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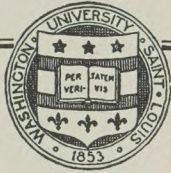
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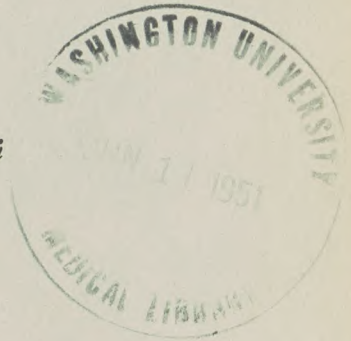
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- The Challenge of Cancer Chemotherapy
Alfred Gellhorn, M.D.
(Second M. G. Seelig Lecture)
- David P. Wohl, Jr., Memorial Hospital Under Construction
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THE CHALLENGE OF CANCER CHEMOTHERAPY

Alfred Gellhorn, M.D.

(From the Medical Service, Francis Delafield Hospital, and the Department of Medicine, College of Physicians and Surgeons, Columbia University, New York)

This address was delivered at Washington University School of Medicine, St. Louis, Mo., on March 7, 1951, as the second M. G. Seelig Lecture, in honor of Dr. Major G. Seelig, professor emeritus of clinical surgery. Dr. Gellhorn is a 1937 graduate of Washington University School of Medicine.

It is a privilege to participate with you in this expression of affection and respect for Dr. Major Seelig. Dr. Seelig's boundless energy, keen insight and broad experience brought him to preeminence in both clinical surgery and scientific research. Dr. Graham has reviewed some of the medical contributions made by Dr. Seelig, and many of us in a variety of medical disciplines have made use of the knowledge that he added. Besides the well-deserved recognition that Dr. Seelig has won in his profession, it is also to be recalled that his stature was great as a citizen of this community. To mention but a few of Dr. Seelig's extrascientific activities, we can remember that he was a founder of the Liberal Forum, an important medium of adult education in St. Louis; and he was a long-time and constructive member of the Public Library Board. As a member of the Social Planning Council and founder of the Blue Cross Hospitalization Insurance plan, he gave generously and skillfully of his talents toward the solution of

broad economic, social, and health problems of this city. As a tireless worker on the Board of the People's Hospital, Dr. Seelig made a major contribution to the improvement of community relationships. This only partial list of Dr. Seelig's activities is an impressive measure of the man, and the work that he has done is a living memorial to him.

Dr. Seelig recognized many challenges in his professional and community life and met them successfully. Tonight I wish to discuss with you one phase of a problem which bristles with challenges.

THE CHALLENGE OF CANCER CHEMOTHERAPY

The chemotherapy of cancer is ages old. Long before the development of the techniques of radical surgery and the methods of irradiation, malignant disease was treated by drugs in a variety of forms. The approach was characterized by the application of naive and erroneous concepts and the therapeutic

results were uniformly bad. When it was demonstrated that certain malignant diseases could be cured by surgery and/or radiotherapy and when critical laboratory and clinical evaluations were made of cancer remedies such as crab soup, purgation, blood-cleansing potions, heavy metals externally and internally administered and black or red pastes, cancer chemotherapy fell into well justified disrepute.

During the past half-century, however, the accumulated experience with conventional surgical and irradiation treatment has taught the medical profession that there still is a desperate need for additional therapeutic weapons in the management of human malignancy. With this realization attention is once again focused on the potentialities of chemotherapy and vast efforts in this field are in progress.

A powerful stimulus to research in cancer chemotherapy has been the dramatic successes achieved by anti-microbial chemotherapy. The demonstration that a chemical compound can selectively destroy an invading micro-organism has spurred the hope that a similar effect on the neoplastic cell may be achieved. Sober reflection of the comparative difficulties posed by the therapy of infection and of cancer leads to the realization that there are a number of fundamental differences in the two problems. Probably the most striking difference is that in microbial infections the offending invader is foreign to the host and efficient defense mechanisms provide strong support to supplement and complement the effects of therapeutic drugs; the malignant cell, on the

other hand, is qualitatively indistinguishable from the normal cells of the body and no innate restrictive defenses are mobilized against it. A distinguished scientist who had devoted his life to experimental cancer research took cognizance of the basic difficulties which theoretically raise the odds impressively against successful chemotherapy of malignant disease when he said that the problem of treatment with chemical compounds is "almost — not quite, but almost—as hard as finding some agent that will dissolve away the left ear, yet leave the right ear unharmed: so slight is the difference between the cancer cell and its normal ancestor."

In spite of the obvious obstacles to a chemotherapeutic solution of cancer and in spite of the understandable skepticism of many, the challenge presented by the practical problem of the medical management of disseminated malignant disease is so great that all efforts must be made to meet it. Tonight I wish to evaluate with you some phases of modern cancer chemotherapy to determine whether there are as yet any auspicious signs for the future.

At this time it must be recognized that there are no drugs now available which completely eradicate any malignant disease. There are, however, chemical compounds which modify the course of certain malignant tumors and which are indicated in the clinical care of patients with these tumors.

The important observations of Huggins and his associates, which led to the recognition that malignant prostatic epithelium requires male sex hormone for

its survival, have firmly established estrogens as a part of androgen-control therapy of disseminated cancer of the prostate. Both estrogens and androgens have found application in the palliative treatment of metastatic breast carcinoma and the relief of bone pain, improvement in appetite and sense of well-being which may follow their administration is of significant importance to the patient. The pituitary adrenal cortical stimulating hormone and cortisone have been found to produce remissions in acute leukemia, particularly of children, with some regularity and have also been reported to benefit patients with lymphomas and multiple myeloma. Urethane may substitute for radiotherapy in the treatment of chronic leukemias and perhaps more importantly it can be used to modify the course of multiple myeloma in a significant proportion of cases. The judicious use of the nitrogen mustards in conjunction with radiotherapy offers significant palliation to patients with Hodgkin's diseases, lymphosarcoma and bronchogenic carcinoma. Finally, the folic acid antagonists have the distinction of being the first therapeutic weapons ever to alter the course of acute leukemia.

It is neither feasible nor pertinent to discuss the laboratory and clinical data on each of these chemotherapeutic compounds. Rather I will present a brief summary of the biological actions on normal and tumor cells produced by two of the drugs, followed by the story of a chemical compound which we are studying in the laboratory. This, it is hoped, will provide orientation to the present status of cancer chemotherapy.

Let us consider first the nitrogen mustards which were introduced into the therapeutic management of malignant disease by Gilman and Goodman at Yale and Jacobson and Spurr at the University of Chicago in 1942. The developments which led to the clinical study of this agent are closely linked to the history of dichloroethyl sulfide, the dreaded "mustard gas" of World War I. In 1886 a German chemist, Victor Meyer, described the properties of this latter compound. Meyer appreciated the highly toxic local actions of the sulfide because he and his associates in the laboratory sustained severe skin contact-burns from working with the chemical compound; in addition, Meyer noted that following the administration of small doses parenterally to rabbits, the material produced death rapidly. The toxicological properties of this compound were disregarded until the first World War.

During the spring of 1917, however, the Germans carried out secret field tests with such satisfactory results that they adopted dichloroethyl sulfide as an artillery shell filling and accumulated a large quantity of these (yellow cross) shells without the knowledge or at least understanding of Allied intelligence. On the night of July 12, 1917, the Germans bombarded the British positions near Ypres in Flanders with these shells. The devastating effects produced by this unexpected chemical offensive warfare are indicated by the statistics of 14,276 casualties processed through British casualty stations in the first three weeks of mustard gas use.

Descriptions of sulfur mustard intox-

ication soon appeared in the medical literature, with initial attention focused on the local actions as manifested by skin vesication progressing to deep ulceration, conjunctivitis, photophobia and lacrimation; irritative laryngitis, bronchitis with intractable cough and aphonia; secondary bronchopneumonia associated with severe damage to alveolar epithelium, massive pulmonary edema and death. Somewhat later, however, serious systemic toxicity was recognized as a major complication of mustard intoxication and descriptions of profound hemopoietic depression, dissolution of lymphoid tissues and gastrointestinal ulceration were recorded. Laboratory studies to define the mechanism of cytotoxic action were undertaken, but the termination of World War I led to the discontinuation of these investigations before a careful evaluation of the problem had been completed.

In the interim between World Wars I and II only scattered studies on the biological effects of sulfur mustard were reported; however, there was continued activity in the chemical warfare laboratories of the French and Germans directed toward the discovery of more toxic agents. With the advent of the Second World War new compounds were proposed as potential offensive agent. Sulfur mustard shared interest with a series of nitrogen analogs, bis- and tris-(*B*-chloroethyl)-amines. It was rapidly demonstrated that the nitrogen mustards were also contact vesicants and careful pathological studies revealed the cytotoxicity of these compounds on a number of tissues follow-

ing their absorption. As had been noted in the studies with sulfur mustard, lymphoid structures were especially susceptible to damage by the nitrogen mustards. These observations, coupled with the fact that the hydrochloride salts of the nitrogen mustards were crystalline compounds, thereby facilitating their handling, led the groups at Yale and Chicago to explore the therapeutic possibilities of these agents in the malignant lymphomas.

The biological actions of the nitrogen mustards are impressively demonstrated following the administration of minimum lethal doses to dogs. The delayed lethal syndrome thus produced is of real pertinence to the clinician using nitrogen mustard. The events which characterize this syndrome are encompassed within three to seven days and either result in death of the experimental animal or uneventful recovery. Anorexia is evident in the first day following the injection of the drug and persists throughout the period. Associated with this there is loss of weight which exceeds, however, the effect of starvation alone. Usually profuse vomiting occurs within several hours after intoxication and continues for two or three days. On the third day there is the onset of diarrhea which progresses to ulceration of the gastrointestinal tract with large losses of fluid, electrolytes and blood. The syndrome is complicated by marked depression of hemato poiesis manifested by progressive lymphopenia, granulocytopenia and thrombopenia. Complex disturbances of electrolyte and water metabolism are also in progress with loss of intra-

cellular potassium and cellular dehydration. Terminally, there is hypothermia and shock, followed in several hours by coma and respiratory failure.

The precise cause of death in nitrogen mustard intoxicated animals is understandably obscure. The disruptions of physiological function produced by the hemorrhagic necrosis of the gastrointestinal tract, by aplasia of the bone marrow, and by alterations of electrolyte and water distribution due to toxic effects on cells, as well as possibly on renal transport systems, are great and interrelated. The entire problem of the mechanism of lethal nitrogen mustard toxicity is further complicated by the fact that correction of the obvious abnormalities by appropriate substitution therapy in the form of transfusions, electrolyte solutions and so on fails to prevent the lethal outcome. This suggests that subtle toxic effects on the cells are produced which irreparably damage their function.

The toxic manifestations and pathological changes produced by nitrogen mustard resemble in many details the effects of total body x-irradiation. The radiomimetic actions of the chemical compound accounts, in part, for the great efforts that have been put forth to discover its intimate mechanism of action because it has been hoped that the understanding thus gained would shed light on cellular effects produced by ionizing radiation.

Turning to the actions of nitrogen mustard in man it may be broadly stated that therapeutic doses produce effects comparable to total body irradiation. As was anticipated from the

observations of the susceptibility of lymphoid tissues to this chemical compound, the most successful therapeutic application has been in the management of the malignant lymphomas. In patients with these tumors, and most strikingly in cases of disseminated Hodgkin's disease, dramatic reversal of the lesions can be achieved by the administration of nitrogen mustard. There can be no doubt of the fundamental effects of this drug on neoplastic cells when one observes patients with high fever, marked weakness and anorexia, generalized lymphadenopathy, and enlargement of the liver and spleen who, forty-eight hours after an intravenous course of nitrogen mustard, have normal temperatures, subjective improvement, a voracious appetite and then a more gradual regression of tumor infiltrations. Unfortunately the remissions so induced are only temporary. Why is it not possible to eradicate these susceptible tumors? The limitation to effective therapy rests on the fact that nitrogen mustard has no true selectivity of action on neoplastic cells. This drug has a devastating effect on the cellular function of normal and malignant tissues in direct proportion to the rate of proliferation of these cells. Thus, because of the high turn-over rate of the cells of the hemopoietic system, even when therapeutic doses of nitrogen mustard are given, depression of bone marrow function is manifested by lymphopenia, granulocytopenia and thrombopenia. Complete destruction of a tumor by nitrogen mustard would also destroy the host.

Here, then, we meet the basic

problem of cancer chemotherapy head-on. The nitrogen mustards interfere with a mechanism of the malignant cell but this mechanism is also vital to the function of normal cells. Under these circumstances it is obvious that only limited therapeutic objectives can be attained. But what are these fundamental cellular mechanisms and what can we learn about them which may be of value in further chemotherapeutic research?

During World War II extensive investigations were conducted on the mechanism of action of nitrogen mustard with the objective of devising rational antidotal measures. A major contribution was made by chemists who demonstrated that the chemical compound underwent an intramolecular transformation when placed in solution at the pH of body fluids. The compound thus formed was shown to be highly reactive chemically. Biochemists then found that a large number of compounds of biological importance reacted with nitrogen mustard in the test tube. These included such varied substances as amino acids, proteins, vitamins and a number of enzymes. The concentrations of the drug required to alter these entities, however, were far greater than occurred in vivo, even following the administration of lethal doses, and therefore it was considered unlikely that inactivation of any of these substances accounted for the observed biological actions. Increasing evidence from biochemical, histochemical, genetic and morphological studies has focused attention on the nucleic acids as the primary site of action of the mustards.

Brilliant cytological experiments at the Chester Beatty Institute in London and at the Wilmer Institute in Baltimore have demonstrated mitotic inhibition of cells exposed to extremely low concentrations of nitrogen mustard and specific alterations of chromosomal structure could be detected and characterized in these cells. Since it has been established that the chromosome is a complex nucleoprotein in which the desoxypentose nucleic acid is the chief polynucleotide, the morphological evidence suggests that the mustards may react with these latter important nuclear constituents. The induction by the mustards of heritable mutations in the fruit fly and in certain fungi also provides convincing proof that the drug alters chromosomal function. The inactivation of viruses, particularly those rich in desoxypentose nucleic acid, the change in viscosity of DNA from thymus and the evidence from dynamic studies, which indicates suppression of desoxypentose nucleic acid synthesis all produced by the mustards, provide additional support to the tentative conclusion that the drug destroys cells by interfering with the functions of the nucleic acids.

Before trying to draw any lesson learned from the clinical and basic investigations of the nitrogen mustards let us review briefly the current status of knowledge about another group of cytotoxic agents, the folic acid analogs. These compounds, which are very closely related chemically to pteroylglutamic acid, or folic acid, are noteworthy because they can produce remissions in acute leukemia and because studies of

their mechanism of action have illuminated some fundamental aspects of cellular physiology. There are a number of folic acid analogs which have been synthesized and studied in the laboratory and in the clinic. Although they vary in potency, their biological actions are qualitatively identical and therefore we will typify them all in discussing just one of them, aminopterin.

The toxicity of the folic acid analogs in experimental animals has been carefully studied in order to throw light on the mechanism of action of the drugs and in order to anticipate the hazards in their clinical application. Animals receiving single, fatal doses of aminopterin, survive for at least 48 hours and usually succumb between the third and fifth day. The characteristic syndrome of toxicity is manifested by progressive weight loss, anorexia, bloody diarrhea, leucopenia, depression, terminal collapse and coma.

As could be anticipated from the clinical course of fatal intoxication with the drug, the chief pathological changes have been found in the intestinal tract and the bone marrow. Microscopic examination of the small and large intestine reveals swelling and cytoplasmic vacuolization of the epithelium as early as six hours after the parenteral administration of the drugs. The initial changes are followed by desquamation of the epithelial cells, plasma extravasation into the intestinal lumen and intensive leucocytic infiltration of the submucosa. Within three days after acute poisoning or within a somewhat longer period after chronic intoxication, the whole mucous membrane from the duo-

denum to the anus is edematous, swollen, and in part, hemorrhagic.

On the third day of acute intoxication, the bone marrow of the experimental animals is found to be grossly abnormal. The peripheral blood showed marked granulocytopenia, reticulocytopenia, and moderate lymphopenia. Serial examination of the bone marrow reveals progressive depletion of all cells in the erythroid and myeloid series.

Apart from the lesions of the bone marrow and the intestines, no outstanding pathological changes have been noted. Decrease in the size of lymph nodes and spleen has been described but histological studies have not revealed striking cytotoxicity to lymphoid cells.

In humans the biological actions of aminopterin can be excitingly demonstrated when a remission is induced in a child dying from acute leukemia. In those patients who respond, the abnormal immature leucocytes in the peripheral blood and bone marrow may completely disappear to be replaced by normal mature forms. Associated with this change, the anemia and thrombocytopenia may be corrected by a spontaneous rise of the erythrocytes and platelets. Hemorrhagic manifestations cease, the hectic temperature curve returns to the baseline, the child begins to eat with relish and to react to his surroundings and associates with renewed vigor and pleasure; bone pain and other objective signs of the leukemic process such as peripheral lymphadenopathy and gross visceral infiltrations disappear. Within a period of two weeks a critically ill child may once again be in good health.

As you well know, the story can not be ended here. The response just described is observed in only about one third of the cases. Another group, comprising about 20 per cent of the total, show only a moderate hematologic response but are nevertheless markedly improved symptomatically. The remaining half of the patients suffer a severe initial bone marrow depression following the administration of aminopterin and hemorrhagic phenomena occur which, along with the depletions of the disease, contribute to death early in the course of treatment.

There are several points which have emerged from the clinical studies with the folic acid analogs which merit attention. As has been stated, only about 50 percent of children with acute leukemia show a favorable response. It is impossible *a priori* to predict which patient will have a remission; this separation of acute leukemias into those which are and those which are not controlled by aminopterin presents a fascinating problem in the biology of the disease. Another striking observation along this line is that the results of aminopterin therapy in acute leukemia of adults are far less satisfactory than in the childhood disease. It is possible that the therapeutic drug will also serve as a tool for investigating these biological enigmas when its mechanism of action is more fully understood.

It has been implied that the folic acid analogs do not cure acute leukemia. This is true, and further, experience has taught us that with each exacerbation of the disease, the response to therapy is less evident until sooner or later no

effect can be detected. Recent experimental studies by Law and by Burchenal have demonstrated that the development of refractoriness to the folic acid analogs is an inherent response of the leukemic cell. Whether this is the acquisition or enhancement of a cellular detoxifying mechanism or whether an alternate metabolic pathway is developed which bypasses the function affected by the folic acid analogs is not yet known.

Finally, clinical studies have emphasized the important toxicity of the folic acid analogs on normal cells. The cells of the hematopoietic system and the epithelium of the alimentary tract are particularly susceptible. Severe bone marrow depression, ulcerative stomatitis and hemorrhagic enteritis are not infrequent concomitants of therapeutic doses of these powerful drugs.

Again we must recognize that aminopterin fails to provide the solution to a therapeutic problem of malignant disease. The drug does have some profound effect on malignant cells, however, and therefore it is important to know how it acts.

When the folic acid analogs were first synthesized their biological action was studied on bacteria which required folic acid for growth. In these microbiological experiments aminopterin was found to inhibit the growth of appropriate bacteria and its action could be reversed by the addition of more folic acid to the medium. This led naturally to the conclusion that aminopterin and related compounds were folic acid antagonists. This concept began to be seriously questioned, however, when it

was found that both in experimental animals and in man, folic acid had only limited success in preventing the toxicity of its analogs. If toxic manifestations had already appeared following the administration of aminopterin, then folic acid was completely ineffective in reversing them. These observations suggested that aminopterin was an antagonist of folic acid, but in addition caused cytotoxicity through some unrelated mechanism. As we shall see, recent advances in our knowledge of the biochemical function of folic acid and of its metabolism indicate that the puzzling discrepancies just mentioned can be adequately explained on a single basis.

From exciting observations made on microbiological systems and in biochemical experiments using radiocarbon and heavy nitrogen tagged molecules, evidence has been accumulated which points to the nucleic acids as the cellular components affected by the folic acid analogs. Since our knowledge of the mechanism of action of these drugs is more precise than in the case of nitrogen mustards, it will be profitable to review briefly and schematically some aspects of nucleic acid metabolism.

In figure 1 there is represented diagrammatically the sequence of events which lead to the synthesis of nucleoproteins. This is an over simplification, but it will facilitate the presentation of the probable sites of action of the folic acid analogs. As can be seen, from the simple precursors glycine, ammonia and active single carbon fragments such as formate, the far more complex purine and pyrimidine molecules are synthe-

sized. The nucleic acids are built up from combinations of purines and pyrimidines to each of which there is added a 5-carbon sugar moiety, either a pentose or a desoxypentose, and phosphorus. It is known that the nucleic acids are complex polynucleotides, i.e., molecules of purine plus sugar and pyrimidine plus sugar joined together through phosphoric acid ester linkages. The formation of the high molecular weight nucleoprotein, is accomplished by the addition of a protein to the nucleic acid. Exact definition of the protein component and the mechanism of its condensation with nucleic acids are areas which are being investigated in many laboratories here and abroad.

How does aminopterin enter into this picture? In figure 2 there are indicated three metabolic functions which are blocked by folic acid deficiency either due to inadequate dietary intake of the vitamin or to administration of the anti-vitamin, aminopterin. In the first example is pictured the reversible reaction in which the amino acid serine is synthesized from glycine plus a single carbon fragment, or in which serine is broken down into glycine and an active carbon fragment. Folic acid is a part of the enzyme system which catalyzes the reaction, and the reaction can be blocked by aminopterin. As you will remember, glycine is one of the precursors of the purines and pyrimidines so that interference with its availability would seriously hamper nucleic acid synthesis.

The second illustration of a site of aminopterin action requires a little amplification. During the past few years evidence has been accumulated which

indicates that folic acid is converted in the animal organism to a related form which is biologically active. This altered folic acid is called the "citrovorum factor" because a bacterial species, *Leuconostoc citrovorum*, requires it for growth. More recently, chemical characterization of the "citrovorum factor" indicates that it is a reduced form of folic acid which has been named folinic acid. When folic acid is given to humans there is a proportional excretion in the urine of folinic acid or the citrovorum factor. Welch has shown that when rat liver slices are incubated with folic acid, the citrovorum factor appears in the medium. This *in vitro* conversion of folic acid to folinic acid is blocked by the addition of aminopterin. When it was found that the citrovorum factor or folinic acid could prevent the toxicity of aminopterin and also could reverse toxic manifestations produced by the drug, a reasonable explanation for the inability of folic acid to accomplish these ends was apparent. Thus aminopterin, by blocking the conversion of folic acid to the active folinic acid, effectively stifles the formation of its own inhibitor.

Finally, as shown in C. of the figure, evidence has been obtained which implicates folinic acid as a part of the enzyme system necessary for the synthesis of the purine nucleus. The particular step consists of the introduction of a carbon atom between two nitrogens, thus completing the purine nucleus. Aminopterin blocks this important synthetic process, thereby further interfering with nucleic acid metabolism. Whether there are further sites

of action of aminopterin in the nucleoprotein synthetic chain is not yet known. Certainly the available evidence adequately demonstrates that the drug strikes at fundamental cellular mechanisms.

From the stories just presented on the mechanisms of action of nitrogen mustard and aminopterin, it is not surprising that interest of many laboratories working in the field of experimental cancer chemotherapy turned to the nucleic acids. The difficulties of interfering with nucleic acid function in neoplastic cells without affecting normal cells has been highlighted in the preceding discussion. I would like to tell you, therefore, about a chemical compound which, as of this time at least, appears to circumvent the dilemma.

Some years ago Roblin synthesized a number of purine analogs and tested their anti-bacterial activity. Although several appeared promising, the advent of penicillin discouraged further studies along these lines. Two years ago Kidder, at Amherst, found that an animal microorganism, *Tetrahymena geleii*, which he was studying, required the purine guanine for its growth. When he added, to the medium, a guanine analog which Roblin had previously prepared, the growth of the *Tetrahymena* was inhibited. Kidder then studied the action of the guanine analog on the growth of a number of other microorganisms and also on several experimental tumors. He reported that the guanine analog inhibited the growth of these tumors. At that time our laboratory was also exploring the chemothera-

peutic action of purine and pyrimidine analogs against experimental tumors. We confirmed and extended Kidder's observations and have become increasingly interested in the compound.

In figure 3 are represented guanine and 8-azaguanine, the analog which inhibits neoplastic growth. The type of response which this chemical produces is illustrated in figure 4, which shows the growth of an undifferentiated squamous cell carcinoma (the Brown-Pearce Carcinoma) growing in the anterior chamber of the eyes of treated and control rabbits. We were particularly interested to note that the therapeutic effect was achieved without apparent host toxicity. This gross impression received additional support from studies of the effect of 8-azaguanine on the mitotic activity of normal and tumor tissue. This is shown in Table 1. Here it can be seen that the mitotic rate in the intestinal crypts and in the testes is the same in untreated and 8-azaguanine treated animals, whereas the mitoses of the tumor have been markedly depressed in treated rabbits. This indication of tumor specificity was sufficient stimulus to learn more about the chemical compound. A further spur, however, was our finding and that of others, that 8-azaguanine inhibited the growth

of a variety of experimental epithelial tumors including squamous cell carcinoma and several mammary adenocarcinomas in mice, but failed significantly to affect sarcomas, lymphosarcomas or leukemias. Because the drug was carcinostatic, rather than carcinolytic, we had no inclination to give it clinical trial; however, the fact that it seemed to have selective action for tumor cells in contrast to normal cells, and also because it had a selective action on a morphologically separate group of malignant tumors, suggested that the chemical compound would be a splendid tool for studying biochemical differences between normal and certain neoplastic cells and between cells of 8-azaguanine susceptible and resistant tumors. For this reason, a program of research on the mechanism of action of the drug has been initiated in our laboratory.

This work is in progress and I am unable to give a complete story. However, the results thus far illustrate a hopeful aspect for future cancer chemotherapy, and therefore may be justifiably mentioned. Evidence which we, and also Skipper in Birmingham, have obtained, indicates that 8-azaguanine interferes with nucleic acid synthesis and nucleic acid function. The precise mechanisms involved are not yet known.

THE EFFECT OF 8-AZAGUANINE ON THE MITOTIC RATE OF NORMAL AND NEOPLASTIC TISSUES IN RABBITS*

	<i>Tumor</i> (mitoses per 100 cells)	<i>Intestine</i> (mitoses per 100 cells)	<i>Testis</i> (mitoses per 100 cells)
Control	8.8	6.3	13.1
8-azaguanine	1.1	6.3	14.7

* Abstracted from: Shapiro, Weiss and Gellhorn. Cancer 3: 896, 1950.

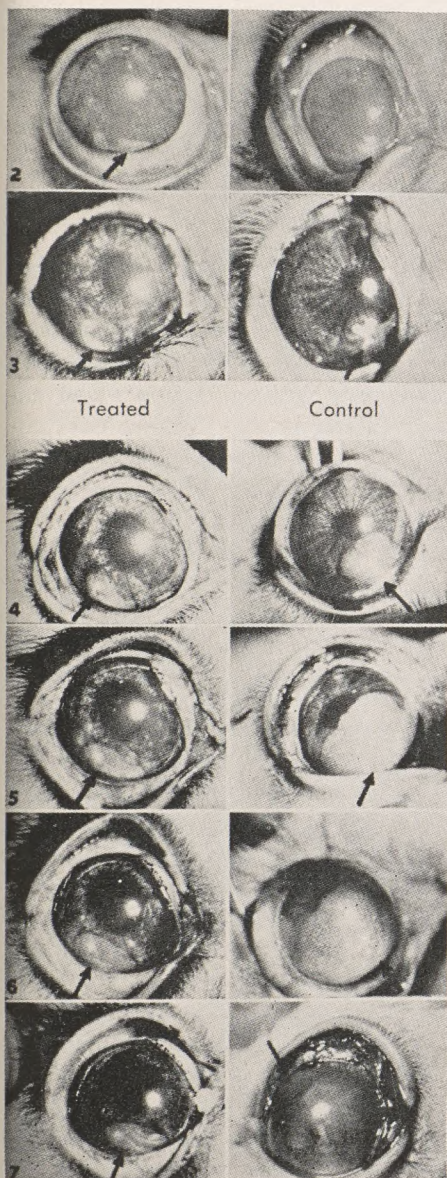


Figure 4. The effect of 8-azaguanine treatment on the Brown-Pearce carcinoma transplanted to the anterior chambers of rabbits' eyes. The small numbers refer to periods after transplantation. The arrows indicate the tumor. Number 2 is immediately after transplantation. Number 3 is two days later. Treatment started on the third day. Number 4 is 5 days after transplantation. Number 5 is 7 days after transplantation. Number 6 is 8 days after transplantation. Number 7 is 10 days after transplantation.

Note that there is little growth of the tumor in the treated animals, whereas the tumor completely fills the anterior chamber of the control animals.

(From Shapiro, Weiss and Gellhorn, *Cancer* 3: 896, 1950.)

We* do believe, however, that we have uncovered an important factor to explain the observed differences in action of 8-azaguanine on normal and neoplastic cells. An enzyme is present in normal tissue cells which deaminates 8-azaguanine to the corresponding xanthine analog, 8-azaxanthine. This reaction is illustrated in figure 5. When we determined the cellular concentration of this enzyme in susceptible tumors we found it to be low, whereas in the resistant tumors thus far examined it was very much higher. These comparisons are shown in figure 6, in which the concentration of the enzyme in the tumors is related to the level in the liver. This observation takes on significance from toxicological and experimental chemotherapeutic studies in which we have shown that 8-azaxanthine, the end product of the reaction catalyzed by this enzyme, is neither toxic nor does it have any growth-inhibiting action on tumors. This leads us to the interpretation that 8-azaguanine inhibits those tumors which are unable to convert the drug to the inactive form; normal cells and resistant tumors are protected by an efficient mechanism.

Obviously, the observations discussed just now are not on the main road to the discovery of effective cancer chemotherapy weapons. They do emphasize the application of an important fact. The fact is that there are many quantitative differences between normal and malignant cells even though qualitative differences have not yet been discovered. The application of this fact in the

case of 8-azaguanine is that the carcinostatic action of the chemical compound can be directly related to the low concentration of a deaminating enzyme in susceptible cells; in normal cells and in certain tumor cells both of which have a relatively higher concentration of the enzyme, no effect of the drug is demonstrable.

The biochemists have shown that metabolite inhibition by an antimetabolite depends to a large degree upon the concentration of the metabolite; the relationship between enzymes and enzyme inhibitors also follows this pattern. From the experience we have had with 8-azaguanine and from other experimental observations in progress in our laboratory, we feel that the observed quantitative differences between normal and neoplastic cells may provide vulnerable points for chemotherapeutic agents to attack cancer cell mechanisms.

In summary, it has been noted that the impressive biological actions of the nitrogen mustards and the folic acid analogs are intimately related to their effects on nucleic acid metabolism and function. This reemphasizes the importance of these cellular constituents and explains the interest of experimental cancer chemotherapists in this field. It has been indicated that these cytotoxic drugs do modify the course of certain malignant tumors and that they are useful in clinical medicine if their indications and limitations are clearly recognized. The nitrogen mustards and aminopterin fail, however, to be truly effective agents because they also are toxic to normal cells. This typifies the major problem of cancer chemotherapy.

* Drs. E. Hirschberg, J. Kream, I. Jaffe, M. Gertler and J. Gang are all associated in this research work.

Figure 5. The intracellular enzymatic diamination of 8-azaguanine.

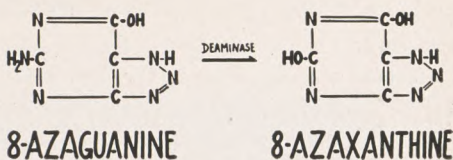
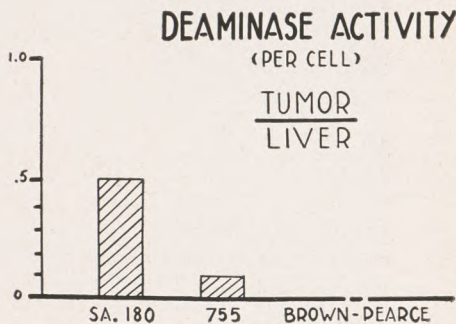


Figure 6. The ratio of cellular deaminase concentrations between tumor and liver.



In the discussion of a chemical compound which is only of interest in experimental cancer chemotherapy, evidence was presented which demonstrates the importance of quantitative differences between normal and neoplastic cells in the attainment of a chemotherapeutic effect. It was suggested that the weakness of the neoplastic cell and the strength of the normal cell might be

illuminated by these quantitative, comparative, biochemical characterizations, thereby providing guidance to the development of more effective anti-cancer drugs.

The challenge of cancer chemotherapy is formidable but the progress of the past ten years offers auspicious signs that it will be met triumphantly.

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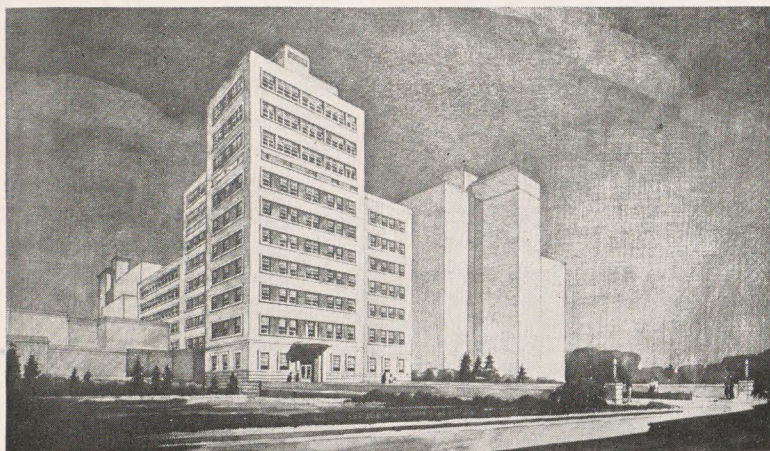
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WOHL HOSPITAL CONSTRUCTION STARTED

Ten-Story Building to Add 82 Beds



Construction on the \$2,000,000 David P. Wohl, Jr., Memorial Hospital in the Medical Center was started during the last week of March. The architect's drawing of the hospital is reproduced above.

The ten-story Wohl Hospital will be adjacent to the Nurses' Home and will connect with the Mallinckrodt Institute of Radiology and other nearby buildings. Designed for a maximum of 82 hospital beds and facilities for teaching and research, it is to be constructed so that three additional floors may be added in the future.

Recent completion of the steel and concrete bridge across the Wabash Railroad tracks made possible the beginning of construction on the hospital. The double-span bridge will provide a front entrance to the hospital from Audubon Avenue, and also will fill the long-felt need for a northern approach to the Medical Center.

Offices for the Departments of Medi-

cine and Surgery will occupy the second floor of the new hospital, with classrooms and a lounge for students on the ground floor, and dining room and additional offices on the first floor. The third, fourth and fifth stories will be devoted to patient care, while the top five floors are to house offices and research laboratories for the surgery and medicine departments.

Named in memory of Lt. David P. Wohl, Jr., the hospital is being built with funds provided in part by Mr. David P. Wohl, St. Louis shoe manufacturer and philanthropist. Lt. Wohl was killed in a bombing raid over Germany in 1944.

Mr. and Mrs. Wohl, the Wohl Foundation, and the Wohl Shoe Company contributed generously to finance the hospital, and the United States Public Health Service made a grant for the construction.

Completion of the structure is expected late in 1952.

W. U. to Admit First Negro to Medical School in Fall

For the first time, a Negro has fulfilled the necessary qualifications and accepted admission to the regular four-year course in the School of Medicine. The student is Edgar R. Thomas of New York City and Kingston, Jamaica, British West Indies, and he will enter with the 1951 freshman class in September.

The School of Medicine was authorized by the Board of Directors of the University in July, 1947, to admit Negroes on the same basis as all other students. There have been several Negroes in recent years who have taken postgraduate work in the Medical Center.

Thomas is 30 years old, was born in New York City, and lived for several years in Jamaica, British West Indies, where he received his secondary education. He was employed by the Medical Department of Jamaica and was secretary to the senior medical officer of the Kingston Public General Hospital.

In 1946 he entered Washington Square College of New York University, and will receive his bachelor of arts degree from there in September. He has been working as a laboratory assistant in the chemistry department, and for two years has been president of the student affiliates of the American Chemical Society at NYU.

Active in many University organizations, Thomas was elected to the honorary pre-medical society, Caducean, and to the honorary German fraternity. Mrs. Thomas will accompany him to St. Louis.

Markle Foundation Awards Third Scholarship to W. U. Researcher

The John and Mary R. Markle Foundation announced in New York on March 4 the awarding of the third Markle Foundation scholarship to a research man at Washington University School of Medicine. The recipient is Dr. Robert B. King, fellow in neurological surgery now on leave of absence to do neurosurgical work at Walter Reed General Hospital in Washington, D. C.

The School will receive a total of \$30,000, to be made available at the rate of \$6,000 for the next five years, to support Dr. King's research in neurosurgery. Dr. King interned at Barnes Hospital following graduation from the University of Rochester School of Medicine in 1946, and was a fellow and assistant resident in neuro-surgery on the staff here before leaving for army service in July, 1949.

Dr. King is the third Washington University man to be named a "scholar in medical science" by the Markle Foundation. Dr. C. Barber Mueller '42, assistant in surgery, received such an appointment in 1949, and Dr. Ralph Smith in 1948.

W. U. Commencement Changed

Washington University commencements hereafter will be held on the Wednesday of the second week in June. The Calendar Committee voted to change the date permanently to avoid conflict with exercises of St. Louis University.

This change places the 1951 commencement on Wednesday, June 6.

W. U. to Be Host to International Gerontology Meeting in September

Plans are well under way for the meeting of the Second International Gerontological Congress, which will meet in St. Louis at Hotel Jefferson, September 9 through 14. Dr. Edmund V. Cowdry, research professor of anatomy, is president of the Congress and several other staff members of the Medical School are serving as chairmen of various committees.

Washington University will act as the official host to the Congress.

Activities will start on Sunday, September 9, with setting up of exhibits and a radio broadcast of the University of Chicago Round Table from St. Louis.

The exhibits will include 20 to 30 of a scientific nature and 60 in the commercial field.

The Congress is being sponsored by the International Association of Gerontological Societies, the Gerontological Society, Inc., and the American Geriatrics Society. Four sections have been established for discussion of the phases of old age study. These are: biology and medicine; sociology, psychology, education and religion; economics and welfare; and medical services, hygiene and housing.

More than one thousand delegates are expected to attend the Gerontological Congress, including representatives and diplomats from many foreign countries.

1951 MEDICAL ALUMNI REUNION

Friday Evening, June 1

Guest Speaker: THE HONORABLE WALTER H. JUDD, M.D.

Representative in United States Congress from the Fifth District, State of Minnesota.

Dr. Judd returned to the United States in 1937 after several years as a medical missionary in China. He is a graduate of the University of Nebraska School of Medicine, class of 1923.

Place: STARLIGHT ROOF, CHASE HOTEL

Kingshighway at Lindell, St. Louis

Time: Cocktails, 6:30 P. M. Dinner, 7:00 P. M.

The 1951 graduating class of the School of Medicine will be our guests on this occasion, so come and help give them a good sendoff!

Please send your reservation to the Medical Alumni Office NOW!

Your class will have its own table

Report of the Dormitory Fund Campaign

Our immediate goal of \$100,000 from the medical alumni is coming closer, but there is still some \$35,000 outstanding before we can approach private philanthropy for contributions and really start work on the Medical Student Dormitory.

The grand total of contributions and pledges is now \$65,284.10, including \$6500 in volunteer gifts from St. Louis friends of the Medical School, as mentioned in the January QUARTERLY. The average gift from 707 donors stands at \$92.00.

There are still more than 2200 graduates of the Medical School who have not responded to our appeals. If you have not contributed yet, please send in your check now to show that you support this important project.

Samuel B. Grant, Chairman

1950—Living Graduates, 85

Edward T. Emura, St. Louis
Joseph D. O'Keefe, Nashville, Tenn.
Robert I. Pfeffer, St. Louis
Richard L. Swarm, St. Louis

1949—Living Graduates, 96

Roger Bumgarner, Kansas City, Kans.
Eugene W. Pearce, Washington, D. C.
Russell D. Sheldon, Kansas City, Mo.
George S. Woodard, Jr., Washington, D. C.

1948—Living Graduates, 89

Virgil R. Bleisch, Boston, Mass.
Walter A. Fernau, Jr., Cincinnati, O.
David A. Guterman, Elgin, Ill.
Hugh R. Harting, St. Louis
Richard F. Huck, Jr., St. Louis
Juro L. Shintani, Perry Point, Md.

1947—Living Graduates, 98

Charles G. Clay, Rantoul, Ill.

Marvin Cornblath, St. Louis
William C. Dunckel, Charlottesville, Va.
Helen Hofsommer Glaser, St. Louis
Burnet W. Peden, St. Louis
Virginia H. Peden, St. Louis

1946—Living Graduates, 86

Drennan Bailey, Clayton, Mo.
R. Robert Bates, Tucson, Ariz.
Gladden V. Elliott, Richmond Heights, Mo.
Lawrence W. O'Neal, Webster Groves, Mo.

James O. Owen, Jr., Skiatook, Okla.
Theodore J. H. Smith, Temple, Tex.
Robert S. Spain, McKinney, Tex.
Frank Vellios, St. Louis
Leonard J. Wiedershine, Aurora, Colo.

1945—Living Graduates, 105

John T. Farrar, Boston, Mass.
Jay O. Gibson, French Camp, Calif.
Samuel B. Guze, Newington, Conn.
John T. Johnstone, Jr., St. Louis
Donald E. Kilker, St. Louis
Louis O. Lambiotte, Salt Lake City, U.
Ceylon S. Lewis, Jr., Salt Lake City
Roscoe Maxwell, Punta Gorda, Fla.
George W. Prothro, Clovis, N. Mex.
Eugene T. Taylor, Mocksville, N. C.
John W. Ubben, Staunton, Ill.
Gary B. Wood, St. Louis
Betty Ben Geren, Boston, Mass.
Charles Wolfson, Amarillo, Tex.

1944—Living Graduates, 95

Guy D. Callaway, Jr., Seattle, Wash.
Albert B. Eisenstein, St. Louis
J. K. Frost, Centralia, Ill.
Robert D. Lange, Kirkwood, Mo.
Ervan Levine, Vandalia, Mo.
Clayton H. Manry, Syracuse, N. Y.
Francis E. Pennington, St. Louis
H. H. Perman, Forest City, Ia.
John J. Rupp, Tucson, Ariz.
David E. Smith, St. Louis
Roy A. Walther, Jr., Overland, Mo.
Virgil Loeb, Jr., St. Louis
Marvin T. Pursell, Dinuba, Calif.
Louis Weisfuse, Brooklyn, N. Y.

1943—(Dec.)—Living Graduates, 113

John F. Blinn, Jr., Stockton, Calif.
J. P. Myles Black, Olive View, Calif.

C. Read Boles, St. Louis
 William P. Callahan, Wichita, Kan.
 Joseph B. Clay, Van Nuys, Calif.
 Terrell Covington, Jr., McKinney, Tex.
 Edward W. Czebrinski, St. Louis
 Harold Grant, McKinney, Tex.
 Mary Jordan, Ridley Park, Pa.
 Walter J. Kennedy, Yakima, Wash.
 Edward H. Kowert, St. Louis
 Elaine K. Lince, Pasadena, Calif.
 Torrence A. Makley, Jr., Columbus, O.
 Walter A. Rohlfling, Fresno, Calif.
 Ernest Schwartz, San Francisco, Calif.
 Burton Shatz, St. Louis
 Donald E. Smith, Salt Lake City, U.
 Tom G. Stauffer, Scarsdale, N. Y.
 Herbert C. Wiegand, St. Louis
 Frances C. Wilson, Tampa, Fla.
 Carl T. Woolsey, St. Louis
 Alfred H. Sudholt, St. Louis
 Harold E. Walters, St. Louis

1943—(March—Living Graduates, 105

DeWayne C. Anderson, Stanhope, Ia.
 Grace E. Bergner, St. Louis
 Raymond M. Charnas, St. Louis
 David Feldman, St. Louis
 Harlan I. Firminger, Bethesda, Md.
 Melvin L. Goldman, St. Louis
 H. Clagett Harding, Portland, Ore.
 F. C. Lawrence, Bartlesville, Okla.
 Ira W. Liebner, Brooklyn, N. Y.
 Eichi Masunaga, T. H.
 Roberts B. Pappenfort, New York, N. Y.
 Ernest S. Rogers, San Francisco, Calif.
 Carvel T. Shaw, Hermann, Mo.
 David A. Stadtner, Stockton, Calif.
 H. A. Uhlemeyer, Jr., St. Louis
 Gerald J. Conlin, Denver, Colo.
 Albert N. Lemoine, Jr., Mission, Kans.
 James L. Petry, Port Arthur, Tex.
 Daniel G. Santer, Milwaukee, Wis.

1942—Living Graduates, 92

William M. Anderson, Richmond, Va.
 Ewald W. Busse, Denver, Colo.
 Frances M. Love, Richland, Wash.
 French H. McCain, Birmingham, Mich.
 C. Barber Mueller, St. Louis
 William G. Reese, Perry Point, Md.
 Herman Rice, Temple, Tex.
 Frank O. Shobe, St. Louis

George L. Watkins, Farmington, Mo.
 Hiraku Ishida, Los Angeles, Calif.

1941—Living Graduates, 93

Robert J. Cook, St. Louis
 Jane Matthews Day, Montgomery, Ala.
 Charles E. Fildes, Poplar Bluff, Mo.
 B. W. Finkel, St. Louis
 Peter O. Fleming, Topeka, Kan.
 Anne T. Goetsch, Berkeley, Calif.
 Samuel W. Gollub, St. Louis
 Leon Kahn, Beverly Hills, Calif.
 Geo. Bruce Lemmon, Springfield, Mo.
 Harold E. McCann, E. St. Louis
 V. A. Mueller, Wichita, Kan.
 C. A. Nielsen, Seattle, Wash.
 Joseph W. Noah, St. Louis
 Carol H. Rehm, Los Angeles, Calif.
 Allan M. Rossen, Los Angeles, Calif.
 William L. Topp, Seattle, Wash.
 Mitchell Yanow, Clayton, Mo.
 Cecil H. Blackburn, Selma, Ala.
 Bruce L. Canaga, Drexel Hill, Pa.
 Jane A. Erganian, Glen Rock, N. J.
 J. I. Moreland, Salem, Ore.
 Bernice A. Torin, St. Louis

1940—Living Graduates, 92

Robert R. Anschuetz, Alton, Ill.
 Donald S. Bottom, Alton, Ill.
 Seymour Brown, St. Louis
 Russell J. Crider, St. Charles, Mo.
 Roland R. Cross, Hines, Ill.
 A. T. Esslinger, St. Louis
 L. R. Fernandez, Laupahoe, T. H.
 James M. Foerster, Wausau, Wis.
 Otto H. Grunow, St. Louis
 R. N. Hirst, Ogden, Utah
 Robert H. Johnson, Tulsa, Okla.
 Robert E. Koch, St. Louis
 James Mann, Boston, Mass.
 Gordon F. Moore, Alton, Ill.
 Charles G. Obermeyer, St. Louis
 Willard D. Rowland, Portland, Ore.
 Llewellyn Sale, Jr., St. Louis
 John S. Skinner, St. Louis
 Robert M. Smith, St. Louis
 W. L. Tomlinson, St. Louis
 Leo A. Sachar, St. Louis
 Harry W. Sawyer, San Francisco, Calif.

1939—Living Graduates, 96

Alfred K. Baur, St. Louis

Irving L. Berger, Cleveland, Ohio
 Vilray P. Blair, Jr., St. Louis
 Leo J. Blum, Jr., Warner Robins, Ga.
 Joseph Borenstine, Kansas City, Mo.
 Sidney S. Boyers, W. New York, N. J.
 Mark J. Brockbank, Petaluma, Calif.
 Heinz E. Cron, San Francisco, Calif.
 William B. Hildebrand, Menasha, Wis.
 Leonard H. Jacobson, Miami Beach, Fla.
 Benjamin Milder, St. Louis
 Edward H. Reinhard, St. Louis
 Minton D. Ritter, Margate City, N. J.
 R. J. Roscow, Evansville, Ind.
 Gerald A. Slusser, Silver City, N. Mex.
 O. W. Towers, St. Charles, Mo.
 John W. Dix, Miami, Fla.
 Leon J. Fox, St. Louis

1938—Living Graduates, 92

Harry A. Baers, North Hollywood, Calif.
 G. W. Blankenship, Anderson, Mo.
 Robert D. Brookes, St. Louis
 Margaret A. Carter, St. Louis
 Adolph H. Conrad, Jr., St. Louis
 Marion J. Dakin, Los Angeles, Calif.
 Lawrence M. Kotner, St. Louis
 Harry Mantz, Alton, Ill.
 Robert G. Moles, Hanford, Calif.
 Anthony Piraino, Oberlin, Ohio
 Joseph H. Pollock, Los Angeles, Calif.
 Philip Rosenblatt, New York, N. Y.
 Samuel Schultz, Clayton, Mo.
 Roy W. Thomas, Redding, Calif.
 J. L. Doenges, Anderson, Ind.
 H. R. Gilbert, Wyandotte, Mich.
 Alexander A. Mueller, Los Angeles,
 Calif.

1937—Living Graduates, 93

Samuel Brady, Gary, Ind.
 Paul A. Brenner, Owensville, Mo.
 G. L. Calvy, Cleveland, Ohio
 R. G. Carter, Austin, Tex.
 Martin A. Compton, Richmond, Va.
 John R. Connell, Denver, Colo.
 Samuel M. Day, Jacksonville, Fla.
 J. M. Dougall, Houston, Tex.
 Thomas S. Boozer, Montgomery, Ala.
 Edward A. Harris, Birmingham, Ala.
 Lester E. Haentzschel, Appleton, Wis.
 A. E. Meisenbach, Jr., Dallas, Tex.
 John E. Miksick, St. Louis

H. L. Townsend, Louisville, Ky.
 Bernard C. Trowbridge, Kansas City,
 Mo.
 J. A. Fiorito, New Haven, Conn.
 William H. Gray, Yakima, Wash.
 Carroll W. Huffman, Los Angeles, Calif.
 Arthur A. Kaplan, Utica, N. Y.
 Robert C. Kingsland, St. Louis
 Carl E. Lischer, St. Louis
 Edgar H. Little, New Orleans, La.
 Lewis E. Littmann, St. Louis
 Elizabeth Lowenhaupt, San Francisco
 M. S. McGrath, Weiser, Idaho
 Ralph C. Petersen, Glendale, Calif.
 Charles M. Polan, Huntington, W. Va.
 William J. Quinn, Alturas, Calif.
 Henry N. Reid, Rome, N. Y.
 Lloyd Rosenbaum, Anderson, Ind.
 Harvey S. Smith, Boise, Idaho
 Walter Stevenson, Jr., Quincy, Ill.
 H. L. Townsend, Louisville, Ky.
 David R. Wall, Wichita, Kan.
 Ellsworth A. Westrup, Webster Groves,
 Mo.
 Marie H. Wittler, Wheaton, Ill.

1936—Living Graduates, 102

James H. Bryant, St. Louis
 F. R. Crouch, Farmington, Mo.
 Norman W. Drey, St. Louis
 Stephen Ellis, Coffeyville, Kan.
 Curtis H. Epps, Springfield, Mo.
 John L. Horner, St. Louis
 W. H. Jacobson, Canton, Ohio
 Nathan R. Kahn, Brooklyn, N. Y.
 George M. Klingner, Springfield, Mo.
 Vernon Lundmark, Seattle, Wash.
 Frank McDowell, St. Louis
 James D. Morrison, Billings, Mont.
 R. A. Nussbaum, St. Louis
 Samuel Schneider, St. Louis
 William L. Sellers, Jr., Mobile, Ala.
 E. H. Trowbridge, Jr., Kansas City, Mo.
 Michael S. Wepprich, Washington, Mo.
 Warren B. West, Ogden, Utah
 Robert A. Wise, Houston, Tex.
 Charles A. Brasher, Mt. Vernon, Mo.
 Lawrence Breslow, Chicago, Ill.
 Hyman Jaffe, Beverly Hills, Calif.

1935—Living Graduates, 88

K. M. Amlin, Honolulu, T. H.

I. J. Flance, St. Louis
 Heinz Haffner, St. Louis
 Alfred W. Harris, Dallas, Tex.
 A. Herman Hutto, St. Louis
 Norman M. Johnson, Clarinda, Iowa
 Jacob Katzeff, Brooklyn, N. Y.
 Bruce Kenamore, St. Louis
 Kenneth V. Larsen, St. Louis
 Ellen S. Loeffel, St. Louis
 Edward Massie, St. Louis
 Sidney Messer, Venice, Calif.
 Clark G. Porter, Three Rivers, Mich.
 Laurence G. Pray, Fargo, N. D.
 David Rothman, St. Louis
 Bernard Schwartzman, St. Louis
 Ben H. Senturia, St. Louis
 A. J. Steiner, St. Louis
 David O. Weiner, Brooklyn, N. Y.
 Irvin Weisman, Granite City, Ill.
 Elmer G. Gaul, St. Louis
 Arthur P. Echternacht, Fort Dodge, Ia.
 John W. Williams, Oak Grove, Mo.

1934—Living Graduates, 88

Helen M. Aff, St. Louis
 Edmund B. Alvis, St. Louis
 James M. Baker, Columbia, Mo.
 Garvey Bowers, Kokomo, Ind.
 Eugene M. Bricker, St. Louis
 L. F. Bush, Danville, Pa.
 Everett S. Caldemeyer, Washington,
 D. C.
 T. C. Campbell, New Orleans, La.
 David Friedman, Granite City, Ill.
 Ben I. Frissel, Phoenix, Ariz.
 Paul O. Hagemann, St. Louis
 Stanley Hampton, St. Louis
 Louis G. Jekel, Phoenix, Ariz.
 Dorothy J. Jones, St. Louis
 Ralph R. Jones, Boise, Idaho
 Morris D. Marcus, St. Louis
 M. Norman Orgel, St. Louis
 H. D. Rosenbaum, St. Louis
 John A. Saxton, St. Louis
 Edna Schrick, Oakland, Calif.
 James G. Telfer, Chicago, Ill.
 William W. Gist, Kansas City, Mo.
 Martin P. Hunter, Kansas City, Mo.
 Fred C. Reynolds, St. Louis

1933—Living Graduates, 89

Henry C. Allen, St. Louis

James W. Bagby, St. Louis
 Russell J. Blattner, Houston, Tex.
 Cecil M. Charles, St. Louis
 Lee W. Dean, Jr., St. Louis
 Truman G. Drake, St. Louis
 Wallace D. English, Cardwell, Mo.
 Charles H. Flynn, Clarinda, Ia.
 George E. Grim, Kirksville, Mo.
 Carl G. Harford, St. Louis
 John R. Haslem, Terre Haute, Ind.
 W. W. Herman, Cleveland, Ohio
 Joseph C. Jaudon, St. Louis
 F. Craig Johnson, Denver, Colo.
 A. A. Loverde, Chicago, Ill.
 R. R. Merrell, Pocatello, Idaho
 Alvin R. Miller, Seattle, Wash.
 Louis A. Motchan, Beverly Hills, Calif.
 Charles Oderr, New Orleans, La.
 Lyman K. Richardson, New Orleans, La.
 J. F. Roufa, St. Louis
 Richard Y. Sakimoto, Honolulu, T. H.
 Robert S. Smith, Boise, Idaho
 Robert T. Terry, Nashville, Tenn.
 Oreon K. Timm, Danville, Ill.
 R. M. Van Matre, Oklahoma City, Okla.
 Wirt A. Warren, Wichita, Kan.
 Lawrence M. Wilson, Olympia, Wash.
 J. J. Wimp, Kirksville, Mo.
 Frank G. Zingale, St. Louis
 George E. Zukovich, San Diego, Calif.
 Lawrence M. Wilson, Olympia, Wash.
 George J. L. Wulff, Jr., St. Louis

1932—Living Graduates, 85

Harry Agress, St. Louis
 Sim F. Beam, St. Louis
 Brian B. Blades, Washington, D. C.
 Louis T. Byars, St. Louis
 B. S. Clark, Spearfish, S. D.
 William Ehrlich, Newark, N. J.
 Leo Gottlieb, St. Louis
 Kikoshi Inouye, Honolulu, T. H.
 D. H. Kaump, Detroit, Mich.
 Paul H. Lefkowitz, Spring Valley, N. Y.
 William H. Meinberg, St. Louis
 Carl V. Moore, St. Louis
 Paul B. Nutter, Spokane, Wash.
 Sydney S. Pearl, Elizabeth, N. J.
 C. O'Neil Rich, Salt Lake City, Utah
 Wendell G. Scott, St. Louis
 Don J. Silsby, Springfield, Mo.

- Barrett L. Taussig, St. Louis
 Dwight H. Trowbridge, Fresno, Calif.
 Sam R. Wallis, Kauai, T. H.
 Helman C. Wasserman, St. Louis
 John C. Wilson, San Jose, Calif.
 Irving Wyle, Brooklyn, N. Y.
 Virgil E. Jeans, Joplin, Mo.
 Donald M. Paton, Houston, Tex.
- 1931—Living Graduates, 73
 Delevan Calkins, St. Louis
 E. W. Cannady, E. St. Louis, Ill.
 Joseph Cieri, Piedmont, Calif.
 D. B. Elrod, Cape Girardeau, Mo.
 A. W. Hankwitz, Milwaukee, Wis.
 W. E. Keiter, Kinston, N. C.
 Morris Krutchkoff, San Francisco, Calif.
 Mary Louise Newman, Jacksonville, Ill.
 Max Magnes, Paterson, N. J.
 H. R. McCarroll, St. Louis
 Robert F. Monroe, Louisville, Ky.
 Ben Friedman, McKinney, Tex.
 W. Wallace Green, Kansas City, Mo.
 Edwin C. Schmidtke, Columbia, Mo.
 John A. Schindler, Monroe, Wis.
 R. B. Wray, Nevada, Mo.
- 1930—Living Graduates, 76
 Harold S. Bowman, Wichita, Kan.
 M. A. Brennecke, Waimea, Kauai, T. H.
 J. Paul Burgess, Hyrum, Utah
 M. A. Diehr, St. Louis
 Donald E. Eggleston, Macon, Mo.
 Virgin O. Fish, St. Louis
 Herbert H. Gass, India
 Joseph J. Gitt, St. Louis
 Stanley Harrison, St. Louis
 Alfred H. Hathcock, Fayetteville, Ark.
 Walter M. Howard, Joplin, Mo.
 James D. Horton, Springfield, Mo.
 I. D. Newmark, Chester, Ill.
- 1929—Living Graduates, 71
 Carl S. Bickel, Wheeling, W. Va.
 Leslie C. Drews, Clayton, Mo.
 A. W. Freshman, Denver, Colo.
 Guerdan Hardy, St. Louis
 Craig B. Johnston, Philadelphia, Pa.
 Louis Kovitz, Kansas City, Mo.
 Sidney Pakula, Kansas City, Mo.
 Frank B. Queen, Portland, Ore.
 A. P. Rowlette, Moberly, Mo.
 Jay Marvin Salzman, Springfield, Ill.
- A. Ford Wolf, Temple, Tex.
 Grace Edwards Barar, Allahabad, India
 F. L. Harms, Salisbury, Mo.
 V. L. Peterson, Charleston, W. Va.
 Arthur E. Varden, San Bernardino, Calif.
- 1928—Living Graduates, 69
 A. N. Arneson, St. Louis
 William Brewer, Hays, Kans.
 Edward Burns, Toledo, Ohio
 Justin J. Cordonnier, St. Louis
 Roland F. Elkins, Springfield, Mo.
 John S. Harter, Louisville, Ky.
 H. R. Hildreth, St. Louis
 Laurence L. Howard, Great Falls, Mont.
 J. Ted Jean, St. Louis
 R. D. Kepner, Honolulu, T. H.
 Guy N. Magness, St. Louis
 L. A. Malone, Terre Haute, Ind.
 Earl L. Mills, Wichita, Kan.
 John F. Patton, St. Louis
 A. Victor Reese, St. Louis
 Paul R. Rollins, Seattle, Wash.
 Verne Ross, Stockton, Calif.
 W. A. Ruch, Memphis, Tenn.
 O. G. Schneidewind, New Athens, Ill.
 B. Wright Shelton, Miami Okla.,
 David M. Skilling, St. Louis
 A. Lloyd Stockwell, Kansas City, Mo.
 Jacob Stolar, St. Louis
 Vincent T. Williams, Kansas City, Mo.
 George H. Wood, Carthage, Mo.
- 1927—Living Graduates, 70
 Everett C. Drash, Charlottesville, Va.
 A. C. Fortney, Fargo, N. D.
 Paul H. Guttman, Sacramento, Calif.
 Alfred G. Henrich, Los Angeles, Calif.
 Irene A. Koeneke, Halstead, Kans.
 C. H. Leslie, Kirkwood, Mo.
 W. R. Merrell, Brigham City, Utah
 Alfred J. Metscher, Enid, Okla.
 Kazuo Miyamoto, Honolulu, T. H.
 Eugene O. Parsons, Kansas City, Mo.
 Willard C. Schwartz, Manhattan, Kan.
 Abigail E. Smith, Lexington, Mass.
 Frances H. Stewart, St. Louis
 Richard T. Taylor, Los Angeles, Calif.
 Louis L. Tureen, St. Louis
 Franklin Walton, St. Louis
 W. B. Wilcoxon, Bowling Green, Mo.

George S. Wilson, Enid, Okla.
 Louis F. Aitken, St. Louis
 A. G. Klein, St. Louis

1926—Living Graduates, 73

Reno A. Ahlvin, Kankakee, Ill.
 Herbert Anderson, Los Angeles, Calif.
 Willard Bartlett, Jr., St. Louis
 James L. Benepe, St. Paul, Minn.
 H. M. Chandler, Waipahu, T. H.
 Erich A. Cunningham, Louisiana, Mo.
 Max Deutch, St. Louis
 Andy Hall, Jr., St. Louis
 William M. James, St. Louis
 William B. Kountz, St. Louis
 John G. Manning, McMinnville, Ore.
 G. Wendell Olson, Fullerton, Calif.
 Walter R. Peterson, Trenton, N. J.
 Bernard Rand, New York City
 Henry A. Romberg, Oshkosh, Wis.
 J. C. Schmidtke, Elgin, Ill.
 E. H. Theis, Granite City, Ill.
 Charles W. Duden, St. Louis

1925—Living Graduates, 67

George P. Bailey, Lakewood, Colo.
 Robert J. Crossen, St. Louis
 H. M. Denny, Union, Mo.
 James J. Donohue, E. St. Louis, Ill.
 B. Y. Glassberg, St. Louis
 A. E. Hiebert, Wichita, Kan.
 Richard K. Kimmel, St. Louis
 James I. Knott, San Diego, Calif.
 S. D. Soule, St. Louis
 Jerome S. Levy, Little Rock, Ark.
 Joseph Magidson, St. Louis
 Carl H. Matthey, Davenport, Iowa
 Loren D. Moore, Wellesley Hills, Mass.
 Sam. J. Roberts, Miami, Fla.
 Melvin A. Roblee, St. Louis
 Roland A. Slater, Peoria, Ill.
 Winton T. Stacy, Fort Sill, Okla.
 R. O. Stickler, Kirksville, Mo.
 Gershom J. Thomson, Rochester, Minn.
 Hugo O. Wagner, Great Lakes, Ill.
 James O. Nall, Marion, Ky.

1924—Living Graduates, 68

Alfred O. Adams, Spokane, Wash.
 Roy F. Baskett, Texarkana, Tex.
 J. William Beckmann, New York, N. Y.
 Harry J. Davis, Topeka, Kans.
 Charles Drabkin, Los Angeles, Calif.

Perry E. Duncan, Springfield, Ill.
 George H. Garrison, Oklahoma City,
 Okla.

H. V. Gibson, Great Falls, Mont.
 William B. Gnagi, Monroe, Wis.
 Scott Johnson, New York City
 Louis H. Jorstad, St. Louis
 Elizabeth E. Koppenaar, Elmhurst, Ill.
 A. E. Meinert, Winona, Minn.
 E. B. Pfefferkorn, Oshkosh, Wis.
 Reuben M. Smith, St. Louis
 O. Earl Whitsell, St. Joseph, Mo.
 Eugene S. Auer, Denver, Colo.

1923—Living Graduates, 47

Oliver Abel, Jr., St. Louis
 William G. Becke, St. Louis
 William L. Bradford, Rochester, N. Y.
 James Barrett Brown, St. Louis
 Ben M. Bull, Ironton, Mo.
 I. Z. Davidoff, Milwaukee, Wis.
 Walter J. Decker, Westfield, Pa.
 George V. Feist, Kansas City, Mo.
 Ben D. Senturia, Chicago, Ill.
 Charles Teel, Bellingham, Wash.
 J. Wm. Thompson, St. Louis
 Clair O. Vingom, Madison, Wis.
 Elias H. Schlomovitz, Milwaukee, Wis.

1922—Living Graduates, 44

K. S. Chouke, Philadelphia, Pa.
 Calvin Clay, St. Charles, Mo.
 James B. Costen, St. Louis
 Aphrodite J. Hofsommer, Webster
 Groves, Mo.
 Armin C. Hofsommer, Webster Groves,
 Mo.
 Kirby A. Martin, New York, N. Y.
 F. E. Sultzman, Hannibal, Mo.

1921—Living Graduates, 42

Lester J. Evans, Jackson Heights, N. Y.
 J. C. McKitterick, Burlington, Iowa
 Harvey S. Rusk, Pueblo, Colo.
 Oscar C. Zink, St. Louis

1920—Living Graduates, 39

Robert L. Andrae, Louisiana, Mo.
 Clifton H. Briggs, Pasadena, Calif.
 Warren H. Cole, Chicago, Ill.
 Alfred Goldman, St. Louis
 Samuel B. Grant, St. Louis
 Guy H. Hopkins, Pueblo, Colo.

- William A. Hudson, Detroit, Mich.
 W. N. Jenkins, Port Gibson, Miss.
 Frederick E. Jostes, St. Louis
 P. H. Kennedy, Hubbard, Ohio
 Herman M. Meyer, St. Louis
 L. J. Owen, Lincoln, Neb.
 M. G. Peterman, Milwaukee, Wis.
 Royal W. Rudolph, Tucson, Ariz.
 H. W. Wellmerling, Bloomington, Ill.
 Harvey Lester White, St. Louis
- 1919—Living Graduates, 45
 Duff S. Allen, St. Louis
 S. P. Funkhouser, Lake County, Calif.
 Howard H. Heuston, Bolder, Colo.
 Fred J. Hodges, Ann Arbor, Mich.
 Carl O. Kohlbry, Duluth, Minn.
 Marriott T. Morrison, Mt. Horeb, Wis.
 E. H. Munro, Grand Junction, Colo.
 Raymond L. Murdoch, Oklahoma City, Okla.
 Howard A. Plank, New York, N. Y.
 A. B. Raffl, Syracuse, N. Y.
 R. P. Roantree, Elko, Nev.
 A. L. Walter, Sedalia, Mo.
- 1918—Living Graduates, 26
 Glover H. Copher, St. Louis
 Wilbur G. Gillett, Wichita, Kan.
 Elmer N. Liljedahl, Hollywood, Calif.
 Arthur G. Mahle, Chicago, Ill.
 J. F. Pessel, Trenton, N. J.
 O. Sundwall, Murray, Utah
 James A. Tesson, Kansas City, Mo.
- 1917—Living Graduates, 25
 Archie A. Skemp, La Crosse, Wis.
 J. E. Wattenberg, Cortland, N. Y.
- 1916—Living Graduates, 13
 E. L. Dallwig, Milwaukee, Wis.
 Earl C. Sage, Omaha, Neb.
 Ray T. Woolsey, Salt Lake City, Utah
- 1915—Living Graduates, 20
 D. K. Rose, St. Louis
 J. E. Strode, Honolulu, T. H.
 W. T. Wilkening, Fort Scott, Kans.
- 1914—Living Graduates, 8
 O. F. McKittrick, Linglestown, Pa.
 John T. McLarney, Brookfield, Mo.
- 1913—Living Graduates, 20
 F. O. Kettelkamp, Colorado Springs, Colo.
- 1912—Living Graduates, 30
 C. F. DeGaris, Oklahoma City, Okla.
 Roy G. Empson, Valmeyer, Ill.
 Edwin C. Ernst, St. Louis
 George S. Gilpin, Cleveland, O.
 W. N. O'Bannon, New Madrid, Mo.
 Wells C. Reid, Goodrich, Mich.
 A. P. Erich Schulz, St. Charles, Mo.
 George L. Watkins, Farmington, Mo.
- 1911—Living Graduates, 20
 Thomas M. Davis, St. Louis
 Clyde P. Dyer, St. Louis
 William H. Fickel, Denver, Colo.
 Charles H. Hecker, Palo Alto, Calif.
 Arthur J. Wagers, Philadelphia, Pa.
- 1910—Living Graduates, 40
 Stanley S. Burns, St. Louis
 Frederic Hagler, Springfield, Mass.
 Robert M. Hardaway, Wheatridge, Colo.
 John P. Keim, St. Louis
 Peter G. Moskop, St. Louis
 Claude D. Pickrell, St. Louis
 Frederick O. Schwartz, St. Louis
- 1909—Living Graduates, 29
 James W. Barrow, Carbondale, Ill.
 Carey B. Elliott, Raton, N. Mex.
 W. N. Pugh, Salt Lake City, Utah
 Richard S. Weiss, St. Louis
- 1908—Living Graduates, 29
 W. A. Olds, Colville, Wash.
 O. J. Raeder, Boston, Mass.
 W. D. Moore, San Pedro, Calif.
- 1907—Living Graduates, 28
 C. C. Nash, Dallas, Tex.
 Grandison D. Royston, Hope, Ark.
 Llewellyn Sale, St. Louis
 Raymond M. Spivy, St. Louis
- 1906—Living Graduates, 33
 Martin J. Glaser, St. Louis
 Arthur Gundlach, St. Louis
 T. A. Lawler, Taylorville, Ill.
 S. P. Martin, East Pairie, Mo.
 S. B. McPheeters, Goldsboro, N. C.
 William H. Smith, Colfax, Calif.
- 1905—Living Graduates, 30
 Jerome E. Cook, St. Louis
 Walter Fischel, St. Louis
 Harry M. Griffith, Pasadena, Calif.
 J. M. James, Henning, Ill.
 O. W. Knewitz, East St. Louis

- 1904—Living Graduates, 31
 Paul Baldwin, Kennett, Mo.
 W. Q. Conway, Kalispell, Mont.
 N. M. Freund, St. Louis
 Harry L. Jones, Kansas City, Mo.
 Roy P. Scholz, St. Louis
 J. H. Woodridge, Pueblo, Colo.
- 1903—Living Graduates, 20
 A. H. Myerdick, Mt. Pleasant, Iowa
 Clive D. Scott, Louisiana, Mo.
- 1902—Living Graduates, 22
- 1901—Living Graduates, 14
 John M. Bradley, St. Louis
 W. C. Forder, St. Louis
 Walter C. G. Kirchner, St. Louis
 M. K. Wyler, Albuquerque, N. Mex.
- 1900—Living Graduates, 2
- 1899—Living Graduates, 34
 J. C. Caldwell, Wellington, Kans.
 C. L. Lawless, Marshall, Mo.
 R. O. Raymond, Flagstaff, Ariz.
 Selden Spencer, St. Louis
 Julian B. Woodson, Lowesville, Va.
- 1898—Living Graduates, 27
 J. G. W. Fischer, Alma, Mo.
 R. B. H. Gradwohl, St. Louis
 John Q. Roane, Carlyle, Ill.
 A. L. Stuttle, Williamsville, Ill.
- 1897—Living Graduates, 21
 Theodore Greiner, St. Louis
 Frederick E. Woodruff, St. Louis
- 1896—Living Graduates, 21
- 1895—Living Graduates, 21
 H. A. Geitz, Monterrey, N. L., Mexico
 Sandor Horwitz, Peoria, Ill.
 Robert J. Terry, St. Louis
 William A. Tolleson, Eufala, Okla.
- 1894—Living Graduates, 13
- 1893—Living Graduates, 12
 Andrew Darling, St. Louis
 R. Clarence Stephens, Plymouth, Ind.
- 1892—Living Graduates, 4
- 1891—Living Graduates, 15
- 1890—Living Graduates, 6
- 1889—Living Graduates, 6
- 1888—Living Graduates, 2
- 1887—Living Graduates, 3
- 1886—Living Graduates, 3
- 1885—Living Graduates, 2
 E. F. Ellis, Fayetteville, Ark.
- 1884—Living Graduates, 2
- 1883—Living Graduates, 2
 W. A. Fries, St. Louis
- 1882—Living Graduates, 1
- 1881—Living Graduates, 3
 James A. Dickson, St. Louis
 Willis Hall, St. Louis
- 1880—Living Graduates, 2

OTHER DONORS

- Mrs. T. R. Akin, Clayton, Mo.
 Mr. William M. Akin, St. Louis
 Harry L. Alexander, M.D., St. Louis
 Robert W. Bartlett, M.D., St. Louis
 Leon Bromberg, M.D., St. Louis
 J. J. Bronfenbrenner, Ph.D., St. Louis
 Samuel S. Bukantz, M.D., St. Louis
 Martin M. Calodney, M.D., St. Louis
 Benjamin H. Charles, M.D., St. Louis
 Drs. Carl F. and Gerty T. Cori, St. Louis
 Gustave J. Dammin, M.D., St. Louis
 Morris Davidson, M.D., St. Louis
 Hollowell Davis, M.D., St. Louis
 Joseph E. Edwards, M.D., St. Louis
 Ben Eiseman, M.D., St. Louis
 Robert Elman, M.D., St. Louis
 Lee T. Ford, St. Louis
 Robert J. Glaser, M.D., St. Louis
 Harry N. Glick, M.D., St. Louis
 Drs. Evarts and Helen Tredway Graham,
 St. Louis
 G. E. Gruenfeld, M.D., St. Louis
 Miss Helen D. Harkness, St. Louis
 Leopold Hofstatter, M.D., St. Louis
 Mr. W. W. Horner, St. Louis
 Alex H. Kaplan, M.D., St. Louis
 J. Albert Key, St. Louis
 John Esben Kirk, M.D., St. Louis
 Paul E. Kubitschek, M.D., St. Louis
 K. Cramer, Lewis, St. Louis
 Grover Liese, M.D., St. Louis
 Robert G. Loeffel, St. Louis
 Sedgwick Mead, M.D., St. Louis
 Albert I. Mendeloff, M.D., St. Louis
 Ivan N. Mensh, Ph.D., St. Louis
 William H. Olmsted, M.D., St. Louis

Ernest H. Parsons, M.D., St. Louis
Joseph C. Peden, Sr., M.D., St. Louis
Lawrence T. Post, M.D., St. Louis
M. Hayward Post, M.D., St. Louis
Herman J. Rosenfeld, M.D., St. Louis
Theodore B. Rosenthal, Ph.D., St. Louis
Harold Scheff, M.D., St. Louis

Arthur E. Strauss, M.D., St. Louis
A. C. Stutsman, M.D., St. Louis
Robert Votaw, M.D., St. Louis
Theodore Walsh, M.D., St. Louis
Carl R. Wegner, M.D., St. Louis
Park J. White, M.D., St. Louis
Ralph B. Wolf, M.D., St. Louis

DEPARTMENTAL NEWS

Anatomy

Dr. Edward W. Dempsey, professor of anatomy, attended a meeting sponsored by the Ciba Foundation in London, England, April 9-12. He presented a paper on "The Experimental Induction of Sexual Behavior by Steroid Hormones," during this conference on the influence of steroid hormones on psychological and behavioural reactions.

The keynote address of the Conference on Aging sponsored by Smith, Kline and French Laboratories in Philadelphia on Feb. 15 was given by Dr. Edmund V. Cowdry, research professor of anatomy. He spoke on "The Importance of Research on Aging in the National Emergency."

An exhibit entitled "The Separate Neural Arch—A Study of the Incidence from the Fetus to Maturity," was awarded the silver medal for second place and a certificate of merit at the American Academy of Orthopedic Surgeons meeting in Chicago, Jan. 27 to Feb. 1. Dr. Maurice B. Roche, instructor in clinical orthopedic surgery, presented the exhibit, which was prepared by him and Dr. George G. Rowe, former instructor in anatomy. They presented a selected series of some 36 lumbosacral columns from the Terry Anatomical Collection.

First prize in the exhibits at the meeting went to Dr. T. J. Stewart, curator of physical anthropology at the Smithsonian Institute in Washington, and former staff member of the Medical School. Dr. Stewart was visiting professor of anatomy during 1943.

Internal Medicine

Dr. Harry A. Schroeder, associate professor of medicine, delivered the annual Alpha Omega Alpha lecture at McGill University, Montreal, Canada, on March 1, speaking on "Congestive Failure." He spoke at the initiation dinner. While in Montreal, he also addressed the Montreal Medico-Chirurgical Society, March 2, on "The Pathogenesis of Hypertension."

On Feb. 1-3, Dr. Schroeder addressed the Recess Commission on Hypertension of the Commonwealth of Massachusetts in Boston on "The Evidence That Essential Hypertension Is Not a Single Disease Entity," and led the discussion which followed.

The United States Public Health Service has renewed a grant to Dr. Harry L. Alexander, professor of clinical medicine, for continuation of research on the metabolism of lipid antigens by Dr. Samuel Bukantz on a joint project with Drs. Gustave Dammin and Frank J. Dixon.

Dr. Alexander is chairman of a committee appointed by the American Academy of Allergy, at the requests of the surgeon general of the army, navy, air force and Public Health Service, to review standards for the induction of men suffering from allergic disorders into the service. Dr. Stanley Hampton is a member of the committee.

Dr. Samuel C. Bukantz, assistant professor of medicine, has been appointed chairman of the committee on clinical investigation on food allergy of the Research Council, American Academy

of Allergy. The committee is in organization and drawing up plans for investigative work.

A research grant of \$7350 has been awarded to the School of Medicine for work in heart disease by the Life Insurance Medical Research Fund.

The grant is for research by Dr. Robert J. Glaser, assistant professor of medicine, for work on the pathogenesis of experimental streptococcal infections and their relation to rheumatic fever. Other fellowships have been awarded to Dr. Joseph Larner, fellow in biological chemistry, and Dr. H. Mitchell Perry, research fellow in medicine.

Neuropsychiatry

Dr. Edwin F. Gildea, professor of psychiatry, will address the third annual neuropsychiatric meeting held at North Little Rock Veterans Administration Hospital, March 1 and 2. His topic is "Research in Psychiatry, Particularly as Exemplified by the Milbank Foundation Symposium on Biological Aspects of Mental Health and Disease."

Otolaryngology

Dr. Theodore E. Walsh was guest speaker at several sessions of the postgraduate course sponsored by the Oregon Academy of Ophthalmology and Otolaryngology. He presented six papers for the course. On Feb. 27, Dr. Walsh was guest speaker for the teaching day session of the Otolaryngology Department at Syracuse University Medical College in New York.

Dr. Hallowell Davis, director of research at Central Institute for the Deaf and research professor of otolaryngol-

ogy, left Feb. 5 for an extensive lecture and inspection tour through Europe under auspices of the Office of Naval Research.

Officially classified as a naval technician on the trip, Dr. Davis visited laboratories and gave lectures in France, Switzerland, Sweden, Denmark, Holland, Belgium and England. Purpose of this tour was to exchange information with scientists in the democratic countries of Europe on research problems about neurophysiology of the ear.

In Sweden, Dr. Davis delivered a series of three lectures describing research work at Central Institute. He spoke before the Karolinska Institutet of Stockholm and the medical faculties of the Universities of Upsala and Lund, and gave informal lectures in Switzerland, England and Holland.

Dr. Davis is in charge of special naval research projects being conducted at C.I.D., and is chairman of the Committee on Hearing of the National Research Council. He is also part-time professor of physiology on the Medical School staff.

Pathology

During the week of April 8, Dr. Robert A. Moore, Dean and professor of pathology, was at the University of Pennsylvania in Philadelphia to take part in meetings of the committee on the survey of medical education, a group formed jointly by the American Medical Association and the Association of American Medical Colleges, which recently completed an extensive survey of medical schools in this country.

Dr. Frank J. Dixon, Jr., assistant pro-

fessor of pathology, has resigned to accept the position of professor of pathology at the University of Pittsburgh, Pa., on May 1. A graduate of the University of Minnesota in 1943, he has been on the Washington University staff since the summer of 1948, when he came here as an instructor in pathology. Dr. Dixon served with the Navy during World War II and attained the rank of lieutenant.

Dr. David W. Talmage of the Department of Medicine, also will leave the staff to accept a position as assistant research professor in the department of pathology at the University of Pittsburgh. His appointment is also effective on May 1.

Preventive Medicine

Dr. Robert E. Shank, '39, professor of preventive medicine and public health, spoke at the meeting of the Food Industries Advisory Council of the Nutrition Foundation at Skytop Lodge, Pa., on April 25.

Radiology

Dr. Hugh M. Wilson, '27, professor of radiology, was elected president of the St. Louis Society of Radiologists at a recent meeting.

Dr. Wendell G. Scott, '32, associate professor of clinical radiology, gave two papers before the Post-Graduate Medical Study Course in Radiology at the University of Kansas Medical Center, Kansas City, Kansas, on January 9. He spoke on "Developments in Cerebral Angiography" and "Technical and Clin-

ical Use of Cardiovascular Angiography."

Surgery

The Henry Jacob Bigelow Medal of the Boston Surgical Society was awarded to Dr. Evarts A. Graham, Bixby professor of surgery, during a meeting of the Society in Boston on April 20. On March 15, Dr. Graham addressed the fifth annual Michigan Postgraduate Clinical Institute on "Common Errors in the Diagnosis of Bronchiogenic Carcinoma."

At the annual meeting of the Society of University Surgeons, held this year at Durham, N. C., from Feb. 8 to 10, Dr. Eugene M. Bricker, '34, associate professor of clinical surgery, was chosen president-elect of the Society for the year 1952. He presented a paper on "The Role of Pelvic Evisceration in Surgery," during the meeting.

Drs. Henry G. Schwartz, George E. Roulhac, and Leonard T. Furlow attended the meeting of the Southern Neurosurgical Society in New Orleans on Feb. 9 and 10. Dr. Schwartz is secretary of the Society.

Gerontology

Participating in a panel discussion on "Better Health for Older People" on Feb. 27, were Dr. William B. Kontz, Dr. John Esben Kirk, Dr. Margaret Chieffi of the Division of Gerontology, and Dr. Sedgwick Mead, assistant professor of physical medicine. The topic of forced retirement of employees at an arbitrary age was discussed before a meeting of the St. Louis Academy of General Practice.

ALUMNI NEWS

1883

William A. Fries, one of the oldest practicing physicians in St. Louis, celebrated his 90th birthday on January 12 by making his regular rounds of patients. His office now is at his home, 3209 Shenandoah Avenue, but for 66 years, until a year ago, he had his office at 1544 S. Broadway. The only reason he moved then was that the roof was blown off in a storm. Dr. Fries lives a quiet life following regular habits and getting exercise by ignoring elevators in hospitals and using the stairs.

1893

Arthur R. Stover has changed his address from Kingman, Ariz., to Box 96, Holbrook, Ariz. He writes that he views with pleasure the progress being made by the School of Medicine.

1895

Forty "old timers" of the School of Medicine and the University gave a party in honor of **Robert J. Terry's** 80th birthday on January 25. The group included maintenance men and secretaries from the School of Medicine, as well as professional staff members and friends. A birthday cake with 80 candles and a special copy of the Medical Alumni Quarterly for January, which was autographed by all those present, were given to Dr. Terry. Among those attending the party were: **Dr. Robert Schlueter '95**, Dr. Borden S. Veeder, Dr. Philip Shaffer, Dr. Joseph Erlanger, **Dr. Sherwood Moore, '05**, Dr. E. V. Cowdry, Dr. Robert A. Moore, Dr. Mildred Trotter, Miss Agnes O'Gorman, Mr. Erik Carlson, Mr. Paul Bauer, Mr. Albert Gigi, and many associates from the Department of Anatomy.

1905

Robert A. (Dr. Bob) Schlernitzauer has been retired from practice for several years and is now in the private order fruit business with his son at Cocoa, Fla., in the Indian River fruit country.

1905

R. Manton Wilson sends word that he is now health officer for Henrico County, Virginia, and celebrated his 71st birthday in January. From 1908 until 1947, Dr. Wilson was a medical missionary in Korea, where he worked with lepers and established a large colony near Soonchun which was named after him. Returning to this country when the second World War began in 1941, he was health officer for the city of Richmond, Va., from then until 1946, when he went back to Korea. He was advisor on leprosy to the U. S. Army in Korea and directed a program of gathering lepers and establishing a colony in an old Japanese fort near Fusan. This latter colony now has 1200 cases of Hansen's disease and is being supplied with food by the U. S. Army. He has had word that the R. M. Wilson colony recently fell into the hands of the Communists and the patients there have been mistreated and scattered. Dr. Wilson came back to this country and since December, 1948, has been in Henrico County. He has five sons, four of whom are M.D.'s, and two daughters.

1911

J. C. Drake, who practiced medicine at Kerman, Calif., for 30 years before retiring in August, 1948, has accepted a position as assistant county health officer of Fresno County "for the duration." He conducts 15 child health clinics each month, three in the city of Fresno and 12 in the county. He now lives at 134 W. McKinley Ave., Fresno.

1917

Robert Mueller has been named chairman of the Missouri Advisory Committee on the Selection of Doctors, Dentists and Allied Specialists under the Selective Service Act. Dr. Mueller served as head of the Physicians' Procurement and Assignment Service in Missouri during World War II. His committee duties are

to apportion Missouri physicians, dentists and allied specialists properly between the civilian population and the armed forces.

1923

R. W. Steubner recently moved his office to 35 N. Central Ave., in Clayton, Mo.

Elmer O. Breckenridge can be reached in care of general delivery at Mason, Texas.

1928

Col. Earl Maxwell recently was named Acting Director of Professional Services, Office of the Surgeon General, U. S. Air Force, in Washington, D. C. Col. Maxwell was Theater Surgeon in the South Pacific from July 1942 to 1944, and for the following nine months was Task Force Surgeon for the Okinawa campaign in World War II. After a period of occupation duty in Japan, he was staff member at Letterman Army Hospital from June, 1946, until he took over his present assignment. He was chief of ENT service, has been certified by the American Board of Ophthalmology, and accepted by the American Academy of Ophthalmology and Otolaryngology.

Wilford F. Hall has been promoted to to the rank of brigadier general, and now is air surgeon for the Military Air Transport Service. His specialty is E.N.T., and he has studied extensively on aerotitis. Dr. and Mrs. Hall have two children, Ronald Dexter, five, and Carol Lynne, one year old. They live at 1213 N. Evergreen St., Arlington, Va.

Paul I. Robinson has been promoted to the rank of brigadier general, and his new title is Chief of Army Medical and Civilian Personnel. His duties include procurement and placement of medical personnel; doctors, nurses, dentists, and medical specialists. The largest division in the Medical Corps also is under Gen. Robinson. In addition to his work at the Surgeon General's office in Washington, Gen. Robinson is on the Medical School staff and teaches eight hours of hospital administration each year.

1929

Craig B. Johnson has moved from the U. S. Naval Hospital in Philadelphia to the Naval Hospital at Bainbridge, Maryland, effective March 10.

1931

Ben Friedman is at the Veterans Hospital in McKinney, Tex.

1932

Paul Lefkowitz lives in Spring Valley, N. Y., and his address is 25 S. Main St.

1934

Jane E. Frisch now lives at 5736 McPherson Ave., in St. Louis.

Charles E. Stindel has moved recently to 341 Violet Ave., in Webster Groves, Mo.

1935

Walter R. Langston has offices in the Professional Bldg., Springfield, Mo.

Arthur P. Echternacht has an address at 728 Crest Ave., Fort Dodge, Iowa.

John W. Williams is living and practicing in Oak Grove, Mo.

1937

The address of **Lester E. Haentzschel** is 228 W. College Ave., Appleton, Wisconsin.

1938

Kenneth L. Carter is in Beloit, Wisconsin, where he is associated with the Beloit Clinic as surgeon.

Joe Parker is now located at 2516 N. Hudson, Oklahoma City, Okla.

Robert R. Robinson, Jr., is engaged in the private practice of maxillo-facial and plastic surgery in the Brockbank Professional Bldg., in Salt Lake City at 141 E. 2nd South St., and reports that he likes Salt Lake City very much. He and Mrs. Robinson have four sons.

Winfield S. Wilder is director of Montana's Mental Hygiene Clinics, with offices at Great Falls and at Butte. His address is 1401 Second Avenue, North, in Great Falls. He writes that he frequently saw **Cornelius Meeker**, '38, who was practicing pediatrics in Butte, before Dr. Meeker left for navy duty in July, 1950.

1939

Raymond F. Kuhlmann is living at 21 Elson Parkway, South Burlington, Vermont. He is a member of the Crippled Children's Division of the Vermont Department of Health.

1940

Mary E. Bowen has a new address at 7449 Cottage Grove Ave., in Chicago, Illinois. Her practice is limited to obstetrics-gynecology.

James H. Robertson recently announced the opening of his new offices at 1405 San Marino Ave., in San Marino, California. He is a diplomate of the American Board of Otolaryngology, and limits his practice to ear, nose and throat.

1941

The office of **D. Cramer Reed** is located in the First National Bank Building in Wichita, Kansas.

Cecil H. Blackburn's office is in the Swift Building, Selma, Alabama.

Henry Schwarz is on the staff of the Veterans Administration Hospital in Aspinwall, Pa.

Mitchell Yanow recently moved his office to 35 N. Central Ave., in Clayton, Mo.

1942

Hiraku Ishida is practicing in Los Angeles, with his office at 2630 W. Jefferson Blvd.

James R. Herz has moved from Kansas City to 508 Humboldt, Reno, Nev.

Sven L. Melgaard now lives at 6831 Cherry St., in Kansas City, Mo.

Glenn O. Turner is now located at 920 E. Elm St., in Springfield, Mo.

Walter P. Graul has moved from Philadelphia to St. Louis, where his office is in the Beaumont Medical Building, 3720 Washington.

Bill Reese writes the following: "Dear Alumni (particularly of '42): I recently assumed the duties of professor and head of the department of neuropsychiatry at the School of Medicine of the University of Arkansas, Little Rock, Ark. The clinical departments are now all on a full-

time basis. As you know, Jim Growden is professor of oncology here. Last fall Dr. Hayden C. Nicholson, formerly secretary of the National Research Council, came here as dean. In general the future of the school looks bright, particularly since the legislature finally provided funds to begin construction of a model 400-bed Medical Center, as the core clinical facility. I believe that Dr. E. F. Gildea has given much consultative help to the establishment of our department.

"At the moment we are looking particularly for a full-time neurologist and would welcome applications.

"Betty, Billy, Bob and I are already comfortably settled into this congenial city, and would welcome any of you who wish to see us at 5501 Grandview Road, Little Rock. Drop us a line, Sincerely yours, Bill Reese."

1943

Edward H. Dunn has been transferred to A.N.S. Hospital in Tanana, Alaska.

Hans-Karl Stauss can be reached at 1200 N. State St., Jackson, Miss.

Glenn L. McElroy is now at Shriner's Hospital for Crippled Children in St. Louis, where he will be until he enters private practice this coming December.

1944

Marvin T. Pursell was a visitor to St. Louis early in April and stopped by the Alumni Office. He is doing general practice in Dinuba, California.

1945

Samuel B. Guze is a fellow in psychiatry in the Division of Psychosomatic Medicine at W. U. School of Medicine.

Edmund V. Cowdry, Jr., is a fellow in psychiatry on the Medical School staff and lives at 14 N. Kingshighway Blvd.

William F. Andrew recently moved to 3410 Tulane Dr., University Hills, West Hyattsville, Md., from Richmond, Mo.

Marshall B. Conrad has moved to 7018 Southland Ave., St. Louis.

The address of **Betty Ben Geren** is 372 Longwood Avenue, Boston, Mass.

1946

Theodore J. Smith is now a captain in the U. S. Air Force and is stationed at Station Hospital, Randolph Field, Texas, where he is chief of medical service. Before entering service in January, he was on the staff of Scott and White Clinic in Temple, Texas, in the department of internal medicine.

Garrett Deane is resident in pediatrics at University Hospital, Baltimore, Md. He stopped in the alumni office recently during a visit to St. Louis.

1947

Paul F. Brown is at Pfeiffer Memorial Hospital, Clinica Americana, Cajon 9, La Paz, Bolivia. Before moving to La Paz, he was in training at Fresno County (Calif.) General Hospital.

Jack A. Gregory is at Huntington Memorial Hospital in Pasadena, Calif.

H. Glenn Kellogg is stationed at U.S. Naval Hospital, San Diego, Calif. On January 13, he was married to Ensign Dorothy Zulick of Philadelphia, who is a navy nurse and also is at the Naval Hospital.

1948

Robert Friedman now lives at 4616 Lindell Blvd., in St. Louis.

Robert W. Petty is on active duty as senior medical officer on a naval transport ship plying the Pacific. His home address is 1305-27th St., Ogden, Utah.

Duane R. Taylor is in his second year of residency at Jefferson Barracks Veterans Hospital. His home address is 815 Dugan, Jefferson Barracks 23, Mo.

In Memoriam

1883

Brice Edwards of Richmond Heights, Mo., passed away recently.

1889

John D. Kessenger of Salt Lake City, Utah, passed away last fall at the age of 85.

1891

T. C. Richards of Fayette, Mo., passed away recently.

1892

Harry Sturgeon Crossen, widely-known St. Louis gynecologist, died March 10 at the home of his son, Dr. Robert J. Crossen, at the age of 82 years. Dr. Crossen, who was professor emeritus of obstetrics-gynecology on the Medical School staff, had been ill for a long while. He joined the Washington U. medical staff in 1901 and was chief of the gynecological dispensary at the old Washington University Hospital from 1901 to 1911. He was

associate on the medical school staff until 1934, when he became emeritus professor. Dr. Crossen was author of several textbooks which are still widely used in medical schools. In 1940, he was honored at a testimonial dinner for his 40 years of service with Washington University, and the oil painting of him which now hangs in the Medical School Library was presented to the University at that time.

1893

Cornelius A. Mann of Glendale, Calif., passed away recently at the age of 79.

1895

Albert H. Thornburgh died August 15, 1950, at the age of 80, in West Plains, Mo.

1897

William D. Francis of Lampasas, Texas, passed away recently at the age of 97 in Austin, Tex. He was 92 years old and

had served as city and county health officer of Lampasas.

1898

William H. Hays, of Hannibal, Mo., Mo., passed away recently.

1903

Carl Althans, who had practiced in St. Louis for 46 years, passed away April 1 of a heart ailment at his home, 3248 Lafayette Ave. He was 69 years old and had maintained offices in his home since entering private practice 46 years ago.

1904

Harry L. Jones, who was associate professor of medicine at the University of Kansas, died in Kansas City December 13, 1950, at the age of 73.

1905

Arthur M. Gregg of Joplin, Mo., passed away December 14, 1950, at the age of 66.

1910

T. P. Gronoway of Macon, Mo., died March 4, 1951.

1911

John F. Beatty of Everett, Wash., passed away December 15, 1950, at the age of 61.

1920

W. Roger Moore, a pediatrician practicing in St. Joseph, Mo., died August 16, 1950, at the age of 54. He was past president of the Buchanan County (Mo.) Medical Society.

1935

Robert H. Swinney of Portland, Oregon, was drowned in a fishing accident on the Lewis River, February 8, 1951. Dr. Swinney had practiced surgery in Portland since 1941, and is survived by his widow, Mrs. Ruth Erlanger Swinney, and two daughters, Peggy, 7, and Patsy, 5.

WASHINGTON UNIVERSITY

Arthur H. Compton, Ph.D., Sc.D., LL.D., *Bridge Chancellor*
Charles Belknap, B.S., *Vice-Chancellor*
Leslie J. Buchan, Ph.D., Acting Dean of Faculties
Thomas Edward Blackwell, Ph.B., M.S., J.D.,
Director of Business Administration

- The College of Liberal Arts
Thomas S. Hall, Ph.D., Dean
- The School of Engineering
Lawrence E. Stout, Ph.D., Ch.E., Dean
- The School of Architecture
Joseph D. Murphy, Dean
- The School of Business and Public Administration
Leslie J. Buchan, Ph.D., Dean
- The George Warren Brown School of Social Work
Benjamin E. Youngdahl, A.M., Dean
- The Henry Shaw School of Botany
Henry N. Andrews, Jr., Ph.D., Dean
- The Graduate School of Arts and Sciences
Carl Tolman, Ph.D., Dean
- The School of Law
Wayne L. Townsend, A.B., LL.B., J.S.D., Dean
- The School of Medicine
Robert A. Moore, M.D., Ph.D., Dean
- The School of Dentistry
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Louise Knapp, R.N., B.S., A.M., Director
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- University College
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- The Summer School
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