth, and Edward A. Doisy. Within a period of a few years the three laid the foundation of our present knowledge of the sex hormones. Today, each of them occupies a professorship in a prominent university, and the work begun at Washington University has been continued at Yale, at Stanford, and at St. Louis University. A copy of their recently published book on *Sex and Internal Secretions*, inscribed by each, has been presented to the Library of the Medical School. It forms a prized part of the shelf of books inscribed by former and present members of the Faculty.

The following books have been received in the library recently:

- American Association for the Advancement of Science. Some fundamental aspects of the cancer problem. N. Y., 1937.
- Armstrong, H. G. Aviation medicine. Baltimore, 1939.
- Bailey, Percival, et al. Intracranial tumors of infancy and childhood. Chicago, 1939.
- Barker, Llewelys F. Psychotherapy. N. Y., 1940.
- Bentley, M., and Cowdry, E. V. Problem of mental disorder. N. Y., 1934.
- Blalock, Alfred. Surgical care, shock and other problems. St. Louis, 1940.
- Compton, Arthur H. X-rays in theory and experiment. 2nd ed., N. Y., 1935.
- Coon, G. P., and Raymond, A. F. Review of the psychoneuroses at Stockbridge. Stockbridge, 1940.
- Duke-Elder, Sir W. S. Text-book of ophthalmology. St. Louis, 1939. 3 volumes.

- English, O. S., and Pearson, G. H. J. Common neuroses of children and adults. N. Y., 1937.
- Flexner, Abraham. I remember. Autobiography of Abraham Flexner. N. Y., 1940.
- Gladstone, R. J., and Wakeley, C. P. G. Pineal body. Balt., 1940.
- Gunn, J. A. Introduction to pharmacology and therapeutics. 6th ed., Lond., 1940.
- Harris, Seale. Clinical pellagra. St. Louis, 1941.
- Hart, Bernard. Psychology of insanity. 4th ed. N. Y., 1931.
- Hawley, E. E., and Maurer-Mast, E. E. Fundamentals of nutrition. Springfield, Ill., 1940.
- Krogh, August. Osmotic regulation in aquatic animals. Cambridge, 1939.
- Langworthy, Orthello R., et al. Physiology of micturition. Balt., 1940.
- Lowsley, O. S., and Kirwin, T. J. Clinical urology. Balt., 1940. 2 volumes.
- Mason, R. L. Preoperative and postoperative treatment. Phila., 1938.
- Maxson, L. H. Spinal anesthesia. London, 1938.
- Miller, Emanuel, ed. Neuroses in war. N. Y., 1940.
- Moon, Virgil H. Shock and related capillary phenomena. Lond., 1938.
- Muncie, Wendell. Psychobiology and psychiatry. St. Louis, 1939.
- Roesler, Hugo. Atlas of cardioroentgenology. Springfield, Ill., 1940.
- Ross, T. A. Enquiry into prognosis in the neuroses. Cambridge, 1936.
- Vaughan, H. S. Congenital cleft lip, cleft palate and associated nasal deformities. Phila., 1940.
- Visscher, Maurice B., ed. Chemistry and medicine. Minneapolis, 1940.
- Whitnall, S. E. Study of anatomy. 3d ed. Balt., 1936.
- Wilder, R. M. Clinical diabetes mellitus and hyperinsulinism. Phila., 1940.

GIFT

- Menninger, Karl A. Man against himself. N. Y., 1938. Gift of Dr. Sydney B. Maughs.

In Memoriam

- Clinton Beasley, '82, Bonner Springs, Kansas, died March, 1941.
- Louis C. Boisliniere, '82, St. Louis, Mo. died January 11.
- Edwin Cass, '99, Vancouver, Wash., aged 79, died February 1.
- Charles B. Cooper, '89, Honolulu, T. H., aged 75, died November 11, 1940.
- W. G. Cowan '92, Roswell, N. M., died July 9, 1940.
- Montrose Day, '81, Haynesville, La., aged 85, died October 27, 1940.
- Arthur H. DeMasy, '11, St. Louis, Mo., died January 15.
- Oscar R. Engelmann '06, St. Louis, Mo., died March 8.
- Edwin O. Gable, '03, Chicago, Ill., died January 9 .
- Willard E. Gant, '84, Hardin, Mo., deceased.
- J. B. Gathright, '82, St. Louis, Mo., deceased.
- E. J. Goodwin, '94, St. Louis, Mo., aged 76, died February 18.
- W. G. Harwood, '82, Dover, Mo., aged 66, died January 28.
- Herbert S. Langsdorf, '15, St. Louis, Mo., died January 16.
- Joseph F. Miller, '89, Palmer, Ill., deceased.
- Leonard Niess, '12, Trenton, Ill., aged 62, died January 19.

CLASS OF '26: MEET YOUR CLASSMATES AND RENEW
OLD FRIENDSHIPS AT THE ALUMNI BANQUET
MAY 31ST

Alumni News

A letter relating a very interesting incident that happened during the practice of his father, S. H. Redmon, '80, has been received from Mr. W. L. Redmon. He writes that some forty-seven years ago his father was called on an obstetrical case and found that in order to reach his patient it would be necessary for him to swim across a creek swollen by flood waters, which he did. On this case he performed what is thought to be the first blood transfusion in his section of the country and made the needle himself from a piece of hard rubber syringe. Mr. Redmon writes that his father is nearing 90 years of age and is in feeble health. He has been retired for the last fifteen years and is residing in Tipton, Mo.

James H. Lacey, '83, Denver, Colo., writes that he has passed the eighty-fourth mile stone in his life, and would like very much to attend the alumni reunions but feels he is not physically able to do so.

C. A. Hadsell, '85, tells us he has lost all contact with his classmates and would be very glad to hear from them. Dr. Hadsell is 87 years of age and resides in Littleton, Colorado.

Jeff D. Dorbrandt, '91, after 45 years of general practice in Texas has retired and is now living in Monrovia, Calif. He wishes good health and a long life to all of his classmates and states that he would enjoy hearing from them.

A meeting was held on October 3, 1940 of the San Joaquin County Medical Society to honor Dr. John D. Dameron, '94, and named him "Dean of the Active Practitioners of Medicine of the San Joaquin

County Medical Society." Dr. Dameron's experiences in practice have been many and varied, ranging all the way from the horse and buggy country practitioner to the streamline era of today. Dr. Dameron is 73 years of age and the oldest member of the Medical Society.

Carmen A. Newcomb, '94, is Assistant Health Officer of the Los Angeles City Health Department. He writes that he "would like to hear from any of the old crowd."

A. J. Gardner, '01, recently moved his office for the practice of general medicine to Norborne, Mo.

Herbert L. Thompson, '03, Long Beach, Calif., has just returned to his office after a year's absence, the result of an auto accident. Dr. Thompson specializes in ophthalmology.

F. S. Marnell, '04, is on the resident staff of the State Hospital for the Insane at Stockton, California. Dr. Marnell has been connected there for the past twenty-two years and for the past two years has been devoting much of his time to treatment of syphilis of the central nervous system and to research work along that line. He writes that he "enjoys the Alumni Quarterly and is always glad to see or hear about any of the Washington University doings or people."

Lt. Col. Ray Mercer, '06, Quincy, Ill., left in March for a year's military training with the 33rd Division of the Illinois National Guard.

Bert W. Hardy, '08, Huntington Beach, Calif., writes "I am fair—fat—past fifty—and doing industrial surgery for many years."

L. H. Slocumb, '13, has offices for

his practice, which is limited to proctology and general surgery, at 1355 Wilshire Blvd., Los Angeles, Calif.

Charles H. Hecker, '11, is retired from practice and residing at 219 Washington Ave., Palo Alto, California.

William Bonner James, '15, Manhattan Beach, Calif., retired as Lt. Comdr. in the Medical Corps of the U. S. Navy in 1932. Dr. James is married and has one child, a boy eight years old.

William C. Pollock, '16, is Assistant Chief of the Medical Service and Chief of the Enlisted Tuberculosis Service at Fitzsimmons General Hospital in Denver, Colorado. He writes that the mobilization of the nation's defenses has increased their work there tremendously.

Elmer N. Liljedahl, '18, is radiologist at the Hollywood Presbyterian Hospital in Los Angeles, California.

James D. Dean, '18, is a Lt. Colonel, 115th Medical Regiment, and was inducted into the regular army from Los Angeles on March 3. He is in field training at Camp San Luis Obispo, San Luis Obispo, California.

Lloyd J. Thompson, '19, is a Major in the Medical Reserve with the Hospital Unit of Yale University School of Medicine, and psychiatrist on the Medical Advisory Board No. 2 of Connecticut. Dr. Thompson resides at 330 Cedar St., New Haven, Connecticut.

H. H. Heuston, '19, Boulder, Colo., writes, "Just returned from California with my wife (Louise Curtis), and sons, Bob and Phil. We visited our other son, Bill, who works for Consolidated Aircraft in San Diego. Saw classmates Geistweit and Blondin in San Diego and Gundrum in

Los Angeles. All on the upgrade as usual."

Duff S. Allen, '19, St. Louis, was honor guest at a noonday luncheon given by Dr. C. R. Rountree, '24, at the Oklahoma Club, Oklahoma City, March 15th. Other invited guests, confined to local Washington University medical alumni, were Doctors C. F. DeGaris, '12, R. L. Murdoch, '19, L. J. Starry, '19, Grider Penick, '20, G. K. Dickson, '22, G. H. Garrison, '24, G. N. Barry, '30, J. L. Glomset, '30, S. S. Ellis, '36, C. H. Epps, '36, and W. D. Read, '40.

G. E. Christensen, '21, Los Angeles, writes that he is practicing gynecology and abdominal surgery "in California's unusual weather area."

Leon G. Campbell, '22, has been practicing internal medicine in Pasadena, California for 15 years. He is on the Senior Medical Staff of Huntington Memorial Hospital and is president of the Pasadena-Alhambra Branch of the Los Angeles County Medical Society. Dr. Campbell is married and has three children.

Eugene S. Auer, '24, is in private practice, limited to obstetrics and gynecology, in Denver, Colorado, and is an instructor in the University of Colorado School of Medicine. He writes that "Denver is a great place to live and practice." Dr. Auer is the proud parent of two children; Marilyn, age 11, and Dickie, age 7.

J. I. Porter, '24, practiced in Benicia, California, until March 17 at which time he reported for duty in the Navy as Lieut. Comdr. at the Marine Base in San Diego, Calif.

Jerome Levy, '25, Little Rock, Arkansas, recently visited the Alumni Room. Dr. Levy was in St.

Louis attending a Missouri Pacific Hospital Convention.

J. Lester Henderson, '29, has just received his call to active duty in the Navy. Dr. Henderson is a specialist in psychiatry and will follow this specialty at his station, the Naval Hospital, Great Lakes Naval Training Station, Great Lakes, Ill.

Clarence E. Jump, '29, has specialized for the past ten years in neuropsychiatry and for the past four has been with the Veterans Administration in Roseburg, Oregon. Dr. Jump is married and has three children. He tells us that he would appreciate a visit from any alumni who happen to pass through his vicinity.

G. E. Garrison, '31, is in general practice in the Robertson Bldg., Fort Collins, Colo. Dr. Garrison's hobby is aviation. He pilots his own ship and expects to fly to St. Louis during the coming summer. He is married and has a daughter, Patricia, four years old.

Paul B. Nutter, '32, is connected with Chicago University doing research on conditions of the gastrointestinal tract. Dr. Nutter has published several papers on his work, the latest being "Anatomical Foundation of Anacidity": *Arch. Int. Med.* 66; 1060, 1940.

O. B. Doyle, Jr., '33, is in general practice in Fresno, Calif., and writes that he is "not doing so badly." Dr. Doyle has two children; O. B., III, age 5, and Susan, age 4. He says there is always open house there for anyone who can make it.

Ralph Knewitz, '33, is a Captain in the Army Medical Corps and is stationed at Fort Bliss, El Paso, Texas.

Louis G. Jekel, '34, is associated in the practice of dermatology with

Dr. Gerald M. Frumess. Their office is at 210 Republic Bldg., Denver, Colorado.

John M. Nelson, '34, is practicing pediatrics at 1578 Humboldt Bldg., Denver, Colo. He was recently certified by the American Board of Pediatrics.

Oliver P. Schureman, '34, recently moved to a new and larger office in South Pasadena, Calif. He and Mrs. Schureman are receiving congratulations on the birth of their daughter, Lucille Louise, on March 29, 1941.

Clement J. Molony, '34, has a daughter, Kathleen, born January 30, 1941. Dr. Molony is practicing pediatrics in Hollywood, California.

Alexander Silverglade, '36, says that he is enjoying army life very much. First Lieut. Silverglade is with the Medical Detachment, 30th Infantry, Presidio, San Francisco, Calif.

Ivan J. Miller, '36, recently received an appointment as instructor in Radiology at Stanford University.

James W. McMullen, '37, is radiologist at Glockner Hospital, Colorado Springs, Colo., and assistant to Dr. Henri Coutard (French roentgen-therapist). Dr. McMullen holds the rank of Major in the Medical Reserve.

A. Edward Meisenbach, Jr., '37, is a clinical instructor of ophthalmology at the George Washington School of Medicine in Washington, D. C. He is a member of the Medical Advisory Board "A" of the District of Columbia, and is a First Lt. in the Medical Reserve. Dr. Meisenbach recently published "Hemangioma of the Orbit. Report of Six Cases with Clinical and

Anatomic Findings." *Am. J. Oph.* 23: 286-295, Mar. 1940.

Roy W. Thomas, '38, is finishing his surgical residency this year at St. Luke's Hospital in San Francisco, Calif. Dr. Thomas plans on going into private practice next year.

George A. Peck, '38, is a Captain, Medical Corps, Army, and is Flight Surgeon at Lowry Field, Denver, Colo.

Wayne P. McKee, '38, is in private practice in Ripon, California.

Eleanor Steindorf, '38, is resident in obstetrics at Children's Hospital, San Francisco, Calif. Dr. Steindorf expects to practice obstetrics and gynecology in Cleveland, Ohio next year.

J. William Shuman, Jr., '38, was married March 8 to Miss Helen Blackman of Beverly Hills, California. They are residing at 3513 W. Adams, Los Angeles.

Harry Baers, '38, attended the School of Aviation Medicine, Randolph Field, Texas, and will be on

duty as Flight Surgeon with the Air Corps, Hawaiian Department, Honolulu, in the near future. Doctor Baers was married in October, 1939 to Donna Norwood, R.N., '38, Washington University School of Nursing.

Howard T. Robertson, '40, was married December 21, 1940, to Miss Mary Ellen DeMotte of Chicago, Illinois. He is interning at the Denver General Hospital in Denver, Colorado, and since he is a ski enthusiast, feels that Denver is an ideal place to live.

Harry W. Sawyer, Jr., '40, is interning in the Southern Pacific Hospital, San Francisco, Calif. He will have a residency at St. Francis Hospital, San Francisco, "unless called to active duty in the army," during the coming year.

Paul Guggenheim, '40, will continue his internship at Los Angeles County Hospital until July, 1942. Dr. Guggenheim has announced his engagement to Miss Delores Casey of Hollywood, Calif.

ALUMNI BANQUET, MAY 31

MAKE YOUR RESERVATIONS NOW

Student News

Since the last issue the students have been showing definite signs of life and with spring just around the corner sports and social affairs are becoming prominent extracurricular activities.

SOCIAL

The big social affair of the year is the Junior-Senior Prom given each year by the Juniors for the Seniors. It was held on April 5, at the Forest Park Hotel and was anything but a disappointment to those who attended.

Several of the fraternities have held initiations and entertained their new members. Nu Sigma Nu initiated four men on March 1, and followed the initiation with a dance at the Blackjack Country Club. On the same date Phi Rho Sigma initiated seven and entertained at a house dance. Phi Delta Epsilon followed their initiation of eight men with a formal dinner-dance at the Westwood Country Club, again of March 1. Phi Beta Pi held their initiation on March 29, and entertained the twenty initiates at a formal dinner-dance at the Coronado.

In addition to the initiation dances each fraternity has had at least one house dance since January and the Phi Deltas manage to have a dance about every two weeks.

The Sophomores finally broke through with some class spirit and threw themselves a party at Albrecht's on March 26.

ATHLETICS

The students have, as usual, entered a team in the St. Louis Rugby

League. The Medics did not do as well this year as in the past but at least managed to tie for second place in the first half of the schedule. Perhaps we can pull up to the top before the season is over.

The Freshman, Junior, and Senior classes each entered a team in the Washington U. intramural basketball tournament. The seniors showed the freshmen and juniors a thing or two about how the game is played, but lack of practice kept them from shining against the undergraduate teams.

A softball league has been formed among the medical fraternities, and, with a barrel of beer at stake, it looks like we are going to have some hot games.

JOURNAL CLUBS

In January the Phi Betas were given a talk by Dean Shaffer on "Recent and Planned Changes in the Curriculum." In February Dr. Alexis Hartmann talked to them on "Chemotherapy," and in March Dr. T. K. Brown presented a movie on "Standard Obstetrical Routine."

The Phi Rho's heard Dr. Frank McDowell talk on "Skin Grafting in the Treatment of Burns" in January, and in March Dr. Wilson Brown discussed "Some Interesting Recent Cases at the City Hospital."

Journal Clubs are one of the most important contributions of the Fraternities to the life of the School and are invaluable in promoting more intimate acquaintance between the students and members of the Faculty. Here's hoping that we can have more of them in the future.

Charles M. Huguley, '42

PLEASE CONTRIBUTE NEWS

for the Quarterly and Information for the Alumni Office

using the following form as a guide and sending your response
to Miss Louise Hunt, Washington University
School of Medicine

Full name (print)

Class of

Office address: number and street, town and state

Membership in medical and other scientific societies and offices
held

Field of work (as general practice, ophthalmology, public
health, pathology, teaching, investigation, etc.)

Connection with hospitals and schools

Army and Navy (branch and rank)

Papers published in present year (title, journal, volume,
pages, and date)

Books published (give full title, publisher, place, date, number
of pages, illustrations)

(OVER)

Editor or associate editor of medical or other scientific journal. Election to honorary societies (name of society and date of election). Honorary degrees, citations, medals, prizes

.....

Member of scientific expedition, medical survey

.....

Recipient of fellowship or of grant-in-aid of investigation

.....

Connection with or activity in any other province of medicine not covered by the above

.....

Have you a son or daughter entering the School next year?

.....

Recent marriage—name, date and place

.....

Recent birth—sex, date

Death—name, class, date of death, place

.....

Desirable location for practice: town and state, number and street

Remarks

.....

.....

Write a letter of 200-250 words to the Quarterly for publication.

Please donate to the Library of the School of Medicine copies of books and reprints of papers you have published. You will confer a benefit to the Library and help to establish a record of the literary contributions of our graduates and faculty.