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# MEDICAL BULLETIN

UNIVERSITY OF *Minnesota*

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*in this issue*

- THE WILD BLUE YONDER
- GLUCOSE TOLERANCE TEST
- CARCINOMA OF THE CERVIX
- THE CLASS OF 1962

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VOLUME XXXV

October 1963

NUMBER 2

**C O N T E N T S**

**SPECIAL ADDRESS**

*The Wild Blue Yonder*

WILLIAM F. MALONEY, M.D. . . . . 58

**STAFF MEETING REPORTS**

*The Cutaneous Glucose Tolerance Test*  
(A New Technique for Clinical and Basic Research)

RAMON M. FUSARO, M.D., M.S., JOHN A. JOHNSON, B.S.,  
and JOHN F. VAN PILSUM, Ph.D. . . . . 72

*Carcinoma of the Cervix: The Relation of Irradiation*  
*Treatment Leukopenia on Survival and on*  
*Tumor Recurrence*

EDGAR L. MAKOWSKI, M.D., FRED A. LYON, M.D., . . . . .  
GEORGE W. FLIGHT, M.D., and JOHN L. MCKELVEY, M.D. 75

*The Structure and Function of Renal Glomerular*  
*Capillaries in Health and Disease*

ROBERT L. VERNIER, M.D. . . . . 78

*Human Endotoxin Shock with Renal Insufficiency*

JACK L. REDDIN, M.D., and WESLEY W. SPINK, M.D. . . . 82

**CLASS SURVEY**

The Class of 1962 . . . . . 84

**MEDICAL SCHOOL NEWS**

91

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## Special Article

### The Wild Blue Yonder\*

WILLIAM F. MALONEY, M.D.†

Statistics first stimulated the title, "The Wild Blue Yonder." For me, statistics have always been something akin to the vast unknown, quite "wild" and quite "yonder."

As a warm-up session, let's look at a couple of cute and commonly used tricks with statistics. The idea for these comes from an entertaining little book entitled, *How To Lie With Statistics* by Darrell Huff.<sup>1</sup> That old prognosticator, H. G. Wells, was right when he prophesied that, "Statistical thinking will one day be as necessary for efficient citizenship as the ability to read and write." In a day when too many people are trying to prove too many things, individuals, particularly those so responsible for their own continuing education, as are we, must be alert to the fallacies of figures.

The first little trick is called the "Gee Whiz" graph. It is a plot of applicants to United States medical schools 1947-48 through 1956-57 (Fig. 1). Note that there has been some fluctuation over the ten year period but nothing of much alarm. But wait, let's look again (Fig. 2)—Gee Whiz, what a serious situation! Yes, the figures are the same—nothing has been falsified except the impression given. All that has been done is to alter the scale on the ordinate which changes the proportion between the ordinate and the abscissa. It's legitimate, there's no rule against it and it does give your graph a more impressive shape. However, you can see how the scale can be manipulated to accomplish a desired impression. It is a more subtle equivalent of editing, "National income rose ten per cent" into "climbed a whopping ten per cent!"

Let's look at another (Fig. 3). This graph appeared in the September 2nd issue of the *AMA News* and was taken from a group of figures recently released by the Blue Shield Plans. Again, the subject is not germane to the subject of this discussion, but it's interesting to see the growth in Blue Shield. Now, if one takes a magnifying glass and looks at the important figures printed beneath, (and that truly was necessary in the original print-

\*Minnesota Medical Foundation Lecture, September 23, 1963.

†Associate Director, Association of American Medical Colleges, Evanston, Ill.

ing), your suspicion is aroused. Sixteen million here and 50 million here—that's approximately three times as many, but that last figure looks many more times the size of the first. Indeed, by measurement the last figure is at least five times as high as the first. But aside from that unexplained discrepancy, this graph points up a more obvious device called "the one-dimensional picture." To explain, let's consider that the picture is only three times as high, but it is also three times as wide; therefore, it occupies not three times but nine times the area on the page. In addition, pictures of objects having, in reality, three-dimensions are thought of as also three times as thick. Thus by increasing the width as well as the height and using a normally three-dimensional figure, this ingenious chart gives the visual effect of a 27-fold increase.

This is a cleverly manipulated version of the simple bar graph. The true bar graph of this increase gives a somewhat different impression. (Fig. 4)

The first example I rigged, but it's done in actual practice every day. This second one is real as is the third. As Disraeli once said, "There are three kinds of lies: lies, damn lies and statistics."

The third example involves tonight's subject. The generic name given this one is "*the semi-attached figure*," in which the implication is permitted to exist that the derivation of the figure is identical with that of the previous figures with which it is compared.

The number of physicians per 100,000 people in the United States has commonly been used to indicate the size of our medical manpower pool. This ratio has been calculated generally as 132 per 100,000 for the past twenty years. The number of physicians has increased over this period but so has the total population. In 1963 the ratio remains about the same if one bases the calculation on the same group composition used in past years.

However, both the composition of the total population and the composition of the group identified as "physicians" in a national medical manpower pool are open to interpretation. The nation's total population figure may variously be considered to include the fifty states, Puerto Rico and the outlying areas, and the Armed Forces in this country and abroad. The national medical manpower pool may or may not be considered to include among others: physicians in military service; retired physicians; interns and residents who are graduates of United States medical schools; foreign doctors in this country for training but who intend to return home; immigrant physicians who

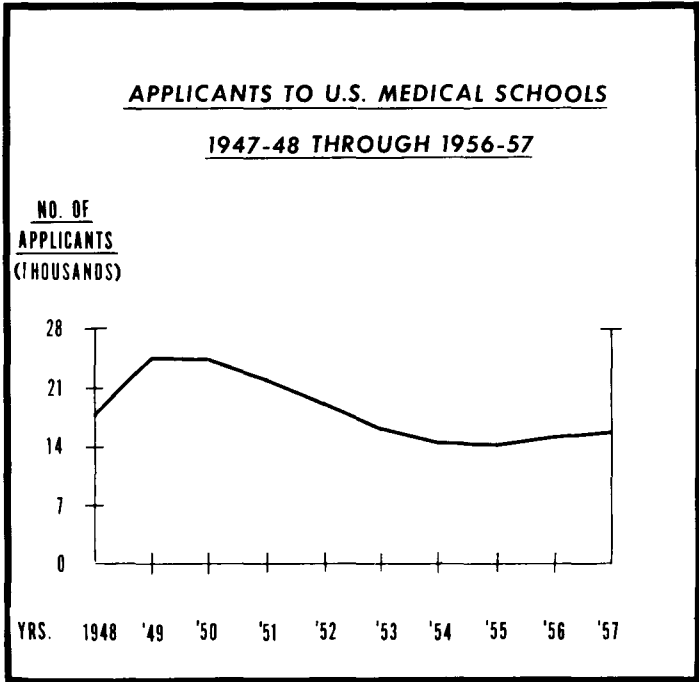


Fig. 1

are awaiting citizenship and consequent licensure; medical students who have just graduated or are about to graduate; and, practitioners and new graduates in osteopathy.

As can be surmised, therefore, the ratio is amenable to considerable manipulation. For example, one recent calculation purports a ratio as high as 147 physicians per 100,000 people and here, then, again is our third example in the numbers game—the *semi-attached figure*.

The agency reporting this markedly increased ratio did not explain that included in the total count of physicians, in addition to what had been counted traditionally, were the current year's medical school graduates (over 7,000) plus Canadian and foreign physicians in this country temporarily for internship and residency training (about 7,000 more). Also, although the total physician figure included all physicians in the 50 states, Puerto Rico and outlying areas and federal physicians here and abroad, this number was related to a total resident population

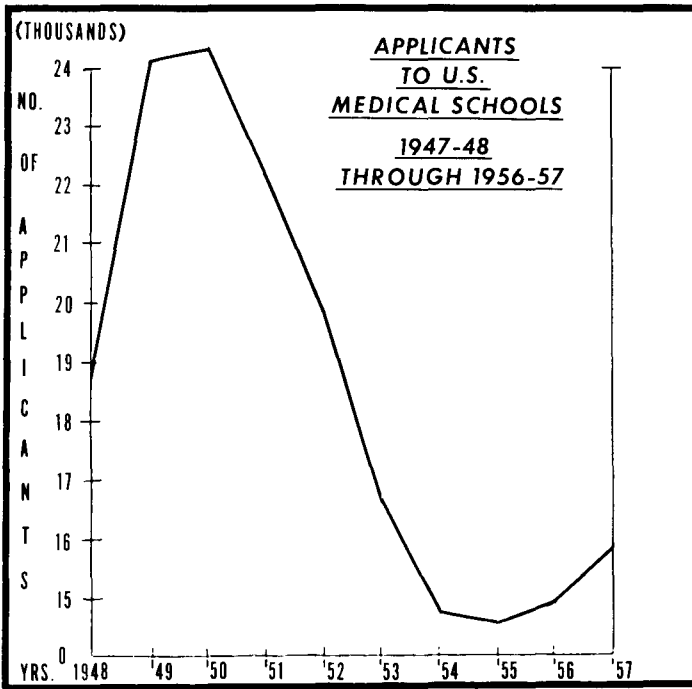


Fig. 2

base of the 50 states only.<sup>2</sup> These alterations were sufficient to produce what appeared to be a really remarkable increase in our physician-population ratio. As you see, this venture into physician-population ratios can indeed be into the Wild Blue Yonder.

A more fundamental shortcoming of the physician-population ratio, other than the fact that it is open to significant manipulation, is the invalidity of any head count as an indication of the adequacy of medical manpower.

Many factors in addition to numbers of physicians are important. Those that would seem to call for an increased number of physicians include: the increasing size of our population; the increasing numbers of older people and children; the increasing prevalence of public health services of government, industry, public schools and colleges; the development of new specialties; the better distribution of physicians into areas now not supplied adequately; the expanding horizons of health and medical serv-

## Growth of Blue Shield Membership— 1950-1962

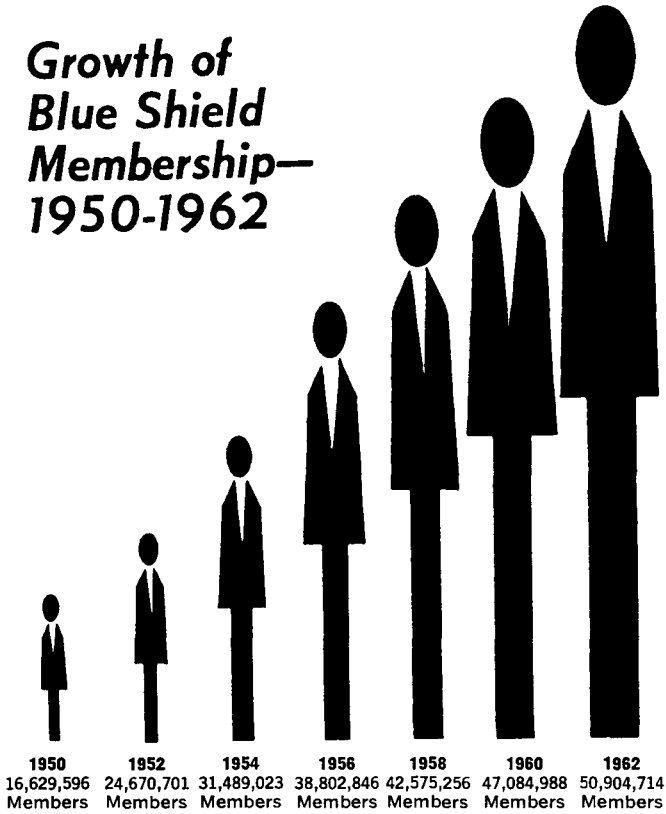


Fig. 3

*Courtesy of AMA News*

ice into the areas of health management and disease prevention and with this the discovery of more but earlier illness; and the growing awareness on the part of our people of the increasing effectiveness of medical care and along with this their increasing ability to purchase this care.

Those factors that would seem to point to the need for fewer physicians, would be improved transportation and communication, the concentration of population, the development of group practice, the visiting of patients in hospitals instead of in their homes and the increasing use of technicians, assistants and instruments. Other factors might be: the further development of drugs and surgery, the increasing effectiveness of preventive



## Growth of Blue Shield Membership— 1950-1962



Fig. 4

medicine which may mean less illness, particularly serious illness; and the increasing amount of medical care being rendered by residents, interns and even medical students.

Thus a multitude of variables influence the adequacy of the manpower pool. Yet a physician-population ratio that is reasonably accurate is important because it provides a method of measurement which can reveal changes in the numbers of physician personnel as they are related to definite units of population. Such a measurement is essential if national planning is to have comparable points of reference.

Just how the previously discussed factors will ultimately balance out, no one can tell. Evidence continues to accumulate that the first set calling for increased numbers of physicians will outweigh those that point to a need for fewer. If this is so, we will need many more physicians than we can graduate with the increase in facilities currently in prospect.

Most important is the fact that, even with the present ratio of physicians to population, however calculated, the need for the personnel who render medical services, as defined by the public itself or by experts in the health field, is not being met. This matter has obvious implications for all of us but the greatest for the student of medicine who will be most active in dealing with the many resulting problems in the future.

THE MEDICAL BULLETIN

Only two sources of new medical manpower are available to this country: graduates of our own medical schools and graduates of foreign medical schools who immigrate to this country. To depend upon importation of physicians to enrich ourselves medically, at the expense of countries which have much greater medical need than ours, cannot be justified.

Consequently, the one source of physician manpower to which this nation should or can look with confidence is the graduates of its own schools of medicine. A study of this source reveals a downward trend. The United States medical graduate-population ratios show that, since 1955, the increase in output of this nation's medical schools has not kept pace with the increase in population. This figure has fallen from 4.2 graduates per 100,000 people in 1955 to 3.8 in 1963. (Table 1) This table is a tabulation of actual numbers of graduates and of population. It serves to further emphasize the failure of the medical education plant in spite of increases to keep up with population increase.

| Year | Total Population in Thousands | Number of M. D. Graduates | M. D. Graduates per 100,000 Population |
|------|-------------------------------|---------------------------|--|
| 1955 | 165,270                       | 6977                      | 4.2                                    |
| 1957 | 171,198                       | 6796                      | 4.0                                    |
| 1959 | 176,912                       | 6860                      | 3.9                                    |
| 1960 | 183,239                       | 7081                      | 3.9                                    |
| 1962 | 189,209                       | 7168                      | 3.8                                    |
| 1963 | 191,700                       | 7257                      | 3.8                                    |

In 1962, 1,357 foreign trained physicians were licensed to practice in the United States. That is 17 per cent of the total number of licentiates last year. The maintenance of the physician-population ratio in recent years is entirely due to the influx of graduates of foreign medical schools. Therefore, the decreasing ratio of United States medical graduates to population should be a matter of serious national concern.

There seems to be general agreement that, with the anticipated rate of population growth, the most that we can hope to accomplish is to maintain the present ratio of physicians to population. If we project ahead to 1975 it means that by 1971, just eight years from now, there must be an addition of more than 4,000 new places for first-year students.

The expansion of existing medical schools can provide for half of the required 4,000. The other 2,000 additional first-year places will have to be provided by the creation of new schools. If each of these new schools admits a class of 100 students, more than 20 institutions will be needed. At this time, ten universities have committed themselves to starting new programs in medicine.

With the present ever-broadening opportunity for career choice, the number of qualified applicants to medical schools has been progressively declining. Last year, for the first time in several years, the number of applicants totaled significantly more than the previous year.

If well qualified applicants are to be available to fill expanding accommodations for medical study, it is essential that this upward trend be sustained.

Now let's take another flight into the Wild Blue Yonder. This time into areas as blue as the sun-filled sky but really not so wild and not so yonder. Let us consider only three factors among those just enumerated as essential for careful evaluation in characterizing our health manpower pool. These are new equipment and new learning techniques, our changing society and the future health team. What does the future really hold for us in these three areas? We can make some pretty good predictions.

Some of you will remember a cartoon strip and radio serial popular in the 1930's called "Buck Rogers in the Twenty-Fifth Century." It predicted a world 500 years hence equipped with rockets, space ships, disintegrator ray guns, and a new source of power. Last month, 25 years later, two men flew the length of the huge McCormick Place Exhibit Hall in Chicago with individual rockets strapped on their backs; atomic power is in use; men have successfully entered and returned from space for the past six years and the recent development of the Laser beam adds one more device to the fast completing picture thought to be five centuries. away.

This kind of acceleration in the realm of science is frightening. It poses tremendous problems of adjustment. Society still lags breathlessly far behind the scientific progress made to date. Men toil articulately but clumsily in the United Nations to make one scientific advance—atomic energy—a compatible part of our social, economic and moral life.

Another aspect of this dilemma at times, I suspect, operates subconsciously to our detriment. The curve of scientific achievement in its rise has so outstripped man's assimilation of this knowledge that the gap may be greater than today's power of

imagination can bridge. To have the inventive dream confront known facts before it can be used to stimulate man's work and thought can be devastating.

What about this brain that has been so prodigious in its production of knowledge? Loren Eiseley writes beautifully about its beginning:

*"Mammalian insects perhaps we should have been—solid-brained, our neurones wired for mechanical responses, our lives running out with the perfection of beautiful, intricate, and mindless clocks. More likely we should never have existed at all. It was the Snout and the ooze that did it. Perhaps there also, among rotting fish heads and blue, night-burning bog lights, moved the eternal mystery, the careful finger of God. The increase was not much. It was two bubbles, two thin-walled little balloons at the end of the Snout's small brain. The cerebral hemispheres had appeared."*

*"Among all the experiments in that dripping, ooze-filled world, one was vital: the brain had to be fed. . . . It could only exist as a thing of thin walls permeated with oxygen."*

*"It was not that his thinking was deep; it was only that it had to be thin. The little bubbles of the hemispheres helped to spread the area upon which higher correlation centers could be built, and yet preserve those areas from the disastrous thickening which meant oxygen death to the swamp dweller. There is a mystery about those thickenings which culminate in the so-called solid brain. It is the brain of insects, of the modern fishes, of some reptiles and all birds. Always it marks the appearance of elaborate patterns of instinct and the end of thought."*

*"Wherever, instead, the thin sheets of gray matter expand upward into the enormous hemispheres of the human brain, laughter, or it may be sorrow, enters in. Out of the choked Devonian waters emerged sight and sound and the music that rolls invisible through the composer's brain."*

But the fascinating question came from Alfred Russel Wallace, a contemporary of Charles Darwin and co-discoverer of the Principle of Natural Selection. Many years ago he propounded a simple question still unanswered: "How was this organ (the human brain) developed so far beyond the needs of its possessor?" No adequate explanation has been put forth yet to account for so large a cerebrum as that found in man.

"Wallace," as Eiseley points out, "challenged the whole Darwinian position on man by insisting that artistic, mathematical, and musical abilities could not be explained on the basis of natural selection and the struggle for existence." "Why else

would men of simple cultures possess the same basic intellectual powers which the Darwinists maintained could be elaborated only by competitive struggle?"

Might it not be possible then that we yet have no real concept of the brain's capacity and capabilities? Is it too far fetched to conceive that new methods of learning even now being developed may be the pathway to demonstrating the brain capable of performing work of a kind and degree far beyond that which we expect or require of it today? The savage possesses a brain capable, if cultivated and developed, of performing as does the brain of the most civilized man. Today we see our own children, by the use of an entirely new method of teaching, understanding concepts of mathematical reasoning far earlier and sometimes beyond what the brains of some of us are even now trained to comprehend. The average person reads 250 words per minute; the good reader 500. In an experimental educational program now going on in Pittsburgh schools, students read 10,000 words per minute and 25,000 is considered achievable. Might not this be the real significance to medicine as well as to other fields of the new media being developed from television and other audio-visual devices, from programmed learning and on out to the use of subliminal stimulation?

The accumulation of knowledge is confounding both student and teacher but the capacity of medical students and physicians alike to comprehend the new knowledge will conceivably be increased immeasurably by new methods and concepts of instruction and learning. New attitudes and total revision of the medical education program are required for this as well as other cogent reasons.

With the additional aid of storage devices such as the electronic computer, a vast storehouse of facts can be made available in time second only to the time of our own neuro-electrical impulse transmission. Next January a computer based information retrieval system will be in operation at the National Medical Library. It will be possible to search five years of literature in less than three hours.

We see modern electronics and cybernetics already at work for us. In one bakery a computer stores recipes and completely controls the baking operation from measuring ingredients to electronically testing the quality of the finished product. In medicine the administration of anesthetics is rapidly approaching the point where administration of the agent will be automatically controlled, vital signs monitored and compensations effected electronically throughout the entire procedure. With the

electronic brain acquired by the cattle industry, a three generation ancestry of any one of 3,700,000 registered Aberdeen Angus beef cattle is available in 40 seconds. Surely this is the forerunner of a national health registry in which the life health history of every individual will be available to any doctor, anywhere in the United States, at any time in a matter of moments, printed, in fact, on an electronic typewriter in the doctor's office. Immediate consultation with a specialist anywhere in the United States will be available to the local practitioner via telephone and television. Even now the electrocardiogram can be recorded directly from the patient by a computer which will analyze the tracing and offer a printed diagnosis.

Perhaps the most important application is that related by *Time Magazine*: "Georgia Tech assigns football seats for old grads strictly on a computer reading of how active they have been as alumni."<sup>4</sup>

The application of electronics, computers and other instrumentation to the problems of medical science and practice is just beginning. The point of this is that medicine already today, but certainly in the tomorrow in which most of today's students will be practicing, will be very different. It requires the development of different educational content to assure the use of other talents—some never used and some dormant through disuse.

But the computer is not a brain. It is only a creation of man's brain and its functional limits are human limits. Automation and machinery can never substitute for personal human judgment in diagnosis or treatment. Medical schools must prepare graduates for practice not as it is the day they graduate but for practice any day—20, 40 or 50 years hence. How is this possible? How can physicians graduate secure with change, facile in assimilating the amassing intelligence and sophisticated in utilizing new technology? Our trust must lie in developing with the aid of every fresh device available the understanding of principles, the ability to observe, to reason, to think and evaluate objectively and critically, and a passionate dedication to lifetime continuing self-education.

Much money is available today for research in medical science and medical care but precious little for research in how to best help coming generations learn that science. Might this not be a field worthy of support by such organizations as the Minnesota Medical Foundation? The Foundation's objectives are to aid *medical education* and research. While assisting the student in his study and the faculty member in his teaching, is it not also at the heart of the matter to attempt to assure that

the educational environment is optimal in terms of preparation for tomorrow's medicine?

Before leaving this area of technology, one more most important point must be made. A moment ago "talents dormant through disuse" were mentioned. May not this avalanche of technological aids to diagnosis and management re-direct the physician back to his most important role: namely, to the comfort he can provide as one fellow human being to another; in other words to the use of his own personality as a therapeutic force? The good practitioner of a century ago, lacking the scientific tools, provided, as his most important contribution, an understanding and supportive relationship based on his personal concern and knowledge of his patient as an individual in society. Our present early period of technological development and solid scientific advance too often is characterized by a failure to bring the magnificent products of research ultimately to the care of our fellow men in a personal manner becoming the most perceptive, understanding traditions of the healing professions. The patient too frequently is viewed as "the host of a diseased organ who lies in the sick bed handy to the test tube and microscope."<sup>5</sup> Might we not now of necessity, with the elaborate tools at hand to automate many laboratory and bedside procedures, return to a point at which the major contribution that the physician has to make as an individual is the doctor-patient relationship and the personal element of care?

Compassionate, personalized, comprehensive care has been requisitioned. People recognize their need for this kind of care and will find it—elsewhere if necessary.

Let's return for a moment to Eiseley as he continues to discuss the development and potential of man as a hollow brain rather than solid brain creature:

*"He is totally dependent, in the achievement of human status, upon the careful training he receives in human society. Unlike a solitary species of animal, he cannot develop alone. He has suffered a major loss of precise instinctive controls of behavior.*

*"We are now in a position to see the wonder and terror of the human predicament: man is totally dependent on society. Creature of dream, he has created an invisible world of ideas, beliefs, habits, and customs which buttress him about and replace for him the precise instincts of the lower creatures. In this invisible universe he takes refuge, but just as instinct may fail an animal under some shift of environmental conditions, so man's cultural beliefs may prove inadequate to meet a new situation, . . .*

*"It is not beyond the range of possibility that this strange reduction of instincts in man in some manner forced a precipitous brain growth as a compensation—something that had to be hurried for survival purposes. Man's competition, it would thus appear, may have been much less with his own kind than with the dire necessity of building about him a world of ideas to replace his lost animal environment."*

Scientific studies are forwarding the concept of evolution through social adaptation as contrasted with environmental adaptation. We cannot ignore the fact that society creates its own environment and man has prodigious ability to alter that environment. Medicine itself has brought about a major revolutionary change in society, one with which medicine is now struggling, thus far somewhat ineptly. Once prepared to endure temporary or permanent imprisonment by disease, man now expects to enjoy the freedom of health. The transition from acceptance of disease to rejection of disease has altered completely the demands of society upon the medical establishment. Its ability to enforce those demands has altered also. We must surmount the complicated problems involved in transposing the comprehensive care concept and pattern to an urban society and a highly specialized matrix of medical workers. Medical care must be personal and coherent in a manner that best combines the concentrated skill of the specialist with the broad understanding and continuing care of the generalist.

Education must reckon with these facts. Additional revisions are required in the educational environment to communicate the mature, broad view of the sick human being. This involves more than integration of specialists and sub-specialists and more than art and intuition. It requires an attitude of mind that must characterize the educational milieu. When it does, inculcation into the student is inevitable. The educational environment is an exquisitely crucial thing.

Finally, in these new demands of medical science and health care multitudes of ancillary and technical personnel and many other professional people, in addition to the physician, are essential. Even today, to accomplish adequate care of only the organic and psychic elements of human disease requires coordinated activity with many other workers long identified with the welfare of the sick human being; however, "sociologists allied with human geneticists, epidemiologists, demographers, physical anthropologists and ethnologists are creating an entirely new picture of man as a social animal."<sup>6</sup> And these professions also become an integral part of the health team.



## THE MEDICAL BULLETIN

Medical education must prepare the physician of tomorrow to lead this team. He must work and learn along with this band of co-workers if he is to be aware of the many resources at hand, to know their capabilities and limitations and how they might participate in the solution of each problem.

And so the problems are before us. We must have more physicians. Furthermore they must be educated to accept, even anticipate, change, and make as certain as possible that change is confined to the free-flowing stream of progress—not dammed back by the status quo.

To deny this role, this future, this “Wild Blue Yonder” is quite like the caterpillar which, on seeing the butterfly fluttering above him, observed, “You’ll never get me up in one of those contraptions.” *The only way he will not fly* is to die.

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# Staff Meeting Report

## The Cutaneous Glucose Tolerance Test\* (A New Technique for Clinical and Basic Research)

Ramon M. Fusaro, M.D., M.S.†

John A. Johnson, B.S.‡

John F. Van Pilsun, Ph.D.§

For many years we have known that certain dermatologic conditions in some patients were aggravated by dietary changes. That an eruptive flare in acne vulgaris may be precipitated by the ingestion of chocolate is widely known. In some disorders the ingestion of fat and/or carbohydrate has been implicated as one factor which may cause an exacerbation. It is a general impression that patients with poorly controlled diabetes mellitus have considerably more difficulty with pyoderma than do normals or well controlled diabetics. Because of these various problems numerous clinicians have restricted the dietary intake of patients with certain dermatoses. These restrictions have had varying degrees of success and in some patients the restriction had no effect on the course of the disease.

About 30 years ago Urbach and his coworkers proposed an oral cutaneous glucose tolerance test as a method of evaluating patients so that those patients could be selected who would benefit from carbohydrate dietary control. His test was an effort to evaluate the patient's ability to handle a carbohydrate load. It was hoped that the same sort of information could be obtained from an evaluation in the skin as was obtained with the blood glucose tolerance test. The oral cutaneous glucose tolerance test was used only by a few investigators in research. Besides the obvious disadvantages of needing large samples of skin (6 mm.

\*Presented at the Staff Meeting of University Hospitals on October 11, 1963 and supported by the Upjohn Company (1958-59) and N.I.H. Research Grant No. A-3964.

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‡Associate Scientist, Division of Dermatology.

§Associate Professor, Department of Biochemistry, University of Minnesota.

diameter), the test had certain problems in technique which made it difficult to interpret.

For five years we have attempted to develop a practical and reliable cutaneous glucose tolerance test for both clinical and research work and have just reported our results.<sup>1</sup> Urbach's method for the cutaneous glucose tolerance test used the oral route for the delivery of the glucose. This caused many difficulties, such as: (a) up to 70 per cent of the glucose can remain in the stomach as late as 2 hours after ingestion, and (b) only  $\frac{1}{4}$  of the portal vein glucose passed into the systemic circulation as the other  $\frac{3}{4}$  was stored in the liver partially as glycogen or was unaccounted for in that its fate was unknown. Because of such difficulties which make difficult the meaningful analysis of the data, we used the intravenous method for delivering the glucose to the body and the skin, thereby eliminating such problems.

After 30 gms. of glucose is given intravenously within four minutes, the blood sugar reaches a peak concentration within minutes, after which it decreases at a constant rate. Cutaneous sugar reaches maximum concentration about 30 to 35 minutes after the intravenous injection, after which it decreases in an orderly manner which can be expressed by the mathematical formula

$$S_t = S_0 e^{-kt}$$

where  $S_t$  is the glucose excess in mg/100 gms of whole skin at time ( $t$ ) between the time interval of 30 to 65 minutes;  $S_0$  is the glucose excess in mg/100 gms of whole skin extrapolated to time zero; and  $k$  is the rate of disappearance of glucose from the skin expressed in per cent per minute. The skin sugar is measured from 3 mm. cutaneous biopsy punch specimens of skin with a specific enzymatic method for glucose.

The test has been performed in more than 75 individuals and the mathematical expression fits the data from each of these test subjects. By this test and mathematical expression, the dynamics of glucose disappearance from the skin can be expressed and evaluated, resulting in more meaningful data than the absolute skin glucose concentrations as measured by the older technique.

With this new technique such dermatologic diseases as acne vulgaris, chronic folliculitis, dermatomycosis, and psoriasis, to name just a few, can be investigated more effectively with respect to carbohydrate metabolism. Also, a means other than clin-

<sup>1</sup>Being published in the J. Invest. Derm. (in press), Fusaro, Ramon M.; Johnson, John A.; and Van Pilsum, John F.: The Cutaneous Glucose Tolerance Test I. A Rate Constant Formula for Glucose Disappearance from the Skin.

THE MEDICAL BULLETIN

ical judgment will be available to evaluate the effectiveness of the new oral hypoglycemic agents claimed in these diseases. From such investigations it is hoped a better understanding of the role of carbohydrates in these disorders will be realized along with a practical method for the selection of patients who may benefit from new therapeutic agents having an influence on carbohydrate metabolism.



## Staff Meeting Report

### Carcinoma of the Cervix: The Relation of Irradiation Treatment Leukopenia on Survival and on Tumor Recurrence

EDGAR L. MAKOWSKI, M.D.,† FRED A. LYON, M.D.,‡  
GEORGE W. FLIGHT, M.D.,§ and JOHN L. MCKELVEY, M.D.¶

*P*atient survival and persistence or recurrence of cervical carcinoma are discussed with emphasis on those patients developing radiation leukopenia during the course of their initial therapy with external irradiation. Almost all patients with cervical carcinoma treated primarily at this institution are included in the report. Between January 1939 and January 1956, 1,175 patients were treated in this manner.

Total white blood counts and differential counts were done on admission and repeated biweekly unless leukopenia developed in which instance daily counts were performed.

Five hundred six patients developed either recurrent or persistent tumor for an incidence of 43 per cent. These 506 patients developed their recurrence or persistence of tumor over a period of one month to seventeen years following completion of primary external radiation and radium therapy. As would be expected, the incidence of recurrence increased proportional to the extent of the tumor involvement at time of diagnosis.

While undergoing irradiation therapy, 504 of the 1,175 patients treated developed a depression of their white blood count to 3,000 cu. mm. or less. The total incidence for the development of irradiation leukopenia was 42.8 per cent. A striking decrease was found in the incidence of leukopenia with increasing extent of tumor.

Comparing the five year survival rates by League of Nation Stages of tumor involvement in those patients with and without leukopenia, the five year survival was 70.6 per cent overall for

\*Presented at the Staff Meeting of University Hospitals on October 25, 1963

†Assistant Professor, Department of Obstetrics and Gynecology

‡Instructor, Department of Obstetrics and Gynecology

§Former Resident Physician, Department of Obstetrics and Gynecology

¶Professor and Head, Department of Obstetrics and Gynecology

THE MEDICAL BULLETIN

those with leukopenia and 51.4 per cent for those not developing leukopenia. The differences within each stage are significant in Stages 2 and 3, marginally so in Stage 1 and the Stage 4 group is too small to be evaluated.

The survival rate was found to be greater in the patients who responded with a depression of their peripheral white blood cells than in those who did not. The total survival for all patients with leukopenia is significantly greater than in the non-leukopenic group. The average age of patients in the two groups was not significantly different within any single stage. The average appearance of the first evidence of leukopenia occurred 16 days following daily irradiation and the average duration was seven days.

Three different treatment modalities were used to supply the long focal distance irradiation. From January 1939 to June 1942 a 220 Kv. X-ray machine was used. In 1942 a 400 Kv. machine was substituted and the Cobalt<sup>60</sup> unit was introduced in 1953. Since then alternate patients with tumors of the same stage were treated by X-ray and cobalt irradiation. Three thousand tissue roentgens were delivered to mid-pelvis in as near to 28 calendar days as possible.

OVERALL SURVIVAL

|                      | <i>Non-leukopenia<br/>Total</i> | <i>Per cent 5 Year<br/>Survival</i> | <i>Leukopenia<br/>Total</i> | <i>Per cent 5 Year<br/>Survival</i> |
|----------------------|---------------------------------|-------------------------------------|-----------------------------|-------------------------------------|
| 220 Kv.              | 192                             | 51.0                                | 51                          | 58.8                                |
| 400 Kv.              | 407                             | 50.9                                | 411                         | 71.3                                |
| Cobalt <sup>60</sup> | 72                              | 55.6                                | 42                          | 78.6                                |

The five year survival rates for the patients treated with the 220 Kv., 400 Kv. and Cobalt<sup>60</sup> units were 52.7 per cent, 61.1 per cent and 64 per cent, respectively. A striking difference was noted in the incidence of leukopenia occurring in association with the type of external irradiation source. The total incidence of leukopenia was 21 per cent for the 220 Kv. source, 50.2 per cent for the 400 Kv. machine and 36.8 per cent for the Cobalt<sup>60</sup> source. In Stages 1 and 2 the 220 Kv. machine produced much less leukopenia than the other two machines. Both of these differences are significant. If one compares the survival rates by individual stages for the three modalities there is insufficient evidence to directly relate the occurrence of leukopenia to survival. Comparing the fate of those patients who developed

THE MEDICAL BULLETIN

leukopenia with those who did not, yet were treated with the same source of irradiation, a significant difference was found in the survival rates of patients with leukopenia and those without, disregarding the stages, for the 400 Kv. and Cobalt<sup>60</sup> source but not for the 220 Kv. machine.

When considered by stage, there is a significantly increased survival in the leukopenic group treated with the 220 Kv. machine in Stage 3.

In the group treated with the 400 Kv. source there was a significantly increased survival in the leukopenic group in Stages 2 and 3 as well as marginally significant in Stage 1. The cobalt group is too small to be evaluated properly.



## Staff Meeting Report

### The Structure and Function of Renal Glomerular Capillaries in Health and Disease\*

ROBERT L. VERNIER, M.D.†

One of the more interesting and unexpected observations derived by light microscopic study of biopsy specimens of the kidney in children with the idiopathic nephrotic syndrome was that the morphology of the glomeruli was often normal. Normal glomerular capillaries were nearly always found early in the course of the disease, in spite of the obvious renal disease and the abundant evidence that the proteinuria found was the result of increased permeability of the glomeruli to protein. In 1955, we began to examine renal glomerular capillaries by electron microscopy, in the hope that the increased magnification and resolution of this technique might reveal new facts relative to the problems of capillary permeability to protein and pathogenesis of renal disease. Space will permit only brief description of some of the findings and hypotheses which have resulted from our continuing study of these challenging problems.

Electron microscopy of normal glomerular capillaries reveals the complex structure which is illustrated in figure 1. Glomerular capillaries in the nephrotic syndrome show a diffuse and characteristic abnormality which consists of fusion of the foot processes of the epithelial cells around the circumference of the capillary wall (figure 2). Studies of more than 50 renal biopsy specimens from nephrotic children have demonstrated the uniform association of this lesion with massive proteinuria and numerous studies of a variety of experimental forms of the nephrotic syndrome in laboratory animals have confirmed this association.

Early in our investigation the significance of this abnormality to the observed proteinuria became a prime interest and several experiments were designed to answer the questions: Were these

\*Presented at the Staff Meeting of the University Hospitals on September 27, 1963.

†Assistant Professor, Department of Pediatrics, Established Investigator, American Heart Association.

This study was aided by grants from the Minnesota Heart Association, Graduate School of University of Minnesota, and the United States Public Health Service.



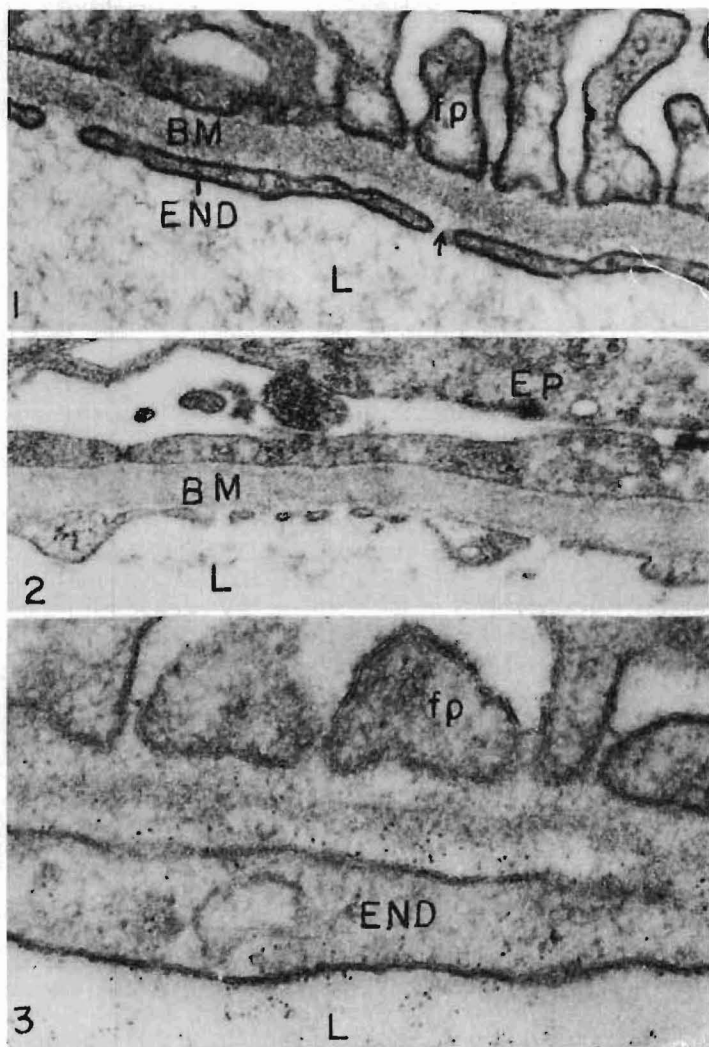


Fig. 1. Normal glomerular capillary wall. Epithelial cell foot processes (fp), basement membrane (BM), endothelium (END) with pores (arrow) and lumen (L).  $\times 30,000$ .

Fig. 2. Capillary wall from a 6-year-old child with nephrotic syndrome. No absence of epithelial cell foot processes, normal basement membrane and endothelium.  $\times 30,000$ .

Fig. 3. Portion of a capillary wall from a human fetus injected with ferritin 3 minutes before biopsy. Note that the ferritin (small dots) accumulate within the basement membrane.  $\times 90,000$ .

abnormalities of the epithelial cells the cause or the result of proteinuria? One of these experiments will be cited since it appeared to give a fairly clear answer to the question posed.

When dogs were given continuous or prolonged daily infusions of canine albumin, they developed what had been termed "threshold" proteinuria, but they were otherwise well. We showed that kidney biopsy specimens from these dogs during proteinuria demonstrated fusion of the foot processes of the epithelial cells and concluded that this morphologic abnormality was probably the result, rather than the cause, of proteinuria. The basic defect was thus thought to reside in the basement membrane, even though we and others had not been able to demonstrate "holes" or pores or other changes in the membrane which would give morphologic support to this concept.

It became clear that additional information was needed regarding the function of the various components of the capillary wall. Since large electron dense protein molecules, such as ferritin, may be visualized by electron microscopy, the transport of these and other molecules across normal and diseased capillaries was investigated. Some of these studies were performed by injection of electron dense particles into the circulation of living human fetuses of various ages in order to correlate the function of the capillary wall as a filter with its state of maturation. Figure 3 illustrates a typical example of these studies. It was shown that the central dense zone of the basement membrane was the principal filter of the capillary wall. The majority of particles were trapped within this filter (the *lamina densa*) and the number of particles in the basement membrane lamina densa increased with time after the injection. Some particles are found within vacuoles in the cytoplasm of the endothelium, indicating the phagocytic role of that cell system. A few particles passed through the filter in normal rats given large amounts of ferritin and appeared within vacuoles within the epithelial cells. In nephrotic animals large amounts of ferritin entered the epithelial cell and appeared as dense granules in the cytoplasm, thus demonstrating the increased permeability of the nephrotic basement membrane and the capacity of the visceral epithelium to take up that ferritin which penetrated the filter.

The studies of the developing glomeruli have also provided information regarding the mechanism of formation of the basement membrane of the capillary wall. It seems clear from these studies and from data supplies by others, that the visceral epithelial cells produce or store components of the *lamina densa*. It also seems likely that the increased quantities of basement

## THE MEDICAL BULLETIN

membrane-like material (thickening of the basement membrane and the hyaline deposits) found in disease glomeruli, may result, at least in part, from abnormal activity of these cells.

The development, structure, and function, of another cell system within the glomerulus, the intercapillary or mesangial cells, has also been extensively studied. These cells also appear to be involved in the normal synthesis and/or degradation of basement membrane material. It seems likely that either increased or decreased production or degradation of basement membrane (hyalin) material by the intercapillary (mesangial) cells may account for some of the patterns of pathology which occur in renal disease.

It is hoped that the application of newer methods of study, including electron microscopic autoradiography, chemical analysis of isolated components of the glomeruli, and immunohistochemical techniques, to specimens from normal and pathologic kidneys may eventually permit an improved understanding of the function of these various cells. I am confident that ultra-structural pathology is here to stay and hopeful that these methods may aid in the ultimate development of specific therapy which will make the artificial kidney obsolete, through prevention of glomerular fibrosis.



## Staff Meeting Report

### Human Endotoxin Shock with Renal Insufficiency\*

*A Report of the Treatment of 27 Patients*

Jack L. Reddin, M.D.,† and Wesley W. Spink, M.D.‡

This report is an evaluation of the efficacy of vasopressor agents and cortisol in 27 patients with severe endotoxin shock involving the human. Each patient was studied personally by one or both of the authors, and in each case shock was of sufficient severity to produce definite evidence of renal insufficiency.

The concept of the production of a shock-like state as the direct result of the liberation of endotoxin (a lipoprotein-carbohydrate complex) from the cell wall of Gram-negative bacteria during the course of bacteremia with such organisms has received increasing acceptance over the past decade. Experimental models, primarily involving the dog, indicate that endotoxin triggers the release of a number of vasoactive substances which produce consistent hemodynamic alterations. The mechanism of the trigger process remains largely undefined. The hemodynamic alterations found in the dog and in all carefully studied animal species consist of marked venous pooling with consequent impairment of venous return, leading rapidly to a significant diminution in cardiac output and severe arterial hypotension which is, in turn, followed by dramatic arterial vasoconstriction. Severe renal arterial vasoconstriction and consequent cessation of glomerular filtration as well as frank ischemic tubular damage are hallmarks of lethal canine endotoxin shock.

Consequently a preliminary study was made to determine if the development of renal insufficiency in human endotoxin shock would serve as a reliable indicator of severity. Renal insufficiency was defined as a fall in urine output below 30 ml./hr. and/or an elevation of the BUN above 30 mg. per cent. Sufficient data on 40 patients with Gram-negative bacteremia during 1962 was

\*Presented at the Staff Meeting of University Hospitals on November 1, 1963.

†Medical Fellow, Department of Internal Medicine.

‡Professor, Department of Internal Medicine.

available for evaluation. Seventeen of these patients developed shock further compounded by renal insufficiency. With but one exception all fatal cases of endotoxin shock during 1962 occurred in this group of 17 patients.

An analysis was then conducted of all patients meeting these criteria which had been personally studied by one or both of the authors. Ten such patients were observed in 1962, and 17 were observed in the years 1954-1957. Additionally, these two groups were identical in regard to mean age and survival. They were considered as one group in the following analysis.

The mean age was 62 years, and males predominated at a ratio of four to one. A combination of malignancy and/or obstructive disease of the genitourinary or biliary tracts was present in approximately one-third of the patients. Blood cultures were positive in all cases, and *Escherichia coli* was the most frequent isolate. The mortality rate was 66 per cent, which is essentially the same as that observed with endotoxin shock in University of Minnesota Hospitals during the years 1950-1955.

Comparison of the surviving patients and the patients who died revealed no significant difference in the variables of age, underlying disease, duration of hypotension, selection of antibiotic, dose of vasopressor (metaraminol), or dose of cortisol when the latter was used in a dose range of 100-500 mg./day. However, those patients who received cortisol with metaraminol during the first 24 hours of therapy had a mortality rate of 55 per cent compared to a mortality rate of 88 per cent with metaraminol alone.

Noting the continued high mortality rate with the therapeutic regimen just discussed and observing favorable reports of therapy utilizing cortisol in a dose range of 1000-2000 mg./day, the opportunity arose to treat two patients in profound shock with such massive doses. The result in both patients was favorable and justifies further trial.

In summary, this report discloses that the complication of renal insufficiency is a reliable indicator of the severity of endotoxin shock. Over 90 per cent of all lethal cases of endotoxin shock developed this complication. There has been little or no change in the mortality rate of severe endotoxin shock in University of Minnesota Hospitals in the past five years. Limited but encouraging results have been noted with the use of cortisol in doses ranging from 1000-2000 mg./day.



## Alumni Survey



### CLASS OF 1962

*Uncle Sam has beckoned to more than one-third—possibly one-half—of the Class of 1962, now scattered throughout the world following completion of internships last summer. A Medical Bulletin survey collected information on 96 of the 122 classmembers. At least 40 were already in military service; unnumbered others were donning uniforms momentarily to serve in the Armed Forces.*

*Forty-two were in specialized medical training as resident physicians; thirteen had entered private practice; one had become a full time teacher, one a medical missionary, and one joined the Peace Corps.*

**David G. Alexander** was commissioned a captain in the U.S. Air Force and is stationed at Tripoli, Libya, for an anticipated three-year period.

**Harlan G. Alexander** is a resident at Presbyterian St. Luke's Hospital, 1753 W. Congress Pkwy., Chicago, Ill., "for at least a year."

**Capt. C. Arthur Anderson** is an Air Force Flight Medical Officer, assigned to Travis Air Force Base, Fairfield, Calif., for two years of duty.

**Quentin N. Anderson** is stationed in Germany with the U.S. Army. Mail can be sent to his home address at North Branch, Minn. c/o Clayton Anderson.

**Lois A. Anselment** has begun general practice in association with the Seifert Clinic, 675 Water St., Excelsior, Minn.

**Stanley J. Antolak, Jr.** has begun a surgical residency at the Bronx Veterans Administration Hospital, 138 W. Kingsbridge Road, Bronx, N. Y.

**Frederick D. Arny** is taking a residency in medicine at Santa Clara County Hospital, San Jose, Calif. In a year he expects to enter the Air Force.

**Daniel Baker** remains at Minneapolis General Hospital, where he has begun a residency in general surgery.

**Jay T. Ballhagen** expected induction into the U. S. Army medical corps last summer for a two year period. Mail may be sent c/o Olen Helland, Mt. Vernon, S. D.

**Bruce Bayley** expected to begin a general surgery residency at Cook County Hospital, Chicago, Ill., "unless I'm drafted first."

**John Becchetti** is in the Air Force, stationed in France, and expects to remain three years in the service. His address is 317 TAC Hosp. (USAFE) APO 253, New York, N. Y.

**Vernon R. Benson** has entered the U. S. Army medical corps under the Berry Plan for two years.

**James Bilstad** was "going into the Air Force," address unknown. His home address is at Little Falls, Minn.

**John F. Biltz** predicted he would be "overseas somewhere with the U. S. Air Force." His mailing address is c/o F. J. Biltz, Box 32, Minnetonka Village, Minn.

**Eugene F. Binet** "has enjoyed his year at St. Mary's Hospital, Minneapolis," and anticipated entering the U. S. Navy. His home address is 1411 Woodlyn, St. Paul, Minn.

**Leslie R. Bornfleth** entered the Air Force on August 4th for two years, and is to be stationed at Goose Bay Air Force Base, Labrador.

**Kenneth A. Branch** is a captain in the Air Force, and expected to be stationed at the Air Force Dispensary, Los Angeles International Air Force. His home address is 11207 Petit, Granada Hills, Calif.

**Joel Brende** has begun general practice in association with the St. Croix Falls Clinic, St. Croix Falls, Wis. He will live with his family across the river in Taylors Falls, Minn.

**David C. Brown** is at the Minneapolis V. A. Hospital taking a residency in internal medicine. His address is 1951 Kenwood Parkway, Minneapolis 55405.

**Keith Burnes** is in charge of the dispensary at the Naval Radio Station, Ponce, Puerto Rico (Navy 116, Box 60, FPO, New York) for an expected two years. "We had an interesting, tiring, but exciting year of internship," he writes.

**Ken Byce** stayed on at Milwaukee Hospital, Milwaukee, Wis., to take a residency in obstetrics-gynecology.

**Joan Cloutier** is now a first year resident in general surgery at the Union Memorial Hospital, Baltimore, Maryland.

**Daniel C. Conlon** has begun general practice in association with the Bloomington-Lake Clinic, Minneapolis, Minn.

**Gary Cowan** was headed for the Navy for two years, but his station and date of induction were unknown.

**Thomas Crowley** is a residency in psychiatry at University of Minnesota Hospitals.

**David Culligan** entered the Air Force last summer for two years of duty and stationed at Ellsworth Air Force Base, S. Dak.

**Don Dahlstrom** is a resident in radiology at Minneapolis V. A. Hospital, and lives at 3924 Lynn Ave., St. Louis Park, Minn.

**Amos Deinard** is a resident in pediatrics at University of Minnesota Hospitals, for an expected three years. He was married July 4, 1963 to Karen Ann Harris of Mound, Minn.

**Ronald Dietzman** is a resident in internal medicine at University of Minnesota Hospitals, where he also has interned.

**Charles Drage** was called by the U. S. Navy, and went on active duty last summer.

**Rosemarie Christa Eckert** was married June 29, 1963 to Dr. Peter Kohler, resident in medicine at University Hospitals. She also has begun a residency in psychiatry at University Hospitals, and lives with her husband at 709 Delaware St., Minneapolis 14, Minn.

**Joseph Emond, Jr.** has been commissioned a captain and is stationed with the medical corps of the U. S. Army at Fort Lewis, Wash.

**Paul F. Engstrom** is a resident in internal medicine at University of Minnesota Hospitals.

**Donald L. Erickson** will spend a year as a resident in general surgery at Minneapolis General Hospital "in preparation for a neurosurgery residency."

**Leonard T. Fielding** is a resident in psychiatry at University of Minnesota Hospitals, and lives at 2121 Indiana Ave. N., Minneapolis, Minn.

**Joel Finkelstein** is a resident in pediatrics at the Mayo Foundation, Rochester, Minn., under a three-year program.

**Robert D. Flaig** has entered the USPHS for two years of service. He is with the Indian Health Division and is stationed at USPHS Hospital, Eagle Butte, S. D.

**Alan D. Fremland** was awaiting orders from the U. S. Navy and was working at the St. Paul Outpatient Center. His wife, Dr. Harriet Fremland, will go with her husband and practice wherever he is stationed. They have a year-old son and interned together at Miller Hospital, St. Paul.



**Stanley A. Gall** is a resident in obstetrics-gynecology at University of Minnesota Hospitals.

**Gary B. Glomstad** has entered general practice in Deer River, Minn., in association with a classmate, Dr. Albert Roth.

**Barbara W. Gokcen** is a resident in anesthesiology at University of Minnesota Hospitals.

**David W. Grande** is a resident in internal medicine at George Washington University Hospitals, Washington, D. C.

**Margaret L. Grunnet** has begun a three-year residency in psychiatry at the University of Pennsylvania Hospital, Philadelphia 4, Pa.

**Capt. Bernie H. P. Hanson** is in the Air Force, stationed at Pope Air Force Base, N. C.

**Thomas Hart, Jr.**, has entered the U. S. Navy.

**Robert L. Hegrenes** is with the Air Force at Sioux City Air Base, Ia., where he expects to remain two years.

**Thomas C. Hegstad** is in private practice in Windom, Minn.

**A. Ervin Howell, Jr.**, has remained at University of Minnesota Hospitals to be a resident in general surgery. He lives with his wife, Dr. Mary Howell, who is presently interning at University Hospitals, at 2300 Oliver Ave. S., Minneapolis.

**Leon W. Hoyer** remained at Presbyterian Hospital, New York City, to spend a year as a resident in medicine.

**Lowell J. Hyland** and his wife, Shirley, live at 7315 W. 9th Pl., Apt. 4, Denver, Colorado, while Lowell spends a year as a resident in medicine at the Denver V. A. Hospital.

**Roger J. Jackman** entered the Air Force for two years and is at Travis Air Force Base, Calif. His home address is 913 9th Ave. S.W., Rochester, Minn.

**Robert R. Jacobson** stayed on at Harbor General Hospital, Torrance, Calif., to spend an anticipated three years as a resident in internal medicine.

**Gerhard J. Johnson** began a residency in internal medicine at the Mayo Foundation, Rochester, Minn. on October 1st.

**Warren L. Kleinsasser** will live and practice general medicine in Farmington, Minn. He has joined a group currently practicing there, and will live at 1212 Fairview Lane.

**Peter Koontz** has entered the Air Force and is stationed at Shepherd Air Force Base, Texas.

**E. Schrae LaPlante** is a resident in surgery at the West Virginia University Hospital, Morgantown, W. Va.

THE MEDICAL BULLETIN

**Parul H. Larson** is a general medical officer for the U. S. Army at Kenner Hospital, Ft. Lee, Va.

**Ronald Logemann** was awaiting an assignment from the U. S. Air Force. Mail will reach him c/o RFD, Bricelyn, Minn.

**Nancy R. Lund** remains at Salt Lake City, Utah, where she has begun a residency in pediatrics at the University of Utah affiliated hospitals. Her address is 2033 S. State, Box 54, Salt Lake City 15.

**Peter Madden** was assigned by the U. S. Army Medical Corps to duty at Ft. Hood, Texas.

**Douglas Mair** is a resident in pediatrics at the Mayo Foundation, Rochester, Minn., and lives at 329 15th Ave. S.W.

**Deane C. Manolis** is a resident in psychiatry at University of Minnesota Hospitals.

**Donald J. Maus** is in general practice at Monticello, Minn.

**Lawrence C. Mayerle** is a resident in psychiatry at University of Minnesota Hospitals, and lives at 512 Delaware St. S.E., Minneapolis 55414.

**Paul Mertens** expected to enter the field of medical missions with the Lutheran Church of America. He anticipated an assignment in Liberia.

**John Mork** has begun a residency in internal medicine at Highland Alameda County Hospital, Oakland 6, Calif.

**LeRoy E. Mueller** is in general practice in Hendricks, Minn.

**Ronald J. Ohmann** "had a wonderful year of internship in Tacoma, Wash.," and is entering the Army for two years on August 1. He is stationed in Milwaukee, Wis.

**Thomas A. Onstad** is a flight medical officer with the U. S. Air Force, and is stationed for two years at Chanutte Field, Ill.

**Charles S. Ostrov** has begun a three-year residency in ophthalmology under the Berry Plan with the Air Force. He is at the Cincinnati General Hospital, Ohio.

**John D. Palmer** has accepted an appointment as assistant professor of pharmacology at the University of Colorado Medical Center, Denver 20, Colo., and took his new post August 1.

**Larry Pearson** is an Air Force medical officer, and is stationed at Forbes Air Force Base, Kansas, for two years.

**David J. Perry** is a resident in obstetrics-gynecology at St. Mary's Hospital, Minneapolis, Minn.

**Richard Reem** was to enter the Armed Forces for a two year period.

THE MEDICAL BULLETIN

**Phillip Rierson** is a resident in pediatrics at Santa Clara County Hospital, and lives at 972 College Dr., Apt. 2, San Jose 28, Calif. He expected to be there one year.

**Larry Rivkin** is a resident in psychiatry at the University of Minnesota Hospitals, and anticipates three years of training here.

**G. Nicholas Rogentine** is a resident in medicine at Massachusetts General Hospital, Boston, Mass.

**Albert Roth** has joined Dr. Gary Glomstad in general practice at the Community Medical Clinic, Deer River, Minn.

**Lawrence J. Schut** is a resident in neurology at the University of Minnesota Hospitals. He lives at 1611 Newton Ave. N., Minneapolis.

**Jack Sebald** is an Air Force Flight Medical Officer, stationed at Walker Air Force Base, Rosewell, New Mex.

**Marvin S. Segal** is a resident in medicine at the Los Angeles V. A. Hospital, California, where he also was an intern.

**David G. Smith** is with the USPHS, Indian Health Division, for two years, and is stationed at the USPHS Hospital, Chamberlain, S.D.

**Donald A. Stenzel** is a resident in anesthesiology at the University of Minnesota Hospitals.

**John E. Sutherland** has joined Dr. John Eckdale (Med. '39) and Dr. K. A. Peterson (Med. '41) in general practice at Marshall, Minn. His address is 15 Doctors Plaza, 508 E. Second St.

**Willis M. Thorstad** is in the Air Force, assigned to Schilling Air Force Base, Kansas.

**Gordon L. Thurston** is taking a general practice residency at Kings County Hospital, Hanford, Calif.

**Peter H. Ullrich** is a resident in radiology at Minneapolis V.A. Hospital, anticipating a four-year stay, and lives at 1352 E. Maynard Dr., Apt. 239, St. Paul 16, Minn.

**Lowell W. VanDeRiet** has joined Dr. Robert Blomberg (Med. '39) in general practice at the Blomberg Clinic, 2215 N. Snelling Ave., St. Paul, Minn.

**Paul R. Vandersteen** is in the USPHS as an assistant surgeon with temporary promotion to senior surgeon. He is stationed at Turtle Mountain Indian Reservation, and the USPHS Indian Hospital, Ft. Yates, N.D., for the next two years.

**Robert D. Wasson** is in the U. S. Navy, and undertook a training program as a flight surgeon at Pensacola, Fla.

THE MEDICAL BULLETIN

**Robert A. Wengler** is a resident in general surgery at Mt. Sinai Hospital, Minneapolis, Minn. He lives at 1685 Thomas Ave., St. Paul.

**Richard A. Willson** stayed at Mary Fletcher Hospital, Burlington, Vt., for a year's residency in internal medicine. He expects to enter the Navy in 1964 for two years, then return ultimately to practice in Minnesota.

**John K. Wolf** is a resident in neurology at the University of Minnesota Hospitals.

**Capt. James L. Zum Brunnen** is a battalion surgeon with the Second Infantry Division, Ft. Stewart, Ga.

**Robert C. Wood** spent the summer in private practice in Seattle, Wash., and was to enter the Air Force Oct. 1st.





## MEDICAL FOUNDATION NEWS

The Minnesota Medical Foundation distributed \$33,425 in scholarship awards to 62 students at the Medical School of the University of Minnesota in ceremonies September 23rd marking the opening of the Medical School's 75th year. The ceremonies included an address by Dr. William F. Maloney, Evanston, Ill. (*see pp. 58-71*).

The scholarships were won in competition based on academic achievement and financial need. They represent the largest annual group of awards offered since the Foundation's scholarship fund was established in 1949. The Foundation is a non-profit organization of 2,000 physicians and laymen which provides various types of private assistance to the Medical School. It was founded in 1939.

The 1963 awards bring to \$199,925 the amount distributed for scholarship purposes by the Foundation in the last 14 years. Funds for the program are contributed by medical clinics, organizations, business corporations, other foundations, alumni, and private citizens.\* Individual scholarships range from \$500 to \$1,000. Dr. Corrin Hodgson, Mayo Clinic, is president.

Receipt of a \$26,000 endowment gift to the scholarship fund was announced at this year's ceremonies. The gift of Alice and Gale W. Perry, St. Paul, Minn., will provide a perpetual scholarship of \$750.00 annually under the Foundation's program.

The \$500 C. J. Watson Award, sponsored by the Minneapolis Society of Internal Medicine, was awarded to Dr. William N. Spellacy, medical fellow in obstetrics-gynecology at University Hospitals, for his research in the use of insulin in pregnancy.

Winners of 1963 Minnesota Medical Foundation scholarships were:

### Seniors:

Eugene H. Bagley, Ralph W. Bergstrom, Jr., Robert S. Brown, Bernard L. Mirkin, Alvin Shemesh, and William B. Torp.



Dr. Vernon D. E. Smith (Med. '30), right, vice president of the Minnesota Medical Foundation, chatted with Dr. William F. Maloney (Med. '46), at the 1963 Foundation Day Exercises. Dr. Maloney, now associate director of the Association of American Medical Colleges, Evanston, Ill., delivered the 1963 Foundation Lecture. Dr. Smith, a St. Paul surgeon, served as master of ceremonies.

**Juniors:**

Yossef Aelony, Arthur H. Bearon, Jerry Bergstein, William K. Brokken, Daniel B. Collin, Darrel DeVilliers, Jr., Darrel L. Lary, John M. McMillin, Joseph H. Merickel, Daniel J. Murphy, Guy E. O'Grady, Norman D. Olson, Karen L. Pajari, Loren P. Petersen, Gerald C. Peterson, David C. Piepgras, Wallace A. Rogers, Jr., Robert D. Thomasson, Paul W. Vander Kooi, and Alan J. Velander.

**Sophomores:**

Paul E. Carlson, Robert D. Christensen, David C. Dahlgren, Jon O. Flom, T. Dean Gillund, Russell F. Hanson, N. Kurt Langsten, Richard P. Linden, Thomas O. McNamara, Avrin M. Overbach, Roger A. Rabold, Gaylan L. Rockswold, Douglas K. Roszell, Terry A. Sorom, Lewis E. Struthers, David E. R. Sutherland, David L. Trudeau, and Jon E. Wallestad. Two other sophomores received scholarships by virtue of direct designation by donors.

**Freshmen:**

James N. Bertelson, Richard M. Biery, James A. Brockberg, Kenneth A. Bromenshenkel, Donald D. Dickinson, Jr., Thomas M. Donndelinger, John F. Greden, Stephen N. Haas, Dennis R. Jacobson, Andre Nelson, Leroy D. Olson, Charles W. Patterson, Jerry T. Reese, Joseph W. Tempel, Victor H. Tschida, and Stuart P. Westburg.

About 300 guests and members attended the annual awards exercises, at which time five new trustees were elected to the Board of Trustees of the Foundation. They were Raymond A. Scallen, Mal E. Herz, Mrs. G. N. Dayton, and Dr. R. S. Ylvisaker, all of Minneapolis, and Dr. Olaf Heiberg, Worthington, Minn. Dr. Milton M. Hurwitz, St. Paul, and Dr. Corrin Hodgson, Rochester, were reelected.

*\*The Foundation is grateful to the following supporters of the 1963 Scholarship Fund:*

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**Elexious Thompson Bell  
1880-1963**

*Dr. Elexious Thompson Bell, 83, professor emeritus of pathology, died September 16, 1963 of injuries suffered in an auto accident in Missouri. A native of that state, Dr. Bell became a world famous pathologist and author during a 38-year career on the faculty of the University of Minnesota. He joined the pathology department staff in 1911, and was head of the department from 1921 to 1949, when he retired. Dr. Bell is one of a handful of distinguished faculty members whose joint influence changed significantly the course of medical education at the University of Minnesota in the post-World War I period.*

*Portions of the eulogy to Dr. Bell delivered by Dr. C. J. Watson at a memorial service held at the Medical School are quoted below.*

“. . . For so many here this afternoon, Tommy Bell was like a father, not just a scientific father, which he surely was, but a most kind and helpful advisor and guide in the maze of one's earlier endeavors and difficulties.



"The privilege of saying a few words about him when we are gathered to honor his memory surely extends to bringing this characteristic picture before you. This portrays so well what literally *thousands* of his friends and students have in *their* memory, together with their recollection that his door was always open, his microscope available, and above all, his mind ready to consider one's problems. And what an unusually fine combination of gray matter his mind represented—keen, incisive, imaginative, and understanding, with the most delightful leaven of a very special humor. It is not surprising that he became so widely respected and so greatly beloved.

"The other day President O. Meredith Wilson commented that the University of Minnesota will never be quite the same without Tommy Bell. What a significant tribute this is when one realizes that Tommy became emeritus more than ten years before Dr. Wilson came to the University! As we all know so well, Tommy's emeritus status failed to curtail his continued activity in teaching and research. He simply moved his base of operations to the Veterans Hospital and his influence there during the next dozen years was beyond doubt one of the most potent factors in the development of the outstanding unit for teaching and research which the Veterans Hospital has become.

"One feels great admiration and wonder that during these emeritus years Dr. Bell did some of his finest work, turning his attention from his lifelong interest in the kidney, to the more intrinsic problems of diabetes. The results of this work, published in 1960, brought him the medal of the American Diabetes Association more than a decade after his retirement. His earlier studies of kidney diseases are world famous and steadily gain increasing confirmation and solid recognition. His book on the kidney is a classic. His Textbook of Pathology, an outstanding example of simplicity and straight thinking about disease, was a superb contribution to the education of countless students and doctors the world over. This book appeared in eight editions over a period of almost 30 years, and continues to have an important influence.

"This truly great man and his work now belong to the ages. As the years pass his name will come to represent, more and more, the finest tradition of medical teaching and research. Surely the focal point of this tradition and its brightest reflection will be this Medical School and this University. If it were possible, our love and admiration would only grow with the passage of time."

*Memorial gifts may be sent to the E. T. Bell Fund,  
c/o the Department of University Relations, University  
of Minnesota, Minneapolis, Minnesota 54555.*

## *Alumni Deaths*

◆ 1900

**Dr. W. H. Valentine**, Tracy, Minn. Died September 23, 1963 at the age of 88 years. He practiced more than 60 years in Tracy, Minn. before retiring early in 1962. He was a member of the Medical School's first four-year graduating class, and until his death was the oldest living intern of St. Mary's Hospital, Minneapolis. Death occurred in the 35-bed hospital which he founded in Tracy. Dr. Valentine was a native of Cannon Falls, Minn., and attended Carleton College. He is survived by his wife and two daughters.

◆ 1903

**Dr. William F. Coon**, Caney, Kansas. Died March 30, 1963 of arteriosclerotic heart disease at age 87.

◆ 1922

**Dr. Harold R. Leland**, Minneapolis, Minn. Died October 20, 1963 of a heart attack at age 65. A diplomate of the American Board of Obstetrics and Gynecology, Dr. Leland had been associated with Fairview Hospital since 1925 and was former chief of the medical staff. He was a member of Phi Beta Pi and Alpha Omega Alpha.

### Memorial Gifts

The Minnesota Medical Foundation acknowledges with gratitude recent contributions made in memory of:

**Dr. Paul S. Hagen**  
Minneapolis, Minn.

**Mr. A. R. English**  
Tracy, Minn.

**Mr. Harry K. Wrench**  
Frankfort, Mich.

**Mrs. Ada Blumenthal**  
Minneapolis, Minn.

**Mrs. Anastasia Gallagher**  
Chicago, Ill.

**Dr. John J. Boehrer**  
Wayzata, Minn.

Memorial gifts are a thoughtful means of honoring the memory of a relative, friend, or colleague. They serve the living by strengthening medical education and research at the University of Minnesota Medical School. Gifts may be designated for specific purposes. The Minnesota Medical Foundation acknowledges all gifts to both donor and next of kin.

# COMING EVENTS

*University of Minnesota Medical School*

## CONTINUATION COURSES FOR PHYSICIANS

1963-1964

University of Minnesota  
Center for Continuation Study

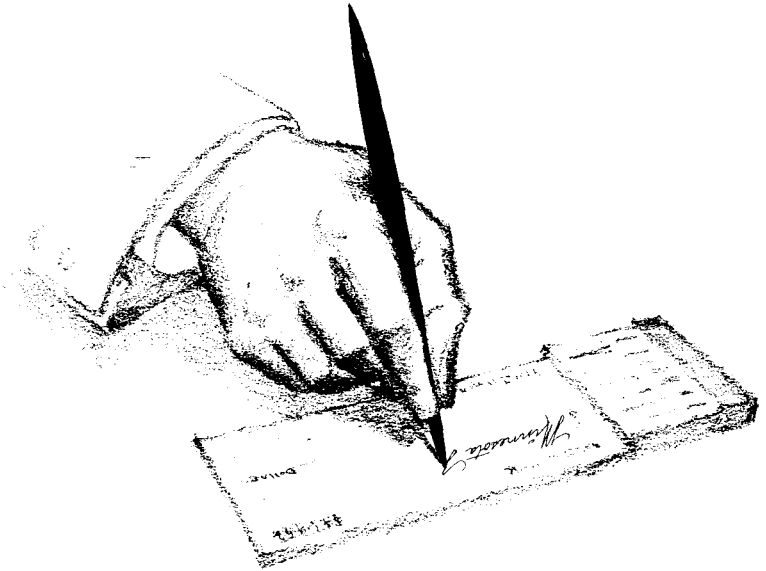
|                  |       |                                       |
|------------------|-------|---------------------------------------|
| October 10 - 12  | ..... | Dermatology                           |
| October 21 - 23  | ..... | Pediatric Neurology                   |
| November 4 - 8   | ..... | Neuroradiology                        |
| November 20 - 22 | ..... | Ophthalmology<br>(Refraction)         |
| November 21 - 23 | ..... | Orthopedic Surgery                    |
| December 6 - 7   | ..... | The Painful Back                      |
| December 16 - 17 | ..... | Respiratory Diseases                  |
| January 6 - 10   | ..... | Electrocardiography<br>(Intermediate) |
| February 10 - 14 | ..... | Proctology                            |
| March 9 - 11     | ..... | Psychiatry                            |
| March 17 - 20    | ..... | Internal Medicine                     |
| April 3 - 4      | ..... | Trauma                                |
| April 23 - 25    | ..... | Gynecology                            |
| May 4 - 6        | ..... | Ophthalmology                         |
| May 14 - 16      | ..... | Surgery                               |
| May 27 - 29      | ..... | Otolaryngology                        |
| June 3 - 5       | ..... | Anesthesiology                        |

The University of Minnesota reserves the right to change this schedule without notification.

Courses are held at the Center for Continuation Study or the Mayo Memorial Auditorium on the campus of the University of Minnesota. Usual tuition fees are \$45 for a two-day course, \$65 for a three-day course, and \$80 for a one-week course.

Specific announcements are sent out about two months prior to each course to all members of the Minnesota State Medical Association and to any physicians who request information for a specific course. For further information write to:

DIRECTOR  
DEPARTMENT OF CONTINUATION MEDICAL EDUCATION  
THE MEDICAL CENTER (BOX 193)  
UNIVERSITY OF MINNESOTA  
MINNEAPOLIS, MINNESOTA 55455



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