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OFFICIAL PUBLICATION OF THE UNIVERSITY OF MINNESOTA HOSPITALS THE MINNESOTA MEDICAL FOUNDATION AND THE MINNESOTA MEDICAL ALUMNI ASSOCIATION

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Human Cell Cultures

Medical Technology

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Staff Meeting Report

Human Cell Cultures for Investigative Studies*†

Jerome T. Syverton, M.D.[1]

A research team in the Department of Bacteriology and Immunology since 1949 has employed human and animal cells in culture for experimental studies of cancer and viruses, more particularly the polioviruses. My associates as staff members, postgraduate and graduate students, have been many. The present summary, for the most part, concerns results during the past two years obtained in collaboration with Doctors L. C. McLaren, J. D. Ross, W. F. Scherer, George Gifford, Richard Crowell and J. D. Gall. Important to our work has been the cooperation of Doctors Richard Varco, Fletcher Miller, N. Logan, Leven, C. Donald Creevy, William Feller, Paul Lober, and the surgical residents in pathology who made it possible to obtain small pieces of operative specimens.

Mammalian cell culture has become a science in itself. Under pressure of virologists' demands for living, actively metabolizing mammalian cells for propagation of viruses, earlier use of animal cell culture as a subordinate extension of animal anatomy and physiology has given way to evolution of a science of animal cell biology. Study of animal cell metabolism and morphogenesis has been intensified because virologists have needed to know the normal body cell to interpret cellular responses to viral infection. Present exploitation of cell culture technics by virologists is being matched increasingly by the interest of researchers concerned with cancer, tissue transplantation, allergy and pharmacology. This growing interest suggests that *in vitro* cultivation of mammalian cells will become a general tool of diagnostic and investigative medicine. Now, when mammalian cell culture is about to emerge from its adolescence so to speak, it is interesting to consider some contributions of virology to cell culture during the last decade because concern with virus diseases is still far from academic, and

*This is a report given at the Staff Meeting of the University of Minnesota Hospitals on December 14, 1956.

†Aided by grants from The National Foundation for Infantile Paralysis, Inc., and The National Cancer Institute, National Institutes of Health.

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because these contributions have provided the bases for further advances and wider applications.

Historical Review

In 1949 cell culture technics for study of virus-host relations were limited to: *a*) the Harrison coverslip-hanging drop[1] for short-term cultures; *b*) and Burrows-Carrel flask-plasma-clot[2], suited to continued propagation and maintenance of cells; *c*) the Gey roller-tube-plasma-clot[3], adaptable to use of large numbers of cultures and long-term propagation of cells by serial transfer; and finally, *d*) the Maitland culture[4] employing suspended tissue fragments rather than true explants. An inability to propagate certain viruses in suspended fragments of host tissue susceptible *in vivo* led to the misinterpretation that such viruses were not propagable *in vitro*. In 1949 Enders and his associates[5] refuted this contention by cultivating poliovirus in human tissue cultures of non-nervous origin. Their work encouraged virologists to reconsider the usefulness of the cultivated host cell. As a result, cell culture technic has become a primary and indispensable tool of virology. The necessary scale of cell culture production was made possible by: *a*) control of contamination by use of antibiotics, *b*) dispersion of cells with trypsin, a procedure described by Rous and Jones in 1916[6] and reintroduced by Scherer, Syverton and Gey in 1953[7], and *c*) mass dispensing of replicate cell cultures with apparatus modified in our laboratories from an earlier design of Evans, Earle and associates[8]. Following these developments, primary cell cultures of human or animal tissue to a great extent replaced animals or embryonated eggs for diagnostic and investigative study of viruses. The next step was to replace the cells cultivated directly from tissue with stable strains of continuously cultivated human cells of a single morphological type. Application of the human cell strain to examination of virus cell interactions, initiated at the University of Minnesota, has resulted here and elsewhere in their widespread use and in the development of a variety of strains. For example, our laboratory each week provides from 2,500 to 4,000 cultures of nine stable human cell strains for intradepartmental investigative studies. Each culture serves to replace an animal, mouse or monkey in these experimental studies. Human strains in use include Gey's HeLa uterine cervical carcinoma[9], Frisch's Maben pulmonary adenocarcinoma[10], Chang's conjunctival and liver epithelium[11], and six strains of human cells that originated in my laboratory. Now in continuous culture are esophageal epithelium

and fibroblasts, liver epithelium, a pulmonary cell, a palate fibroblast, and kidney epithelium. At least 10 other stable human strains are available in other laboratories, and a variety of strains of animal origin are being developed here. This range of normal and malignant cells in continuous culture has simplified and extended study of viruses and virus infections. Continuously cultivated human cells, such as those of strain HeLa, originally studied in these laboratories, are *a*) grossly uniform in morphology, size and metabolic activity, *b*) susceptible to infection by polio and a variety of other viruses, *c*) capable of mass cultivation, and *d*) available by maintenance of stock cultures. Several cell strains are available by purchase from commercial sources. The hardiness of these cells permits shipment of cultures even over long distances[12].

Recent Advances

Further refinement of cell culture technic has been gained by use of pure rather than merely established strains of human cells. The pure or clonal cell strain, derived from the progeny of a single isolated cell, permits control of genetic constitution of cells in studies of cellular metabolism and infection. The first pure line of mammalian cells, strain L, was derived in 1948 from mouse connective tissue by Sanford, Earle, and Likely[13]. Unfortunately, these mouse fibroblasts were not susceptible to many human viruses including poliovirus. In 1955 new methods for encouraging growth of single mammalian cells *in vitro* were described by Puck, Marcus and Cieciura[14]. Single cells were obtained by gentle trypsinization of parent cultures and established in Petri dishes in a medium containing a small amount of agar, where they multiplied into isolated colonies. These clones then were expanded into pure cell lines. Unusually delicate cells were induced to multiply in isolation by use of a "feeder" layer of irradiated cells capable of metabolism but not multiplication.

By a modification of the Puck technic we have derived six pure lines of normal and malignant human cells. The response of one of these strains, a pure line of human liver epithelium, to infection by types 1, 2 and 3 polioviruses has been compared[15] to the responses of primary dispersed monkey kidney cells, cells of stable strains of cervical carcinoma (HeLa) and lung carcinoma (Maben), and cells of stable strains of normal human liver and conjunctiva. All of the different cells in culture exhibited similar cytopathogenic responses and appeared equally susceptible to the three types of poliovirus as measured by 50

per cent infective dose. The three poliovirus prototypes were readily propagable with the usual type of cellular destruction through four to six successive passages in the pure line as well as in the parental strain of liver cells. Cells of the clonal strain of liver epithelium compared to those of the parental strain or of strain HeLa, were fully susceptible to infection by field strains of poliovirus.

Cytopathology and New Viruses

Widespread use of various types of cultivated animal cells for study of viruses has resulted in the accumulation of an increasing body of cytopathologic observations. Since infecting virus parasitizes the synthetic machinery of a host cell, cytologic injury could be expected. The range of cytopathic change is indeed so great as to extend from simple modification of metabolic activity to total necrosis and even to hyperplasia and neoplasia. With cell cultures, the course of virus-induced damage can be observed at the cellular level. Currently five classes of cytopathogenic damage to cells in culture can be described[16]. *Complete destruction* is the usual result of infection by viruses of the polio and Coxsackie B groups, some Coxsackie A types and some of the ECHO viruses. Both epithelial and fibroblastic human cells are susceptible to infectious necrobiosis. In periods of hours to days the process, starting from rounding of cells and retraction of processes, extends to shrinkage of nuclei and disruption of chromatin and to complete cellular disruption. *Incomplete cellular degeneration* is evidenced in cultures by a mixture of necrotic cells and shrunken cells with altered staining characteristics and pyknotic nuclei. This effect is characteristic of the arthropod-borne encephalitogenic viruses and Newcastle disease virus. St. Louis and Japanese B viruses, however, in some cells do not produce this effect. Slow outward-spreading *focal degeneration* is induced by herpes, Japanese B, pseudorabies and vaccinia viruses. Inclusion bodies in various stages of development and occasional amitotically dividing nuclei are seen in cells bordering areas of destruction. With vaccinia virus nuclear changes are absent. Adenoviruses, unlike more virulent agents, attack epithelial cells or fibroblasts to produce *infection without inhibition of cell metabolism.* Affected cells round up, clump, become granular and degenerate, and finally peel off the glass. Culture pH continues to drop despite damage to the cells; the injurious process destroys epithelial cell cultures in from 2 to 7 days while affecting fibroblastic cells more slowly. Rustigian and co-workers[17], Enders and Peebles[18] and others have described

a *"foamy" degeneration* of cells produced by measles virus and simian orphan viruses. Proceeding outward from isolated foci in culture, cells aggregate into multinucleate syncytia with ragged, foamy, vacuolated cytoplasm.

Intracellular alterations underlying visible cytopathology have not been fully characterized. The caliber of investigation required to analyze cellular pathogenesis is exemplified by the work of Lwoff and associates[19] who used time-lapse cinematography and micro-manipulation to correlate visible pathologic changes in single infected cells with production and release of poliovirus.

Widespread laboratory employment of cell culture for diagnostic virology has added increasing numbers of new agents to the list of known human viruses. Reversing the usual history of virology, it has been a task to discover human illnesses associated with these viruses, rather than the converse. The new viruses have been recognized by the cytopathogenic effects in cell cultures inoculated with material of pharyngeal or intestinal origin during population surveys for research on polio and other more familar viruses. *Adenoviruses,* known alternately as the ARD (acute respiratory disease) or APC (adenoidal-pharyngeal-conjunctival) group, have been incriminated as causative agents of some respiratory diseases and keratoconjunctivitis. This group of 12 viruses can be separated by neutralization, but not by complement-fixation test. Serologically distinct viruses of 14 types make up the *enteric cytopathogenic human orphan (ECHO) group,* which are cytopathogenic for monkey and human cells in culture[20]. These viruses, which are not related to other known viruses recoverable in tissue culture, are neutralized by human gamma globulin and by individual human serums. This evidence indicates that the ECHO viruses infect human beings. Laboratory workers employing monkey kidney cells for diagnosis or vaccine preparation have encountered additional cytopathogenic viruses indigenous to monkeys. From the work of Hull, Minner and Smith[21], viruses isolated from the tissues or alimentary tracts of monkeys are known as the S.V. or *simian group.*

Ultimately, the practicing physician may be directly concerned with the new viruses, known currently as "orphan viruses" (originally by Duran-Reynals) because they are "viruses in search of disease". Systematic study and characterization of orphan viruses, and attempted association with specific human diseases, is an assignment currently shared by a number of laboratories, sponsored by the National Foun-

dation for Infantile Paralysis and the United States Public Health Service.

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Staff Meeting Report

Medical Technology*

Ruth F. Hovde, M.S.[1]

The primary purpose of this presentation is to report the development and activities of the Course in Medical Technology at the University of Minnesota. Furthermore it seems appropriate to present general information about this new profession of medical technology in order to promote better understanding and interest in this field of medical science.

Thirty-five years ago the Board of Regents of the University of Minnesota awarded the first degree of Bachelor of Science with the designation of specialization in Medical Technology. Because of the difficulty in finding and piecing together the meager historical facts about the establishment of this course, it seems appropriate to record some of the known events.

Dr. Wesley Spink[1], in speaking about the program here, referred to the "birth of a concept" and the initial planning for a program in Medical Technology as the first of three eras in the development of this curriculum at the University of Minnesota. During this period a committee composed of Dr. S. Marx White, Dr. Wilfred Larson, and Dr. Richard Olding Beard, who served as chairman, directed the course, setting the pattern of high standards of performance and the requirement of a four-year-degree program which have remained to this day. A degree program in medical technology was a complete innovation at that time. Concerning this revolutionary idea Dr. Beard[2] in 1923 wrote:

> "The apprenticeship plan has been the cheapest and the earliest plan and it is still followed, in most institutions, as the only surviving relic in any calling of our educational past. Apprenticeship has been practised under the name training school but in fact and in operation the school has been more like a shop in which novitiates have served a term of almost exclusively practical experience, determined as to its length more often by the demands of the hospital service than by the content of teaching or of the needs of the student."

It is not surprising, then, that under his leadership the original requirements for admission to this course were the same as for admission to

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* This is an address given at the Staff Meeting of the University of Minnesota Hospitals on January 11, 1957.

[1] Assistant Professor in Medical Technology

the College of Science, Literature, and the Arts and that the value of a combined liberal arts and professional education was recognized and established as the basic plan for this program.

The first course bulletin[3] was published on March 10, 1922 with the title, *Courses in Medical Technology for Clinical and Laboratory Technicians.* It contained the following announcement: "The demand for clinical and laboratory technicians trained in the principles and techniques of the medical sciences is increasing. The technician so trained is an aide to the physician, the surgeon, the medical specialist, the group clinic, the hospital, or the teaching and research laboratory. The vocation is one that offers satisfactory objectives, a large measure of usefulness and fair compensation." The course requirements of the first two years in the College of Science, Literature, and the Arts included credits in mathematics, chemistry, English, foreign language, and animal biology.

Four sequences were offered at that time to the student in the third and fourth years of the Course in the Medical School: a. sequence leading to service as a clinical technician; b. sequence leading to technical service in pathology, neuropathology, and gynepathology; c. sequence leading to technical service in bacteriology and serology; and d. sequence leading to technical service in anatomy or neurology.

No specific details about the clinical training were mentioned other than this statement: "Students in clinical technology, as soon as they have adequate preparation, will be assigned to practical work, for one or more quarters, in the technical laboratory of either University Hospital, Minneapolis General, or Charles T. Miller Hospital in all of which a wealth of clinical material is available and where expert supervision and training will be given." Evidently no formal clinical training was established, but rather the student in any of the sequences could do whatever practical work could be managed in between classes, often only a part of two or three mornings each week. This situation is not surprising in view of the many formal requirements of the course.

Upon Dr. Beard's retirement in 1925 Dr. William A. O'Brien was appointed chairman of a special committee composed of representatives from the Graduate and the Medical Schools to direct the Course. Under Dr. O'Brien's leadership the second "era of growth" emerged. During this time the curriculum content and the clinical training program were crystallized.

In 1929 the first program of rotation through the various clinical laboratories with definite assignments in each was established, but classes on the campus still took up a large part of each day. By 1932 the clinical year of 12 months was arranged for each student as follows:

General Laboratory (Hematology, Chemistry, and Bacteriology)	4 months
Tissues	2 months
Metabolism and Electrocardiography	1 month
Serology	1 month
*X-ray	4 months

In 1934 a regular system of submitting grades to the Registrar's office was started. Previous to this time whatever number of credits the student needed to complete 180 credits for graduation was submitted. Since this time a minimum of 45 credits in the senior year of clinical training has been required.

In 1936 the first full-time instructor and a budget of $600 a year to be used for teaching purposes were allocated to the Course. Mrs. Gleva Blain Erskine was appointed the first instructor. Mrs. Erskine had come to the University Hospitals in July, 1924, had served as "technician in charge" of the laboratory, and had gradually assumed the additional responsibility of supervising the student program. With this budget then, according to a department report[4], "sufficient funds were now available for mimeographed examinations, a supply of pipettes and counting chambers with which the students could practice, and textbooks for reference in the laboratory".

In 1939 the third "era of maturity" started with the appointment of Dr. Gerald T. Evans as Director of the Course in Medical Technology and Director of the Laboratory Service of the University of Minnesota Hospitals, in which capacity he serves at the present time. Under his guidance further changes in the curriculum and particularly in the senior clinical year have been made throughout the recent years. The current curriculum includes 2 years in the College of Science, Literature and the Arts and 2 years in the College of Medical Sciences, the second of which consists of 12 consecutive months in a rotating service in the clinical laboratories of the University of Minnesota Hospitals.

The clinical training in the fourth year is dependent on the Laboratory Service of the Hospital. The personnel in both areas contribute

* The inclusion of training in X-ray techniques in the fourth year later became an optional offering with the training in laboratory procedures lengthened to the entire 12 months.

materially to both the teaching and the service functions of the clinical laboratories. The first available detailed report of laboratory determinations appeared in the Hospital Report for 1927-28 and indicated that 24,869 tests had been carried out during that academic year. A similar report for 1955-56 showed that 519,005 tests had been performed.

In 1927-28 only ten different chemical determinations were done, while at the present time the chemistry laboratory is prepared to do 63 different procedures. The same situation exists for almost all the laboratory units and creates the necessity of a flexible training program with changing emphasis from time to time in keeping with the changing demands on the laboratory service.

The Course in Medical Technology here is unique in that the University of Minnesota was one of the first state universities, if not the first, to offer such a program at a degree level. In fact, university training for technical laboratory personnel has only recently been universally accepted. Clinical laboratory work is now beyond mere repetitive mechanical manipulations. Experience has shown that without education, consistent quality of work, let alone advancement in technical skill and knowledge, is impossible. The Course here has always been planned with the objective of teaching our students in such a way that, as graduates, they will be prepared to train other students and will be capable of accepting the responsibility for reliability of work and keeping up with advances in laboratory science. To this end the curriculum includes not only fundamental sciences but also introductory material in pathology and presentation of case material to assist the student in better understanding of the use and value of accurate laboratory tests.

The strength of the Course lies in the excellent cooperation with the other departments in the basic sciences in course offerings for our students and to the interest and encouragement consistently given by Mr. Ray M. Amberg, Administrator of the University Hospitals, and by Dr. H. S. Diehl, Dean of the College of Medical Sciences. The success of the program is dependent upon the efforts of our staff who have willingly accepted increasing responsibilities in teaching and demands for service.

In the 35 years of operation 1,110 students have been graduated from the Course. In the period, 1922-1926, there were 13 graduates, in 1927-1936, 201 graduates, in 1937-1946, 536 graduates, and in 1947-1956, 360 graduates. Along with the decrease in the number

of graduates in the past ten years, there has been an increased demand for more well trained technologists. The situation is further accentuated by the fact that many of the people working in laboratories are inadequately prepared to meet the needs of good laboratory service. The overall decrease in students in this Course specifically appears to be primarily due to a marked decrease in numbers of students transferring here at the third year level to complete requirements for a professional course. Before 1950 the number of transfer students averaged between 20 and 25 students per year. Since 1950, the annual transfer rate has averaged nine students.

The shortage of students in this field is not confined to this school alone but exists as a general situation throughout the country. Nor, in fact, does this situation exist for medical technology alone; there is a general need for more students and graduates in all allied medical professions. Reasons for this situation are complex. A report of the Council on Medical Education and Hospitals of the American Medical Association[5] in 1954 on the continuing shortage of well trained technical personnel stated: ". . . Although great progress has been made throughout the period of active standardization, it has not been possible to meet all of the needs for well trained technical personnel. Shortages are continuing in all areas and may be related to a number of factors such as the increasing competition with other fields, the mounting cost of education, prolonged periods of training, inadequate economic returns, high attrition rates, insufficient publicity, limited resources for recruitment, and the need for additional training centers in various parts of the country . . ."

The actual need for personnel in this field is difficult to determine with any confidence. In 1953 there were 5,832 hospitals in the United States with a bed capacity of approximately 1,170,000. Estimating one technologist for every 25 patients, 47,000 technologists would be needed for hospitals alone. At that time 22,741 full-time and 3,041 part-time technologists were employed by registered hospitals, 23,000 short of the ideal number[6]. These figures do not take into account the need for technical laboratory personnel in physicians' offices, clinics, and research laboratories.

All allied professional groups both at the local level and at a national level have been trying within the last few years to find solutions for this situation. Efforts are being made along the following lines:

1. Creation of the National Committee on Careers in Medical

Technology to provide better information to the public and, through high school counselors and other appropriate agencies, to prospective students about the need for people in this field and about opportunities in this profession as a vocation.

2. Studying and surveying salary levels and working conditions.
3. Conducting critical evaluations of training programs to improve proficiency of graduates.
4. Studying means for scholarship assistance for students in this field.
5. Encouraging use of auxiliary personnel (clerks, aides, dishwashers, etc.) wherever possible.

What effect these efforts will have is difficult to foretell. It is probably safe to assume that in view of the reports regarding predicted increase in college enrollment that the numbers of students in this Course will increase proportionately.

In order to determine the needs for the State of Minnesota, the Minnesota Medical Association and the Minnesota Hospital Association sponsored a statewide survey of physicians in 1951 with the cooperation of the Minnesota Department of Health. The survey was specifically designed to secure information regarding laboratory and X-ray personnel, services, and facilities.

The returns were tabulated by the Hospital Services Program of the Minnesota Department of Health and reported in November, 1951. In summary the report indicated:

1. A real need not only for more technologists but also for better trained personnel for laboratory work.
2. A need for technicians (sub-professional level) well trained in limited procedures for physicians' offices and in hospitals under supervision.
3. An interest in a visiting technologist consultant program.
4. An interest in short courses of refresher type to improve quality of the work of the personnel presently employed.

The first aspect of the Minnesota survey that involved this department was the request that our staff, together with that of the Minnesota Department of Health, participate in planning and teaching an experimental group of refresher courses under the sponsorship of the Minnesota Hospital Association, the Minnesota State Medical Association,

the professional societies of the pathologists and the medical technologists, and the Department of Continuation Medical Education of the University of Minnesota. Seven courses were held in 1952 and 1953 in Little Falls, Mankato, Hibbing, Crookston, and St. Cloud. These courses were designed to assist the laboratory personnel presently working in rural areas to improve service by review and discussions of techniques and methods. These courses were not intended to be training courses for unskilled personnel but rather for those with some training.

In a critical evaluation of this type of an educational endeavor it must be pointed out that many difficulties were encountered. Among them were the following:

1. The people taking the courses presented a great lack of uniformity in fundamental training and experience. Providing appropriate lectures, laboratory exercises, and demonstrations for such a group was difficult.
2. Lectures alone were not successful. Actual laboratory exercises are necessary. This limits the places where such courses can be held and practically makes it mandatory that they be held at teaching institutions where laboratory facilities and equipment are available. A further complication is the provision of sufficient instructors to staff such courses.
3. On the other hand, for many technologists sessions almost have to be held in the evenings at easily accessible locations. Many hospitals in the rural areas have only one technologist who can not be away during the day or for several days at any one time.
4. There is a grave question about the advisability of attempting to teach in a few hours techniques for which regular, approved training schools require several weeks.
5. There is the danger that these courses may be regarded as an easy, cheap way to train laboratory assistants.

In spite of these difficulties however, the response to the program by the registrants indicating an interest in attending future similar courses was heartening. Likewise the sponsoring groups and the instructors indicated continuing interest and cooperation in future courses. In view of these facts and the need for continuation education programs in this field such activities should perhaps be extended and developed. Although the concept of regional educational pro-

grams is not new, the application of this idea to the field of clinical laboratory techniques is unique and has attracted considerable interest.

The second aspect of the Minnesota survey that directly involved this department was the fact that laboratory assistants with thorough training in techniques within limited areas of laboratory work could be effectively used in certain laboratories. Our own observations and experience with the refresher courses in the state as well as with laboratory sessions for physicians who were trying to give good laboratory service with unskilled and poorly trained assistants substantiated this need.

In 1951 a course of study for laboratory aides under the jurisdiction of this department and offered through the General Extension Division of the University of Minnesota was put into operation. The current program includes two phases of training. The first part, 6 months, includes registration on the campus in special classes involving fundamental material in anatomy, chemistry, and bacteriology and special laboratory periods involving instruction and practice in the basic techniques in hematology, urinalysis, blood bank, and chemistry, and in BMR and ECG tests. The second part, 6 months, includes practical experience in these various aspects in the laboratories of the hospitals affiliated with this program.

The hospitals cooperating with the program in the practical experience of the second part of the training include Abbott, Asbury, Deaconess, Doctor's Memorial, Fairview, Mt. Sinai, North Memorial, St. Andrews, Bethesda, St. Lukes hospitals in Minneapolis and St. Paul, and Hibbing General Hospital, Naeve Hospital in Albert Lea, St. Joseph's Hospital in Brainerd, St. Joseph's Hospital in Mankato, Our Lady of Mercy Hospital in Alexandria, Miller Memorial Hospital in Duluth, Virginia Municipal Hospital, and Community Memorial Hospital in New Prague.

Because this course represented such a drastic departure from our previous experience with the professional course, the initial planning was carried out in conjunction with the professional medical, hospital, and medical technology organizations in the state. Periodic consultations have been held with these groups, and the program has their complete support. Dr. Ellis Benson[7] has stated: "(The course) represents an attempt to provide satisfactory training for laboratory workers at a sub-professional level and as such is experimental. Its success will depend in a large measure on the continued interest, support, and guidance of official medical and hospital organizations."

The program is now in its fourth year, and 42 students have received certificates of completion of the course. In examining the distribution of employment of the aides (tabulated below) it is of interest to note that 13 of the aides are employed at the same hospital with which they affiliated during training and that seven sudents in the 1955-56 class who were trained in hospitals outside of Minneapolis and St. Paul are also employed in rural Minnesota.

EMPLOYMENT AS OF SEPTEMBER, 1956, 42 LABORATORY AIDES

	Doctor's Office or Clinic	*Hospital*	*Research Laboratory*	*Total*
In Minneapolis-St. Paul	9	14	1	24
In other Minnesota Cities	1	8		9
Outside Minnesota		3		3
Married and not working				1
Unknown				5
				42

From reports and surveys of employers and graduates, it appears that the original objectives of the experiment are being realized to a satisfactory extent. With careful selection of students, it is possible in 12 months to teach a few basic laboratory techniques, limited in scope, in such a way that the students can learn these procedures well and can do these tests competently. The laboratory aides are employed in situations where they are able to make a real contribution to laboratory service by doing time-consuming "routine" tests, thereby allowing time for the medical technologist to perform more exacting and demanding procedures. Furthermore the return of the students to their community hospitals for practical training will tend to encourage employment of them in the areas where the personnel situation is most critical. The initial experimental period of 5 years will be completed in September, 1958. With present indications of satisfaction with the program it appears that this course merits continuing if funds become available to support it.

The increasing demand for laboratory personnel has resulted in a frequent suggestion that the answer is more "technicians" quickly trained in one specific area. The Registry of Medical Technologists (ASCP) does certify histologic technicians with requirements of high school graduation with one year of training under a pathologist and one year of experience in tissue preparation. In the area of tissue work utilization of these technicians answers the specific need in a practical and satisfactory way. Likewise the laboratory aide program described previously is an attempt to provide technical help in those

situations where the needs can properly be met in terms of personnel with limited training. This program is proving valuable and useful.

There continues to be, however, alarming agitation for "blood bank technicians", "hematology technicians", "cytology technicians", etc. In large hospitals with departmentalized laboratory services where supervision is available such a plan is a tempting solution to some of the pressures of work load and insufficient numbers of graduate technologists available for employment. The facts found in the Arbogast[8] survey deserve sober consideration. Sixty percent of the registered hospitals in the United States are under 100 bed capacity. The medical technologist in the laboratory of a hospital of this size generally has direct responsibility (often with only cursory medical supervision) for all the laboratory work done and must be able to do all types of laboratory tests. Seventy-one percent of the registered technologists in all sizes of hospitals perform all types of laboratory work, and only 29 percent work in fixed assignments. In view of these facts it is hardly reasonable to dispute the fact that teaching programs still have a direct responsibility to meet the greatest need; namely, for technologists well trained in fundamental principles and practices in all clinical laboratory areas.

There remains much to be done in improving the curricula in pre-technical programs and the caliber of clinical technical training. The importance of accurate laboratory work by well trained personnel cannot be minimized in the present day situation where the physician no longer performs his own tests but relies on the work of the medical technologist. Dean Diehl[9] has commented in a recent editorial upon the responsibility of organized medicine in this aspect of high standards for laboratory training and practice as follows:

> "The day seems to be passing in which the physician performs much of his own laboratory work. Important as it may be to the diagnosis and management of disease, he will expect others to perform this role. He will come to rely increasingly on the skill of these other hands. This becomes clear when one considers the large contributions that chemistry, bacteriology, hematology, and other laboratory sciences are making to the advance of American Medicine in this century.
>
> "A physician is by nature a skeptical person. A report from the laboratory may be to him just a slip of paper of questionable value. Still he must come to trust the skills of laboratory workers in order that these skills may help him make the decisions he must make. For this reason, if for no other, each physician and all physicians must be vitally concerned with the establishment of high standards of laboratory training and practice.
>
> "There are now many workers poorly trained; there are many schools that exploit heartlessly the needs for workers in this field. Glowing advertisements promise a short pleasure course, immediate vocational success. At the same time, approved schools of medical technology suffer progressive decrements in enrollment. Perhaps this field needs a sober study such as the one which culminated in the Flexner report on medical education in the early part of this century. After that report, organized medicine developed and enforced high standards of medical

education, closing the "diploma mills". Today, medical technology, an emerging profession under the aegis of organized medicine, needs its strenuous support and encouragement. Under the best of circumstances, it will gradually fill the need for professional clinical laboratory workers."

In this regard the results of the Belk and Sunderman[10] survey might well be reviewed. This study was conducted under well controlled conditions to check on the accuracy of some of the common chemical measurements in clinical laboratories. Fifty-nine laboratories in the Pennsylvania-New Jersey area received several samples for analyses for hemoglobin, glucose, chloride, total protein, albumin, calcium, and urea nitrogen. The results of the determinations were graded as satisfactory or unsatisfactory based on values for the various tests selected by the referee as being within the limits that should be maintained for satisfactory laboratory practice. The survey findings are tabulated below:

Substance tested	*Number of determinations classed satisfactory*	*Number of determinations classed unsatisfactory*
Hemoglobin	38	65
Glucose	60	43
Sodium chloride	54	63
Total protein	18	29
Albumin	9	35
Calcium	28	59
Urea nitrogen	35	48

The authors stated, "The scatter of measurements and the degree of unreliability is surprising. The accuracy of measurements is below any reasonable standard. It will be noted that unsatisfactory results outnumbered the satisfactory and that no laboratory had a perfect score."

In a follow-up survey, the clinical pathologists in that area were asked to give their opinions as to the causes for the inferior laboratory work indicated by the survey. They believed the major contributing factor to be inadequate training of technicians and secondly insufficient numbers of technical personnel to do the amount of work requested of the laboratories.

Efforts toward better educational programs and certification of personnel in clinical laboratories have been made, particularly in recent years, by medical technologists and clinical pathologists through the Board of Schools and the Board of Registry of the American Society of Clinical Pathologists.

The Board of Schools, composed of three medical technologists and six pathologists, assists in the inspection of schools and maintainance of educational standards and acts in an advisory capacity to the

Council on Medical Education and Hospitals of the American Medical Association. The Council in 1936, with the establishment of minimum standards for clinical laboratories for the training of medical technologists, initiated approval of schools for this training. At that time 96 schools qualified for approval. In May, 1955 there were 596 approved schools with a student capacity of 4503 and an enrollment of 2790 students, or 62% of capacity.[6] Three hundred and six hospital schools are affiliated with teaching institutions that grant degrees in medical technology after completion of combined requirements of academic courses and clinical laboratory training[11]. The approved schools for medical technology in Minnesota include St. Luke's Hospital and St. Mary's Hospital in Duluth, Minneapolis General Hospital, Northwestern Hospital, St. Mary's Hospital, and Swedish Hospital in Minneapolis, St. Cloud Hospital in St. Cloud, and Ancker Hospital, Charles T. Miller Hospital, and St. Joseph's Hospital in St. Paul.

The Board of Registry, composed of three medical technologists and six pathologists, was established in 1928 to develop minimum standards for the training and certification of proficiency of clinical laboratory personnel. Since this time the registry has been recognized by the professional medical and hospital organizations as the only authoritative certifying body for medical technologists although there are other so-called registries in the United States. In the period from 1928 to June, 1956 the Board of Registry has issued certificates of registration to 29320 medical technologists of which 22894 remain currently active. Renewal of certification is required each year.

The certification of MT (ASCP) is awarded to the person who qualifies both by satisfactory completion of written examination and by education and training. At the present time the educational requirements include two years of college (90 quarter credits) of which 18 quarter hours must be in biologic science and 14 quarter hours in chemistry. The clinical training requirements include 12 consecutive months of training in all phases of medical technology in a clinical laboratory approved for training. Realizing the fact that more comprehensive and better preparation of laboratory personnel is essential with the expanding needs brought about by the growth of medical and scientific knowledge, the Board of Registry has increased the pre-technical educational requirements for certification, effective January, 1962, to 3 years of college with additional academic requirements in the basic sciences.

Medical technologists are not licensed by the State of Minnesota.

Only three states (California, Florida, and Alabama) have a requirement of licensure for people working in clinical laboratories in those states. Time does not permit here a detailed discussion of the disadvantages or merits of licensure in this field.

Medical technology is young in comparison with the well-established programs and standards in medicine and nursing. Only within the last few years has there been developing nationally a consciousness of our professional responsibility for standardization and development of educational programs. In this connection, the University of Minnesota, long a leader in medical technology education, will continue to be active in this growth not only at an undergraduate level but also at a graduate level. To meet demands for better schools and teaching programs paralleling the growth of medical knowledge and use of clinical laboratory for the care of patients, supplemental programs for the graduate in technical specialties, in teaching, and in administration must be offered.

The importance of supplemental programs in this field has been recognized for many years by the Department of Continuation Medical Education and the Center for Continuation Study. The Medical Technology staff has participated actively in planning and presenting annual courses with the cooperation of the Center for several years. There has always been a gratifying response to the courses (within the limits of the facilities of the Center) by technologists from Minnesota and the neighboring states.

A new activity, the counseling program in medical technology, although influencing only in an indirect way the standards of the Course, perhaps should be briefly mentioned in this report. Within the last decade, in cooperation with the Junior College Office of the College of Science, Literature, and the Arts, a program of counseling students in orientation and registration procedures has been slowly developing. In this way data have been collected pertaining to the abilities of our students and graduates. One potential aspect of the activity is the use of these data in developing a testing program for better selection of students. At the present time the only criterion for selection of students for this course is that of scholastic achievement. Of concern to us is the large numbers of students who start as freshmen in the Course and then cancel, primarily for poor scholarship or change of interest during the first 2 years. Students who reach the fourth year level generally complete the requirements for graduation. The only exception to this in recent years was in 1954 when three

seniors did not graduate for reasons of poor scholastic records. The following table, based on data for the past 8 years, shows the percentage of students cancelling out of the Course in Medical Technology as compared with percentages in the College of Science, Literature, and the Arts.

	Percent of student drop out in Medical Technology	*in SLA*	
		Men	*Women*
from 1st to 2nd year_____	59	18	15
from 2nd to 3rd year_____	43	30	39
from 3rd to 4th year_____	23	31	27

Research on testing programs for students in this field is needed and has potential value and use not only here but also in other schools.

In conclusion, the past years have witnessed the growth and development of educational programs in a new profession of medical technology. The coming years give promise of progress toward improvement and standardization of training programs and emerging of teachers and leaders in this field. No better words can be found to express the objectives toward which the efforts of the staff are directed in continuing to prepare young men and women for this profession than those written by Dr. Beard[12] 35 years ago: "A profession is first of all of a trained body of (men). Its initial test is culture. And culture is a product of education. Its second distinction is that of social privilege, bestowed upon it in consideration of the peculiar office it has to fill. The test it carries with it is fitness. And fitness is the flower of education. Its third distinction is that of social obligation. Its ultimate test is service. And service is the function of (him) who has the capacity and will to serve."

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3. Bulletin of the University of Minnesota, Vol. XXV, No. 2, March 10, 1922.
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8. Arbogast, J. L.: Report of the December 1953 Survey of Medical Technologists, Board of Registry of Medical Technologists, Muncie, Indiana.
9. Diehl, H. S.: Laboratory Medicine, Minn. Med. 39:246, April 1956.
10. Belk, W. P., and Sunderman, F. W.: A Survey of the Accuracy of Chemical Analyses in Clinical Laboratories, Am. J. of Clin. Path., 17:853, November 1947.
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Medical School Activities

New Appointments

Two important appointments in the Medical School Faculty have recently been approved by the Board of Regents.

DR. H. MEAD CAVERT has been appointed *Assistant Dean* of the College of Medical Sciences succeeding DR. WILLIAM F. MALONEY, who will become *Dean* of the Medical College of Virginia on February 1. Dr. Cavert graduated from the University of Minnesota Medical School in 1950 and became a *Research Assistant* in the Department of Physiology immediately following his graduation. He has been an *Assistant Professor* in that Department since 1952 and will continue his teaching and research activities there on a part-time basis. He will share Assistant Deans' duties with DR. N. L. GAULT, JR., who has served in that capacity for the past year.

DR. JOHN H. MOE has been named *Professor and Director* of the Division of Orthopedic Surgery succeeding DR. LEONARD F. PELTIER who has left the University to head the Section of Orthopedic Surgery at the University of Kansas Medical School. A graduate of Northwestern University Medical School in 1930, Dr. Moe received his orthopedic training at Illinois Research Hospital, Gillette State Hospital, St. Paul, and San Joaquin General Hospital, Stockton, California. He has been a member of our Clinical Faculty since 1934.

Both Dr. Cavert and Dr. Moe are well known to our Faculty. We are pleased that they are taking on these important responsibilities which we know they will discharge most capably.

WHO Seminar

MR. HERBERT M. BOSCH, *Professor* of Public Health Engineering, attended a health seminar in Beirut, Lebanon, last November. His account of this experience is of real interest and we quote from it:

"The seminar was originally scheduled to be held from October 28 until November 8, 1956. However, because of the outbreak in hostilities in the Middle East it was shortened, and it was actually held from October 28 to November 3. It was held under the auspices of the Eastern Mediterranean Region of the World Health Organization, and I attended the meeting in the capacity of a Special Advisor to WHO.

The seminar itself was concerned with environmental sanitation, and it was the first such meeting to be held in the Middle East. Somewhat similar meetings have been held in other regions of the world under WHO sponsorship.

"There were participants from the following countries: Cyprus, Egypt, Ethiopia, Jordan, Iran, Iraq, Lebanon, Libya, Pakistan, French Somaliland, Italian Somaliland, the Sudan, Syria, Turkey, Greece, Yemen, and Saudi Arabia as well as six participants from the International Cooperation Administration of the United States Government. All in all there were 52 participants who were nominated by their governments to take part in the meeting. It is of interest to note that of the 52 participants, eight were former students of the School of Public Health of the University of Minnesota. Of these eight, two were Americans and the other six were from the Middle East. I believe that this is further evidence of the impact which the University of Minnesota has on the education of the Middle East.

"With the outbreak of hostilities between Israel and Egypt, it became necessary to curtail the seminar. It was possible to arrange transportation back to their own countries for all the participants (even though in some cases it had to be done by circuitous routes) except those from Egypt and Yemen."

Faculty News

On November 15, DR. H. C. LICHSTEIN, *Professor,* Department of Bacteriology and Immunology, addressed the Henrici Society of Microbiologists. His topic was "Physiological Control Mechanisms in the Bacterial Cell."

DR. DAVID GLICK, *Professor,* Department of Physiological Chemistry, and *Director,* Histochemistry Laboratory, attended the 22nd Ross Pediatric Research Conference, October 25 and 26, on Mesenchymal Diseases in Childhood which was held by the Department of Pediatrics, University of Utah, at Salt Lake City. He presented a paper on "Quantitative Histochemical Studies on the Adrenal Gland in Various Physiological States."

DOCTORS JOHN J. BITTNER and CARLOS MARTINEZ of the Division of Cancer Biology, Department of Physiology, have been invited to present papers before an International Symposium on Mammary Cancer sponsored by the Division of Cancer Research, University of Perugia, Italy. Approximately 60 investigators from 11 countries will

attend the Symposium which will be held from July 24 to 29, 1957. Dr. Martinez will remain in Italy for 10 weeks to give lectures and demonstrations of research techniques for the staff of the Instituto di Anatomia e Istologia Patologica, University of Perugia. Before returning home he will also lecture at the University of Madrid, Spain.

DR. WESLEY W. SPINK, *Professor,* Department of Medicine, and DR. JEROME T. SYVERTON, *Professor and Head,* Department of Bacteriology and Immunology, recently were elected to fellowship in the New York Academy of Sciences.

DR. ELLIS S. BENSON, *Assistant Director,* Hospital Laboratories, has been awarded a Senior Research Fellowship from the United States Public Health Service to further his studies in clinical pathology. Dr. Benson is tentatively planning to study in Europe during 1957-58.

DR. REYNOLD A. JENSEN, *Professor,* Departments of Psychiatry and Pediatrics, was one of five guest speakers at the Third Pediatric Congress of Central America and Panama which was held during the last week in November in Guatemala City. While there he received an Honorary Professorship on the Faculty of the Medical School of the University of San Carlos.

DR. MILAND E. KNAPP, *Clinical Professor,* Department of Physical Medicine and Rehabilitation, and Director of Physical Medicine and Rehabilitation of the Kenny Institute, was awarded the Gold Key of the American Congress of Physical Medicine and Rehabilitation with a citation for the work he has done in developing methods of treatment of poliomyelitis. Dr. Knapp worked with Sister Elizabeth Kenny in pioneering the Kenny method of treatment of poliomyelitis.

DR. JOSEPH J. GARAMELLA, *Clinical Instructor,* Department of Surgery, has been named the first appointee to the Rappaport Professorship of Cardiac Research at Mount Sinai Hospital, Minneapolis. The appointment was recently announced by DR. H. S. DIEHL, *Dean,* and DR. BENJAMIN MANDELSTAM, *Administrator* of Mount Sinai Hospital. The professorship was established in 1955 with an initial gift of $55,000 by the Rappaport family (of NAPCO Industries, Minneapolis) in memory of James Rappaport, and his father, Edward Rappaport, who died during that year. The gift provides for a heart research post to be occupied by a medical scientist designated by the University and doing his major investigative work in the Jay Phillips Research Laboratory at Mount Sinai Hospital.

DR. FRANZ HALBERG, *Associate Professor,* Division of Cancer

Biology, has been invited to participate as the speaker from the U.S.A. at an International Symposium on "Problems of Time in Biology." The Symposium is to be held on the occasion of the sixth congress of the International Society for the Study of Biological Rhythms at Semmering, Austria, from August 26 to 28, 1957. Dr. Halberg's address will be on the effect of daily routine upon physiologic rhythms.

DR. ERNST GELLHORN, *Professor,* Department of Physiology, currently on sabbatical leave, gave lectures on December 13 and 14 at UCLA Medical Center in Los Angeles. Both lectures concerned "New Experiments on Hypothalamic Functions: Their Clinical and Physiological Applications." Dr. Gellhorn has just completed a 500-page manuscript, to be published by the University of Minnesota Press, entitled "Autonomic Imbalance and the Hypothalamus." This will be his seventh book.

DR. WESLEY W. SPINK, *Professor,* Department of Medicine, will give a series of lectures and clinics at the Annual Postgraduate Course sponsored by the Washington State Medical Association and University of Washington Medical School at Seattle on January 23 and 24. He will also address the Seattle Society of Internal Medicine on "Present Day Problems with Antibiotics."

DR. H. C. LICHSTEIN, *Professor,* Department of Bacteriology and Immunology, lectured on "Physiological Control Mechanisms in the Bacterial Cell" to the staff of the School of Medicine, Vanderbilt University, Nashville, Tennessee, December 18, 1956.

Postgraduate Education

Emergency Surgery for General Physicians

The University of Minnesota announces a continuation course in Emergency Surgery for General Physicians which will be held at the Center for Continuation Study next January 31 to February 2, 1957. The management of clinical problems requiring emergency surgical care will be emphasized throughout the course. Guest speaker will be DR. JOHN L. BELL, *Associate,* Department of Surgery, Northwestern University Medical School, Chicago. The course will be presented under the direction of DR. O. H. WANGENSTEEN, *Professor and Chairman,* Department of Surgery.

Cardiovascular Diseases for General Physicians

The University of Minnesota, in conjunction with the Minnesota Heart Association, will present a continuation course in Cardiovascular Diseases for General Physicians from February 7 to 9, 1957, at the Center for Continuation Study. Diagnosis and management of the cardiovascular disorders most commonly met will be stressed. The program will be presented under the direction of DR. C. J. WATSON, *Professor and Head,* Department of Medicine. Guest speaker will be DR. RICHARD V. EBERT, *Professor and Head,* Department of Medicine, University of Arkansas Medical Center. Dr. Ebert will also deliver the annual George E. Fahr Lecture on Thursday evening, February 7.

Notice

All continuation courses presented by the University of Minnesota are approved for formal postgraduate credit by the American Academy of General Practice. Attendance certificates will be furnished on request.

Further information concerning the above programs or others to be presented may be obtained by writing to Dr. Robert B. Howard, 1342 Mayo Memorial, University of Minnesota, Minneapolis 14.

Coming Events

Jan. 31-Feb. 2 ——— Continuation Course in Emergency Surgery for General Physicians

February 7-9 ——— Continuation Course in Cardiovascular Diseases for General Physicians

February 7 ——— GEORGE E. FAHR LECTURE; "Alveolar Function in Pulmonary Emphysema;" *Dr. Richard V. Ebert,* Professor and Head, Department of Medicine, University of Arkansas Medical Center, Little Rock, Arkansas; Mayo Memorial Auditorium; 8:00 p.m.

February 11-13 ——— Continuation Course in Anesthesiology for General Physicians

February 11-16 ——— Continuation Course in Neurology for General Physicians and Specialists

February 13 ——— J. B. JOHNSTON LECTURESHIP; "Human Stereotaxic Surgery and its Applications;" *Dr. Henry T. Wycis,* Temple University Hospital, Philadelphia; Mayo Memorial Auditorium; 8:00 p.m.

February 19 ——— MINNESOTA PATHOLOGICAL SOCIETY LECTURE AND E. P. LYON MEMORIAL LECTURE; "Internally-Deposited Radioactive Isotopes in Relation to Radioactive Fallout;" *Dr. Wright H. Langham,* Los Alamos Scientific Laboratory, Los Alamos, New Mexico; Mayo Memorial Auditorium; 8:00 p.m.

February 21 ——— E. STARR JUDD LECTURE; "Problems of Dysphagia;" *Sir Philip Allison;* Professor of Surgery, Radcliffe Infirmary, Oxford University, Oxford, England; Mayo Memorial Auditorium; 8:15 p.m.

February 26 ——— STUDENT A.M.A. LECTURE; "Total Treatment;" *Dr. A. B. Baker,* Professor and Director, Division of Neurology, University of Minnesota Medical School; Room 125, Mayo Memorial; 8:00 p.m.

Faculty Publications

WORTHEN, H. G., and GOOD, ROBERT A.: The Concept of Renal Tubular Disease. J. Lancet, 75: 473, 1955.

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ZIEVE, L., and HILL, E.: Ibid. IV. Nature of the Interrelationships Among Hepatic Tests in Cirrhosis. Gastroenterol., 28: 914, 1955.

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ZIEVE, L., SKANSE, B., and SCHULTZ, A. L.: Comparative Value of the Basal Metabolic Rate, Chemical Protein-Bound Iodine, and Radioactive Iodine Excretion or Uptake in the Diagnosis of Borderline Hyperthyroidism When Used Individually or in Combination. J. Lab. & Clin. Med., 45: 281, 1955.

WEEKLY CONFERENCES OF GENERAL INTEREST

Physicians Welcome

Monday,	9:00 to 10:50 A.M.	OBSTETRICS AND GYNECOLOGY Old Nursery, Station 57 University Hospitals
	12:30 to 1:30 P.M.	PHYSIOLOGY- PHYSIOLOGICAL CHEMISTRY 214 Millard Hall
	4:00 to 6:00 P.M.	ANESTHESIOLOGY Classroom 100 Mayo Memorial
Tuesday,	12:30 to 1:20 P.M.	PATHOLOGY 104 Jackson Hall
Friday,	7:45 to 9:00 A.M.	PEDIATRICS McQuarrie Pediatric Library, 1450 Mayo Memorial
	8:00 to 10:00 A.M.	NEUROLOGY Station 50, University Hospitals
	9:00 to 10:00 A.M.	MEDICINE Todd Amphitheater, University Hospitals
	1:30 to 2:30 P.M.	DERMATOLOGY Eustis Amphitheater, University Hospitals
Saturday,	7:45 to 9:00 A.M.	ORTHOPEDICS Powell Hall Amphitheater
	9:15 to 11:30 A.M.	SURGERY Todd Amphitheater, University Hospitals

For detailed information concerning all conferences, seminars and ward rounds at University Hospitals, Ancker Hospital, Minneapolis General Hospital and the Minneapolis Veterans Administration Hospital, write to the Editor of the BULLETIN, 1342 Mayo Memorial, University of Minnesota, Minneapolis 14.