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UNIVERSITY OF MINNESOTA

Medical Bulletin

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

IN THIS ISSUE:

Bacteremic Shock

Tumor Growth

University of Minnesota Medical Bulletin

University of Minnesota Medical School

University Hospitals

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UNIVERSITY OF MINNESOTA

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Staff Meeting Report

Studies on the Mechanism of Shock Caused by Gram-Negative Bacteria*

Max H. Weil, M.D.,[1] Lloyd D. MacLean, M.D.,[2]
Wesley W. Spink, M.D.,[3] and
Maurice B. Visscher, M.D., Ph.D.[4]

A clinical problem of growing magnitude is the occurrence of shock in patients with gram-negative types of bacteremia. This alarming, often fatal complication is probably related to endotoxin liberated from microorganisms. Local vascular effects of bacterial products have been studied extensively, but much remains to be learned about hemodynamic changes.

Our investigation into pathophysiology showed a rational basis for treatment by metaraminol (Aramine) and perhaps by related vasopressor compounds. Large quantities of blood collect in the portal venous system, conceivably because of spasm blocking hepatic vessels. As a result, total venous return, cardiac output, and arterial blood pressure are critically reduced. The drug prevents or eliminates shock by selective action on dilated veins.

Shock in the Dog

Endotoxins injected by vein into dogs have effects very like those of human bacteremic shock. In our first experiments, adult animals received purified products of the Boivin type from *Escherichia coli* or *Brucella melitensis*.

After injection, the animal immediately had a well-formed bowel movement, and in two or three minutes pruritus, hyperpnea, agitation, vomiting, and diarrhea were noted. The dogs shivered and became apathetic as systemic blood pressure fell. Gagging and tenesmus predominated during the first hour, then profuse bloody vomiting

*This is an abstract of a report given at the Staff Meeting of the University of Minnesota Hospitals on February 24, 1956. A copy of the complete report, including references, may be obtained by writing to the Editor, UNIVERSITY OF MINNESOTA MEDICAL BULLETIN, 1342 Mayo Memorial, Minneapolis 14, Minn.

[1]Research Fellow, Department of Medicine.
[2]Research Assistant, Department of Surgery.
[3]Professor, Department of Medicine.
[4]Professor and Head, Department of Physiology.

and diarrhea. In some instances, strands of mucosalike material were extruded from the rectum. Coma generally ensued in three to five hours and death in 18 hours.

After intravenous Nembutal anesthesia, injection of endotoxin caused no visible gastrointestinal signs and little hyperpnea. However, blood pressure plunged to shock levels within one minute, as shown by a catheter passed from the femoral artery into the aorta.

Portal vein pressure, determined by a tube inserted through a splenic venous branch, increased up to four times within the first five minutes and subsided to the former value in 15 minutes. However, arterial pressure recovered only part way, then dropped in the next one to five hours and seldom rose again.

Whether or not anesthesia had been provided, the outstanding features at autopsy were severe congestion of the liver, submucosal bleeding and epithelial slough over much of the small bowel, and pronounced edema of the gallbladder.

Hemorrhagic enteritis was particularly severe in the duodenum, though gastric mucosa was relatively intact. In the intestinal submucosa, hyaline thrombi occluded some blood vessels. Thrombotic material closely resembled the fibrinoid seen in glomerular capillaries of rabbits after two injections of meningococcal toxin, as described in connection with the generalized Shwartzman reaction.

Shock in the Rat, Rabbit, and Cat

Endotoxin produced comparable shock in at least four species of laboratory animals. The same abrupt fall of arterial pressure and portal elevation observed in dogs took place with similar tissue changes in rats, rabbits, and cats.

Pathologic Physiology

Severe hypotension induced by overwhelming infection or injected bacterial products is commonly attributed to (1) toxic insult of the central nervous system, (2) diffuse injury to capillary or other blood vessel walls, (3) cardiac damage, or (4) a combination of two or more such factors. Our experiments were designed to test these possibilities.

Shock might well be influenced by neurologic factors but could not be primarily caused by direct toxic action on the higher nervous centers. Dogs were not protected by chordotomy at the sixth cervical vertebral level, with or without vagotomy. Even in the decapitated preparation, endotoxin promptly lowered arterial blood pressure and raised portal value.

Anesthetized cats were more variable. Yet, when the entire spinal cord was destroyed, toxin still caused a profound secondary drop of arterial pressure and slight portal elevation, as well as morphologic changes.

Neither arterial nor arteriolar dilatation was a factor. Using a dye-dilution technic, cardiac output of dogs before and after injection of toxin was measured with the aid of Dr. E. B. Brown and his staff. Although both cardiac output and arterial pressure declined, peripheral resistance did not change.

So-called vasomotor collapse was fully explained by a fall in cardiac outflow to 21 to 36% of control value. When output was kept at a constant level during total body perfusion with a pump oxygenator, blood pressure was not significantly depressed by toxin. This also argued against a shock factor of low peripheral resistance.

Cardiac output was not reduced by congestive heart failure, because, during shock, pressure in the inferior vena cava was either unaffected or decreased. Moreover, a direct view of the dog heart and serial electrocardiograms gave no evidence of myocardial failure.

The hemodynamic changes responsible for shock were demonstrated by our method of determining total venous return. A reservoir system was interposed between the central ends of the great veins and the right atrium. Blood was passively drained from the superior and inferior venae cavae to the reservoir, which was a glass cylinder maintained in a water bath and placed 30 cm. below the animal's heart level.

This unoxygenated blood was then delivered with the aid of a Sigmamotor finger pump to the right atrium. Infusion was established at a flow of about 85 cc. per kilogram, with which blood pressure and reflexes could be well maintained for more than three hours.

The volume of blood in the cylinder was continuously measured by hydrostatic pressure of the fluid column acting on a strain-gauge manometer. The arterial infusion was kept flowing at a constant rate, so that shifts of the reservoir level were entirely due to alterations in the amount of blood returned from the vena cava to the reservoir. Therefore, a rise in the glass cylinder indicated an increase in venous return, and a loss reflected decrease. The system was primed with blood from a donor dog.

During a control period, the volume of blood returned to the reservoir was, after initial loss of about 10 cc. per kilogram of body weight, equal to the amount infused. After injection of endotoxin, the

reservoir level rapidly dropped, indicating a considerable fall-off in venous return.

Since the blood supply to the right atrium was maintained at a steady value, blood pressure did not fall. The heart was fully capable of normal function, with unaltered output and arterial pressure, as long as the large deficit in the cylinder was replaced with additional donor blood.

This showed that large quantities of blood were pooled in the body and that shock resulted from a sharp fall in cardiac output due to reduction in venous return. As peripheral resistance was unaltered, blood necessarily collected in the postarteriolar vascular bed.

The portal system proved to be a major site of pooling. When large amounts of blood pooled in the liver and intestine were quantitated by a gravimetric technic, blood lost from the active circulation was reasonably accounted for. High portal pressure, severe engorgement of the liver and bowel, and edema of the gallbladder were all closely related to accumulation of blood.

Pooling in the portal system was evidently caused by transient obstruction to venous outflow from the liver. We have found that, in open hepatic veins during shock from endotoxin, pressures reflect conditions of the inferior vena cava rather than those of the portal vein.

Other workers have demonstrated that *Ascaris* extract, hydatid cyst fluid, and histamine provoked occlusive spasm of the intrahepatic vessels in dogs and cats. We suspect that gram-negative bacterial endotoxins exert a similar action.

No evidence at the present time supports pooling in systemic veins. In fact, subcutaneous venous pressure fell after injection of endotoxin.

Circulation in the bowel serosa and mesentery was examined microscopically with the help of Dr. J. S. Lee. Remarkable changes occurred after injection of endotoxin. As arterial pressure fell, arteriolar width shrank about 30%, while diameter of venules doubled. Changes were partly reversed during the recovery phase, but venules became fragile, and rupture of venous capillaries caused pinpoint hemorrhages.

Subcutaneous venules in the thigh did not swell after induction of shock, but both arterioles and venules narrowed. When endotoxin was applied directly to vascular beds, no local damage resulted.

Experimental Therapy

The worth of vasopressors for human shock is well known, although epinephrine and other sympathomimetic amines have been thought to overconstrict vessels, thus causing further stagnation of blood.

With the assistance of Dr. Lerner Hinshaw, the effect of metaraminol on venous return was studied. The drug was injected into dogs three to seven minutes after endotoxin, and supplements were added at short intervals.

Much less blood pooled in treated animals. For example, an unprotected animal lost 80 cc. per kilogram of body weight in 30 minutes, in contrast to 18 cc. per kilogram lost by an animal given metaraminol. When 25 cc. per kilogram had already pooled, the process was actually reversed by treatment.

Norepinephrine, the most potent vasopressor clinically available, also counteracted stasis but less rapidly, even at larger dosage.

Staff Meeting Report

Factors Affecting the Transplantability and Metastatic Growth of Tumors in Mice*

Carlos Martinez, M.D.[1]

Of great interest in cancer research are the influences that control development of tumor implanted in a healthy host.

An important factor in mammary tumors of mice is the size of the primary neoplasm at the time of transfer. Inoculated cells from a large cancer will form a new lesion earlier than material from a small growth. Tumors derived from a larger neoplasm also grow faster, metastasize earlier, and kill the host sooner than those from a small source.

Factors in Transplantability of Mammary Tumors

Success or failure in transfer of breast tumors in mice depends primarily on the genetic relationship between the host and the tumor to be received. During experiments, it was noted that both transplanted and spontaneous neoplasms had a typical sigmoid growth curve. That is, slow initial development was followed by a rapid spurt, then by a final retarded phase before the host succumbed.

These fluctuations in growth rate suggested that corresponding changes might be occurring in some other properties of cancer. Accordingly, possible effects of tumor size on transferability were investigated.

Method. Spontaneous mammary tumors in mice of the Z (C3H) or A stock and also tumors maintained in the laboratory by successive passage into genetically related mice were used.

Recipients were young males and females of the ZBC and ABC strains, hybrids designed to grow, respectively, tumors from mice of Z and A strains.

Neoplasms were excised, divided into small bits, and processed in a Potter-Elvejehm glass homogenizer. Saline suspensions of cells

*This is an abstract of a report given at the Staff Meeting of the University of Minnesota Hospitals on March 2, 1956. A copy of the complete report, including tables and references, may be obtained by writing to the Editor, UNIVERSITY OF MINNESOTA MEDICAL BULLETIN, 1342 Mayo Memorial, Minneapolis 14, Minn.

[1]Associate Professor, Division of Cancer Biology, Department of Physiology.

were injected in different concentrations. Subcutaneous implants were made in the right groin with a 22-gauge needle and a 2-cc. syringe. For intravenous inoculation, the tail vein was used.

Tumor size was determined with calipers, measuring the two greatest diameters at right angles. These two widths were multiplied, and mean size was calculated as the square root of the product.

"Take time" was defined as the number of days required for 50% of a group to develop a tumor with mean diameter of at least 0.8 cm. in the inoculation site. "Death time" was the number of days before half the subjects died of cancer.

After intravenous inoculation, groups of mice were killed at various intervals, and the number of nodules on the lung surface was counted under a dissecting scope with magnification of 1.3 by 10. Nodules were also examined histologically.

Results. (a) Take times were determined for two spontaneous tumors, large and small, obtained simultaneously from the same mouse. Mean diameters on excision were 2.6 and 1.25 cm.

Recipients were two groups of young females, which were inoculated, respectively, with 0.25 cc. of cell suspension from the large tumor at 2.5% concentration and the same amount of 3.5% suspension from the small tumor. Take time was 21 days for the large growth and 39 days for the small.

However, two mice, one from each group, had tumors of about the same size, 2.2 and 2.21 cm. After cells from these implants were injected in the same concentration into two groups of normal ABC mice, take times were 20 and 21 days.

(b) Take time and death time were ascertained for animals inoculated with serial samples of the same tumor at different sizes. Cells were transferred at the same concentration.

When a Z spontaneous tumor had a mean diameter of 1 cm., a biopsy specimen was obtained and a 5% suspension in saline prepared. Subcutaneous injection of 0.25 cc. into eight ZBC mice produced no growth. At a diameter of 1.6 cm., tumor was effectively implanted in five of the eight mice, with take time of 51 days and death time of 134 days.

A third sample at 2.56 cm. produced tumor in all animals, with take time now only 24 days and death time 92 days. Results were comparable with Z transplanted tumor and with spontaneous and transplanted A lesions.

(c) Take time and death time were also estimated for mice inoculated with the same tumor at different sizes and with various concentrations of tumor cells.

When Z transplanted tumor was 0.9 cm. in diameter, suspensions were prepared. ZBC females were inoculated in three groups with 0.25 cc. of 5%, 2.5%, or 1% strength. About half the mice grew tumor, regardless of cell concentration. Take time was 28 days for all groups, and death time was 57, 58, and 55 days.

With size of 1.55 cm., all subjects had tumors; take time fell to 10, 14, and 14 days; and death time decreased to 39, 40, and 37 days. When the donor tumor was 2.37 cm. in diameter, all recipients grew cancer and different cell concentrations had almost identical take and death times.

(d) Intravenous inoculation of the same tumor was done at different stages of growth. Z transplanted adenocarcinoma was sampled and injected as a 0.5% concentration into the tail vein of ZBC mice. The total volume was 0.2 cc. Mice were killed 7, 10, and 15 days later. Lungs were excised, and superficial nodules were counted.

When primary tumor diameter was only 0.8 cm., no metastases were found after any interval. At width of 1.5 cm., lung tumors appeared in two of six mice killed seven days after inoculation and in all killed after 10 or 15 days. At 1.85 cm., tumor spread to the lungs in four of six animals killed after a week and in all after longer periods.

Factors in Metastasis of Mammary Tumors

The reasons for spread of malignant tumors are not entirely clear. Suspected factors are the number of embolic cells detached from the primary growth, duration of parent tumor in the host, and final size of the primary growth. Since the size and transferability of donor tumor are related and metastases are essentially autotransplants, the relation of metastasis to size of the primary growth is particularly interesting.

From mice bearing a transplanted tumor, the initial growth was removed at various intervals after inoculation. Forty-five days later, animals were killed and pulmonary metastases determined.

Method. Young ZBC females were hosts for transplanted mammary adenocarcinoma which first appeared spontaneously in a Z female and has been maintained for 52 successive passages into ZBC mice.

In the first of two experiments, a 5% suspension of cells was inoculated subcutaneously into the right groin. Subjects were later divided into four groups, according to mean size of the tumors on excision: 0.6 to 0.79 cm., 0.8 to 0.99 cm., 1 to 1.2 cm., and 1.21 to 1.4 cm.

In the second experiment, the tumor was transplanted subcutaneously into the tail, to facilitate subsequent excision. Each mouse received 0.05 cc. of 8% cell suspension. On removal, implants were 1.15 and 2.6 cm. in mean width.

Results. (a) With tumor of the groin, only eight of 34 animals, or 24%, had pulmonary spread with the smallest growth on excision. Rates increased with greater bulk on removal to 58%, 71%, and 88%.

(a) Outcome was similar after implantation in the tail. Metastasis was more likely in subjects bearing rapidly growing transplants from the larger donor tumors.

Comment

The results imply that transplantability, growth rate, and capacity for metastasis of breast tumor in mice depend upon size of the donor growth at the time of transfer. Even if two spontaneous tumors are taken from the same mouse, the larger one has a shorter take time. Moreover, tumors of the same size transferred from separate groups to normal mice have similar take times.

Differences in take and death times are also seen when the same tumor is transplanted at various sizes but in the same amounts.

Our data agree with those reported by Browning in 1948, suggesting that autonomy is not present in small cancers but appears gradually with increase in tumor age or size. In our experience, this is also true for transplanted tumors after many passages.

These results are rather difficult to explain. If the actual number of cells were important, the number of malignant cells per unit of tumor mass should be less in small than in large growths. Yet, young transplantable sarcomas are said to have a higher percentage of viable cells than old tumors.

Moreover, when inoculating tumors of small and large sizes, Browning introduced bits of tissue by trocar. All concentrations of cells must have been well above any critical value and therefore could not alone account for the phenomenon observed.

As for spread of mammary tumors, size was clearly related to the rate of lung metastasis. The larger the tumor on excision, the higher the incidence of pulmonary implants from either groin or tail.

When adenocarcinoma was removed 10 to 22 days after inoculation, the metastatic trends increased with the time of growth, apparently showing a direct correlation between rate of metastasis and the time during which tumor remains in the host.

Actually, however, rate of growth of the primary tumor seems more important than number of days in the host. When two groups of mice received, respectively, a fast-growing and a slow-growing neoplasm, metastases were always more frequent in animals with the rapid type. This held for any given time after inoculation, though intervals ranged from 5 to 33 days.

Editorial

Antibiotic Sensitivity Studies 1954-1955

The problem of resistance of pathogenic microorganisms to available antibiotics is encountered by every physician using these drugs, particularly in hospital practice. It is of interest, therefore, to review from time to time the status of susceptibility of current strains of various bacterial species to the most commonly used antibiotics. For this purpose the results of 1386 individual sensitivity determinations on 414 microorganisms isolated from patients of all ages at the University of Minnesota Hospitals during 1954 and 1955, were reviewed. Sensitivity determinations were performed by the standard tube dilution technique of Rammelkamp, thus the data are comparable to those available from other laboratories employing this method. The antibiotics used include penicillin, erythromycin, bacitracin, neomycin, Streptomycin, polymyxin, chloramphenicol, and tetracycline. Tetracycline was the only member of its group studied, since it has been shown that no major differences in sensitivity are demonstrable among the group.

The results are given in Table I. The numbers of strains exam-

Inhibiting level of antibiotic tested	*Microorganism*									
	Staphylococcus (coagulase pos.)		*Escherichia coli*		*Aerobacter Aerogenes*		*Proteus sp.*		*Pseudomonas aeruginosa*	
	No. strains tested	*No. sensitive*	*No. strains tested*	*No. sensitive*	*No. strains tested*	*No. sensitive*	*No. strains tested*	*No. sensitive*	*No strains tested*	*No. sensitive*
Penicillin 7.8	90	18 (20%)	2	0	3	0	17	3 (18%)	3	0
Erythromycin 7.8	101	73 (72%)	4	0			2	0	2	0
Tetracycline 7.8	83	32 (38%)	41	32 (78%)	49	12 (24%)	56	3 (5%)	41	27 (66%)
Chloramphenicol 7.8	71	43 (61%)	27	24 (89%)	46	17 (37%)	61	8 (13%)	24	0
Neomycin 7.8	28	18 (64%)	7	1	7	4	12	0	4	3
Bacitracin 6.2	48	25 (52%)								
Streptomycin or dihydrostreptomycin 7.8	25	0	19	2 (10%)	26	1 (4%)	20	1 (5%)	11	1
Polymyxin 3.9					4	0	6	0	39	35 (90%)

ined, and the number and percentage of these strains inhibited by the given level of the various antibiotics are indicated. The levels chosen to depict are somewhat arbitrary, but reflect achievable levels for most of the drugs. Since no statistical difference in data from the years 1954 and 1955 was found, they are combined in the table.

It may be seen that a majority of the staphylococci are still sensitive *in vitro* to erythromycin, neomycin, and bacitracin. The percentage of strains showing sensitivity, while similar to results obtained in 1953, is lower than in 1952 (Wise and collaborators). Of particular interest is that the sensitivity to chloramphenicol has increased since 1952. This may reflect the decreased use of this agent subsequent to the reports of unfavorable reactions to chloramphenicol. The present data suggest that chloramphenicol is among the best available drugs for treatment of staphylococcal infections.

A high percentage of Proteus and Aerobacter strains remain extremely insensitive to most available antibiotics. Pseudomonas strains isolated during this period are surprisingly sensitive to tetracycline, in contrast to data obtained elsewhere, and continue to be uniformly sensitive to polymyxin.

It should be stressed that the data presented are from a selected group of patients with unusual or resistant infections. Nevertheless, the results do represent trends and serve as a guide in choosing antibiotics to treat infections which will be encountered in general practice.

ROBERT A. BRIDGES, M.D.
ROBERT ABERNATHY, M.D.
DOROTHY NESS, B.S.

Alumni Association

DR. ROBERT B. RADL, '24, Bismarck, North Dakota, is Governor for North Dakota of the American College of Physicians. He is also Councillor for the Sixth District of the North Dakota State Medical Association.

DR. THEODORE B. RASMUSSEN, '34, is *Professor of Neurology and Neurosurgery* at McGill University and Montreal Neurological Institute, Montreal, Quebec, Canada.

DR. REINERT T. RAVENHOLT, '51, is serving as Director of the Division of Communicable Diseases of the Seattle-King County Health Department in Seattle, Washington. He is also a member of the faculty of the University of Washington Medical School.

DR. LYLE J. ROBERTS, '16, Rear Admiral (Retired), U.S.N., holds the Legion of Merit award. Dr. Roberts is now serving as Health officer of District 6 in West Virginia. His home is in Martinsburg, West Virginia.

DR. JAMES S. ROBERTSON, '44, Upton, Long Island, New York, is head of the Medical Physics Division of the Brookhaven National Laboratory.

DR. LOUIS H. RODDIS, '13, San Diego, California, received the Sir Henry Wellcome Gold Medal and Prize in Military Medicine in 1943.

DR. JOHN M. RUMBALL, '34, Coral Gables, Florida, is serving as Secretary of the Section on Gastroenterology of the Southern Medical Association for the period 1954-56 and will become Chairman of the Section in 1957. He is a *Clinical Associate Professor of Medicine* at the University of Miami School of Medicine.

IN MEMORIAM

DR. FRANK LLOYD RICHARDSON, '36, Vancouver, Washington.

DR. FREDERICK S. RICHARDSON, '22, Oakland, California

DR. LEON G. SMITH, '10, Montevideo, Minnesota

DR. J. DOUGLAS WALKER, '09, Los Angeles, California

DR. STELLA L. WILKINSON, '03, St. Paul, Minnesota

Medical School Activities

Professorship Established

The University of Minnesota Regents recently established the Rappaport Professorship in Cardiac Research. They approved a proposal of the board of governors of Mount Sinai Hospital to use a gift from the Rappaport family providing $10,000 a year for the new research position. Appointment of the professor will be announced later.

The research professor will do most of his work in the Jay Phillips Research Laboratory at Mount Sinai Hospital. An initial gift of $55,000 has been made by Max and Fred Rappaport and their sister-in-law, Mrs. James E. Rappaport. It is a memorial to the late Edward Rappaport, father of Max and Fred, and to the late James E. Rappaport, their brother.

Special Course in Medical Physiology

During the fall and winter quarters, the Department of Physiology has conducted a special course in Medical Physiology for the faculty members of the Medical School of Seoul National University of Korea who are visiting our campus this year. In addition to regular members of the Physiology Department staff, several visiting lecturers have participated in this course. These have included DOCTORS C. ADRIAN M. HOGBEN, FREDERIC C. BARTTER, ERNEST COTLOVE, and STANLEY J. SARNOFF of the National Institutes of Health; DR. WARD FOWLER, Mayo Foundation; DR. COSMO MACKENZIE, University of Colorado Medical School; DR. ROBERT SPEIRS, Brookhaven National Laboratories; and DR. ARMAND QUICK, Marquette University Medical School. These visiting lecturers have preseneted seminars for the staff on their current research interests in addition to lecturing for the course.

Faculty News

DR. LEMEN J. WELLS, *Professor of Anatomy*, participated in the Third Conference on Gestation, sponsored by the Josiah Macy, Jr. Foundation, March 6-8, Princeton, New Jersey. Dr. Wells' contribution dealt with the secretory activities of fetal endocrine glands and their effect upon target organs. Twenty-three American and two European workers attended the conference, on invitation of DR. GEORGE B. WISLOCKI, Chairman.

DR. J. FRANCIS HARTMAN, *Associate Professor of Anatomy,* attended a Symposium on Tissue Fine Structure, sponsored by the U.S. Public Health Service, January 16-18, at Arden House, Harriman, New York. Dr. Hartman presented a short summary on mitochondria in the central nervous system.

DR. RAYMOND BIETER, *Professor of Pharmacology,* attended a meeting of the Committee on Drug Addiction and Narcotics of the National Research Council at the National Academy of Science on January 30 and 31. He was also the representative of the Minnesota Basic Science Board at the meeting of the National Association of Basic Science Boards in Chicago on February 13.

DR. M. B. VISSCHER, *Professor of Physiology,* participated in a Symposium in celebration of the thirtieth anniversary of the founding of Biological Abstracts in Philadelphia on February 17. His contribution dealt with an analysis of trends in zoological and medical literature.

The Board of Directors of the Radiological Society of North America has appointed DR. CHARLES M. NICE, JR., *Instructor and Acting Head, Department of Radiology,* as Counselor for the State of Minnesota.

DOCTORS JEROME T. SYVERTON, WILLIAM H. MURPHY, JR., and JOHN DOUGLAS ROSS, *Department of Bacteriology and Immunology,* attended the Tissue Homotransplantation Conference sponsored by the New York Academy of Sciences, New York City, February 1-3.

DR. THOMAS M. RIVERS, *Rockefeller Institute for Medical Research,* and DR. HENRY W. KUMM, *Director of Research, National Foundation for Infantile Paralysis, Inc.,* were visitors of the Department of Bacteriology and Immunology on February 8.

PROFESSOR M. R. CHUMAKOV and DR. M. K. VORSHILOVA, *Poliomyelities Research Institute,* Russia; PROFESSOR A. A. SMORODINTSEV, *Institute of Experimental Medicine,* Russia; DR. LEV LUKIN, *Junior Scientific Employee,* Russia; DR. ALEXIS I. SHELOKOV and MR. WILSON, representatives of the *U.S. Public Health Service,* Washington, D.C., were visitors of the Department of Bacteriology and Immunology on February 9 and 10.

DR. R. DOROTHY SUNDBERG, *Associate Professor of Anatomy,* spent February 6, 7, and 8 at Children's Medical Center, Department of Pediatrics, Harvard Medical School, Boston, as a guest of DR. LOUIS K. DIAMOND. She participated in a three-day session of hematology for present and past pediatric residents and also gave a formal lecture, "Anemias Which Present Peripheral Leuko-Erythroblastotic Reactions."

MRS. MYRTLE COE, *Assistant Professor, School of Nursing,* has accepted the appointment as liaison member from the Council on Rheumatic Fever and Congenital Heart Disease of the American Heart Association to the Committee on Nutrition of the Council on Community Service and Education. Mrs. Coe became the official representative of nursing on the Council on Rheumatic Fever at the time of its organization in 1944 and is presently a member of its Committee on Education. She is also a member of the Executive Committee of the Council on Community Service and Education.

IN MEMORIAM

DR. WATER H. UDE

The entire Faculty of the Medical School was saddened to learn of the death, on February 10, of Dr. Walter H. Ude, Clinical Professor of Radiology. Dr. Ude died suddenly of a heart attack while vacationing with his wife in Hawaii.

For more than 25 years Dr. Ude had been a most active member of our Clinical Faculty. Despite a busy private practice in Minneapolis, he devoted his time generously to undergraduate, graduate, and postgraduate teaching at the University. He was the first resident to receive training in radiology under Dr. Leo G. Rigler, thus beginning a long and satisfying association.

Born in Vernon Center, Minnesota, Dr. Ude attended the University of Minnesota Medical School, graduating in 1924. He served his internship and fellowship at Minneapolis General Hospital. He was a Fellow of the American College of Radiology and a member of the American Roentgen Ray Society and of the Radiological Society of North America. He had been elected Third Vice-President of the latter society shortly before his death.

We shall, of course, miss Dr. Ude's contributions to our teaching programs. Perhaps to an even greater extent, however, we shall miss his softspoken friendliness and his readiness to share his valuable time with those seeking his advice and counsel.

He is survived by his wife, Valborg, and two brothers. To these and other members of his family we wish to express our most sincere sympathy.

Postgraduate Education

Trauma for General Physicians

The University of Minnesota, the Minnesota Academy of General Practice, and the Minnesota Committee on Trauma of the American College of Surgeons will join in sponsoring a continuation course in Trauma on April 7. The one-day program will be held in the Mayo Memorial Auditorium on the University of Minnesota Campus. No attempt will be made to cover all aspects of trauma in the brief time allotted. Instead, head and face injuries, shock, and urinary tract injuries will be taken up in detail. Management will be stressed throughout. It is proposed that a program of this type will be an annual event and that other aspects of trauma will be dealt with in future years.

Endocrinology for General Physicians

The University of Minnesota announces a continuation course in Endocrinology for General Physicians which will be held at the Center for Continuation Study from April 9 to 11. Management of the more common endocrine and metabolic abnormalities will be stressed. Guest speaker will be DR. PETER H. FORSHAM, *Associate Professor of Medicine and Pediatrics,* and *Director of Metabolic Unit,* University of California Medical School, San Francisco. The course will be presented under the direction of DR. C. J. WATSON, *Professor and Head,* Department of Medicine.

Notice

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

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

Coming Events

March 19-21	Continuation Course in Cardiovascular Diseases for General Physicians
March 20	MINNESOTA PATHOLOGICAL SOCIETY LECTURE; "Streptococcal Cardiac Lesions in Rabbits"; *Dr. Joel G. Brunson,* Instructor, Department of Pathology, University of Minnesota; Owre Amphitheater; 8:00 p.m.
March 21	GEORGE FAHR LECTURE; "The Circulatory Action of the Veratrum Alkaloids"; *Dr. Otto Krayer,* Professor and Head, Department of Pharmacology, Harvard Medical School; Mayo Memorial Auditorium; 8:15 p.m.
April 7	Continuation Course in Trauma for General Physicians
April 9-11	Continuation Course in Endocrinology for General Physicians
April 16-18	Continuation Course in Radiology for General Physicians
May 7-12	Continuation Course in Electrocardiography for General Physicians
May 14-19	Continuation Course in Proctology for General Physicians
May 15	DULUTH CLINIC LECTURE; "Experimental Hepatic Injury in its Relation to Hepatic Disease in Man"; *Dr. Paul Gyorgy,* Professor, Department of Pediatrics, Hospital of the University of Pennsylvania, Philadelphia; Mayo Memorial Auditorium; 8:00 p.m.

WEEKLY CONFERENCES OF GENERAL INTEREST

Physicians Welcome

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

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