VOLUME XXVII • NUMBER 6 • JANU

UNIVERSITY OF MINNESOTA

Medical Bulletin

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

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University of Minnesota Medical Bulletin

University of Minnesota Medical School

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UNIVERSITY OF MINNESOTA

Medical Bulletin

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VOLUME XXVII *January 15, 1956* *NUMBER 6*

CONTENTS

Published semi-monthly from October 15 to June 15 at Minneapolis, Minnesota.

Staff Meeting Report

Host-Parasite Factors in Group A Streptococcal Infection*

Dennis W. Watson, Ph.D.[1]

Many workers have focused attention on streptococci of group A because of its relation to rheumatic fever and other nonsuppurative sequelae. The bacterial cell and its extracellular products have been extensively studied, and results are described in recent excellent reviews. Much progress has been made in identifying intrinsic factors. However, no single factor or combination of factors accounts for the various mechanisms by which these organisms cause disease.

The investigation reported here is based on a concept first proposed by Bail in 1904 and lately revived in studies on *Bacillus anthracis.* This theory assumes that the bacterial parasite growing in the dynamic environment of the host may be modified either by selection or by adaptation. As a result, the organism produces substances needed for its life in the host, and, therefore, important in the pathogenesis of the disease. The same organism removed to ordinary culture media may fail to continue the synthesis. However, conditions within the host can be simulated in vitro. For example, the protective antigen of *B. anthracis* may be reproduced in a well-defined and carefully controlled environment.

Simple technics have been devised to furnish and isolate the cellular and metabolic products of the parasite as well as modified toxic products of the host, all of which may have a part in the etiology of disease. This outline presents the over-all approach to a single host-parasite relationship. Various types of group A streptococci were injected into the American Dutch rabbit, a highly inbred strain. In addition, a single streptococcal type was employed with several inbred strains of mice.

Experimental results are grouped in four categories: [1] methods of producing and fractionating host-parasite factors from bacterial

*This is an abstract of a report given at the Staff Meeting of the University of Minnesota Hospitals on December 9, 1955. 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]Professor, Department of Bacteriology and Immunology.

lesions, [2] toxic host factors from host-parasite interaction, [3] parasite factors induced by the host environment, and [4] host factors and liability to infection.

One cannot even speculate on the mechanisms involved, nor can effects in animals be extrapolated directly to the human disease. These experimental models may serve as guides to future interpretations and illumine data directly bearing on group A diseases in man.

1] *Production and fractionation of host-parasite factors.* Group A lesions are produced in rabbits by intracutaneous inoculation at 40 to 60 sites over the abdomen and thorax. After twenty hours, the animals are killed and lesions are excised and immediately frozen. Specimens are later thawed and ground, stirred in cold saline solution, and filtered through gauze. Host and parasite factors are then separated by various technics of centrifugation and filtration. During the entire procedure, temperatures never exceed 5° C.

2] *Host factors from host-parasite interaction.* [a] Toxic thromboplastin-like factor. Apparently, streptococci act on normal tissue thromboplastin to reduce its molecular weight and increase solubility. When group A organisms are injected into this modified substance, either intravenously into rabbits or intraperitoneally into mice, virulence apparently rises. More rabbits die with endocarditis, and fewer mice survive.

The modified thromboplastin may surround bacteria with fibrin clots, favoring multiplication in the colonial effect. Treatment with heparin prevents increase of virulence. Possibly, the factor is related to a toxic necrosin-like substance isolated from human serum during acute rheumatic fever.

[b] Antimicrobial factors from necrotic tissue or cells. Basic polypeptides obtainable from thymic and other host tissues combat group A organisms. A factor with different properties is extracted with lactic acid from leukocytes taken from rabbit peritoneal cavity. Significantly, factors of both types are inhibited by hyaluronic acid, a polymer that comprises the capsule of streptococci in the mucoid phase. Thus, antimicrobial factors of the host may influence selection of the resistant capsular form of streptococci in vivo.

3] *Parasite factors induced by the host environment.* [a] Biosynthesis of a hyaluronate-protein complex. When the initially rough group A streptococci are converted to mucoid form, hyaluronic acid at the surface of the capsule is probably combined with protein.

A relatively pure hyaluronic acid-protein complex can be iso-

lated by a simple method. Streptococcal strains in the mucoid stage are grown in broth, harvested by centrifugation, washed with Rogers' maintaining solution (which contains glycerophosphate, thioglycolic acid, and glutamine), suspended for seven hours with 7% glucose added, and centrifuged. The supernatant is dialyzed against distilled water. The final product is collected by lyophilization. Cells from one liter of medium yield 27 mg. of electrophoretically homogeneous material. The isolated fraction contains a significant amount of tyrosine.

When the product is treated with acid according to the Lancefield method of typing, a strong reaction is obtained with M-antiserum. This indicates that the protein portion of the hyaluronic acid complex is related to the M-protein, the type-specific substance of group A streptococci.

The nature of the conjugated protein is of interest, as well as the influence of hyaluronic acid on elimination of the protein from the host. The mechanism by which antigens are removed may be related to late sequelae of streptococcal infections. Presumably, some antigen of group A bacteria is distributed through connective tissue during infection, and damage results from interaction of antibodies and persisting antigen. The similarity of hyaluronic acid in ground substance and that produced by group A streptococci may greatly affect retention of the conjugated protein.

Many factors are involved in the biosynthesis of the complex. At minimal levels of glutamine, penicillin considerably increases synthesis of hyaluronic acid. As noted by other workers, cells made resistant to penicillin in vitro produce more hyaluronic acid, while, at the same time, M-protein is apparently lost. This may explain why no penicillin-resistant strains of bacteria are obtained from live sources or natural infections, since resistance to penicillin may be accompanied by loss in virulence.

[b] Type-specific potentiating factor. A great variety of substances can induce fibrinoid necrosis. A preparative or potentiating factor in this process is found in the soluble extracts prepared from group A streptococcal lesions. This agent enhances lethal and cardiotoxic properties of typhoid endotoxin, streptolysin O, erythrogenic toxin, and anaphylaxis.

Though properties are difficult to determine, the potentiating factor is clearly antigenic and conveys type-specific immunity. It is heat-labile, being destroyed at 60° C. maintained for half an hour,

and is produced by all types of group A streptococci tested, except a single type 4.

Activity of the enzyme transaminase, which increases in human serum after acute myocardial infarction, has been used to demonstrate independent toxicity of the potentiating factor. Transaminase also measures the extent of tissue damage after provoking injections of erythrogenic and other toxins.

As a working hypothesis, the potentiating agent may be assumed to be associated with the type-specific M-protein. The M-substance may exist as a complex. Under the described in vivo conditions, the M-substance behaves as a toxin, the physiologic unit of which is labile. In other environments, the M-substance may exist only as stable protein with no physiologic activity and simulate a toxoid. The immunologic specificity, however, is directed toward the heat-stable portion of the complex. Experiments to test this theory are now being made.

4] *Host factors and liability to infection (susceptibility of inbred mice to type 18 streptococci).* A spectrum of diseases can be produced with four strains of mice and a single type of group A streptococci. These vary from acute infection with highly virulent organisms in D_2b and male Balb strains to chronic disease in C58 mice, where bacteria may persist for months in focal abscesses.

In Swiss and female Balb mice, with highly resistant hosts, the organism manifests low virulence. Sex differences, with ten thousand-fold greater sensitivity in males, may indicate the effects of hormones. All these differences may be useful in observing acute and nonsuppurative sequelae of group A streptococcal infections.

Staff Meeting Report

Some Observations on the Fetus in Utero*†

Irwin H. Kaiser, M.D., Ph.D.[1]

Little is known of fetal life in utero, owing to the formidable difficulty of actual observation.

During collection of data in animal experiments, mother and fetus may be so disturbed that experimental results are meaningless.

New and relatively safe experimental methods, however, have lately been employed for withdrawal of blood. Unnecessary manipulations are avoided, and rupture of membranes can frequently be prevented.

In these experiments specimens are obtained from the cord and elsewhere, and the same fetus may be used repeatedly. Moreover, substances can be injected intravenously and their effects observed later, either before or after delivery. A biochemical study of fetal anoxia and acidosis is under way.

The developing infant has huge supplies of water and metabolites, an environment of constant temperature and humidity, and a highly efficient circulatory system. Yet these idyllic surroundings have limitations, which require adaptive mechanisms well worth investigating.

The embryo begins life under hypoxic conditions; only after formation of the placenta and the fetal circulation is progress made toward oxygen tensions of adult tissues.

Newborn infants are definitely known to have uncompensated acidosis and an unexplained increase of organic acid anions. After birth at term, conditions rapidly shift toward adult patterns.

The evidence implies that the unborn child derives some energy from anaerobic glycolysis in a state of acidosis. Steady maintenance of this acidotic situation is not understood. That a non-diffusible anion is produced by anaerobic glycolysis has been postulated but

*This is an abstract of a report given at the Staff Meeting of the University of Minnesota Hospitals on January 6, 1956. A copy of the complete report, including tables, may be obtained by writing to the Editor, UNIVERSITY OF MINNESOTA MEDICAL BULLETIN, 1342 Mayo Memorial, Minneapolis 14, Minnesota.

[1]Assistant Professor, Department of Obstetrics and Gynecology.

†These studies were supported by grants from the Louis W. and Maud Hill Family Foundation.

not yet proved.

The first step in research was to demonstrate that acidosis of the newborn is not a result of labor and delivery. Blood samples were obtained at elective cesarean section in otherwise normal human pregnancy, and pH was determined in fetal specimens withdrawn before delivery.

Average pH in the umbilical artery, which bears blood from fetus to placenta, was 7.26; in the umbilical vein, 7.32, and in the maternal uterine veins, 7.36. Since mean values corresponded remarkably well with those reported of infants at natural birth, acidosis is not a consequence of labor.

The next step was to select an experimental animal with fetuses of large size and fairly long gestation. Sheep are easily handled, pregnancy lasts about 150 days, and birth weight at term is 4,500 gm. Invaluable help was given by Doctors L. M. Winters and J. N. Cummings, of the Department of Animal Husbandry, and by the Institute of Agriculture.

Ewes about 6 years old were bred, and blood samples were obtained from ewe and lamb about 70, 88, 106, 124, and 142 days later.

Subjects were prepared for operation by intraperitoneal injection of nembutal, placed on their left sides, and held gently in position. The right lower quadrant was infiltrated with 1 per cent procaine.

The abdominal wall was opened and the uterus exposed. Since tapping of the uterine artery caused extreme spasm, blood was obtained from the right femoral artery. Venous blood was taken from a uterine vessel.

A radial incision was made over the fetus down to the amnion, frequently with little bleeding. The cord was palpated, and, if possible, vessels were punctured without rupturing the amnion. In twin pregnancies the procedure was repeated with the second fetus, which has its own membranes.

Ewes tolerated these procedures with surprising docility, and the majority remained in excellent condition throughout.

Blood samples were drawn into oiled heparinized syringes and refrigerated thereafter.

On each sample, the following determinations were done in duplicate: pH, carbon dioxide, oxygen, hemoglobin, total protein, sodium, potassium, calcium and magnesium, chloride, phosphate, pyruvate, and lactate.

Satisfactory data were obtained from 65 ewes. Of 106 lambs sampled in this group, 21 were excluded because of severe anemia,

obvious hypoxia due to experimental conditions, or loss of specimens.

A primary question as to whether the least possible anesthesia and manipulation preserved physiologic conditions was answered in the negative. In ewes, mean arterial oxygen saturation was substantially below the normal range of 97 to 99% at all stages and in every animal, even with no special disturbance in the ewe's general welfare.

For example, in the final test on day 142, maternal oxygen saturation was only 80% in arterial blood and 58% in the uterine vein. But hypoxia did not seem to exceed the sheep's adaptive capacities. Depletion probably resulted from the lateral recumbent posture, which this animal never assumes spontaneously. Yet no good way was discovered for obtaining fetal blood with the mother prone.

Fetal hemoglobin rose steadily from the seventieth day to term, though values never approached human levels of 18 to 22 gm.% at birth. Late in pregnancy, oxygen saturation of venous blood tended to fall. Venous hemoglobin averaged 8.3 gm.% on day 70 and 12.6 gm. on day 142; venous oxygen saturation dropped from 71 to 62%, and umbilical artery saturation from 28 to 22%.

Data on oxygen content could be used further, for instance, in learning about adaptations to needs of twins. Hemoglobin and oxygen content were similar for single and twin lambs until late pregnancy, when single values were slightly higher.

The arteriovenous oxygen difference between maternal arterial and uterine venous blood was always greater with twins, but was nowhere near double at any stage, except perhaps by day 142. Uterine blood flow was increased though not doubled, and blood was more completely cleared of oxygen. Thus the adaptive mechanism was twofold, and was both fetal and maternal.

Twins threw light on the effect of experimental manipulation. The side on which the lamb was situated and the order of sampling made little difference in mean values for pH, carbon dioxide content, or hemoglobin, but the second fetus sampled always had a lower oxygen content than the first, supposedly from time lost between samplings, from uterine manipulations, or both.

This point was settled by data gathered at later stages of pregnancy. The umbilical artery, which returns blood from the fetus to maternal circulation, contains a mixture of biochemically arterial and biochemically venous blood. Not much is known about pure venous blood of the fetus, though just this information might explain processes at the cellular level.

True venous blood was therefore withdrawn by puncture from the jugular vein. The neck of the fetus was brought under the uterine wall, maternal tissues were incised down to the membranes, and skin of the neck was clamped to the edges of the uterine incision, a proceeding to which the lambs regularly objected. The incision was then completed, and the fetal skin was anesthetized with procaine.

The neck was incised and the deep jugular vein dissected out. A second incision was made in the uterus over the cord, the cord was secured, and blood was taken simultaneously from the umbilical vessels and the jugular vein.

Although dissection took at least as much time as previous sampling of a first twin, oxygen level in the umbilical vein did not differ from values for single fetuses at a corresponding stage of pregnancy. This contrasts with findings in first and second twins at an earlier phase of development. Obviously, oxygen levels were reduced by manipulation of the uterus rather than by the time consumed in operation.

True venous blood values are of interest in themselves. For jugular pH levels, like oxygen content, are notably lower than those of mixed umbilical artery blood returning to the placenta, and carbon dioxide content as a rule is correspondingly higher. On day 124, for instance, vein and umbilical jugular artery pH may be 7.28 and 7.31, respectively, and carbon dioxide 56.4 against 53.2.

This confirms the expectation that on the venous side of the fetal capillary, at any rate, there is severe hypoxia with uncompensated acidosis.

The abilities of lamb and ewe to survive under adverse circumstances were observed in a single case, which holds great promise for future investigations.

After all blood sampling was completed without membrane rupture, the uterus and abdominal wall were closed. Despite total lack of aseptic precautions, the ewe did remarkably well, and the uterus was reopened on the following day. Amniotic fluid was clear and the lamb in excellent condition.

Editorial

The Minnesota Basic Science Law

The granting of a medical license in America has always been a function and right of the separate states. Examining boards for this purpose were set up by the legislatures in the various states early in their history. In Minnesota the original legislation controlling medical licensing was changed in 1927 with the enactment of the Basic Science Law. This law recognized a number of types of "Healing" and proceeded to set up, as a requirement, an examination in the basic sciences, for the successful completion of which a candidate is given a Basic Science Certificate. This certificate must then be presented to the examining board in healing at the time an application is submitted to obtain a license to practice.

The following quotation from the Act will serve to define "Basic Sciences" and the "Practice of Healing":

"Wherever the term 'Basic Sciences' is used in this Act and not otherwise specifically defined, the same shall be understood and construed to mean and include all matters pertaining to anatomy, physiology, pathology, bacteriology, hygiene and after 1931 chemistry, so far as the same relates to the human system or mind as generally treated in each or all of said subjects. Wherever the term 'Practicing Healing' or 'Practice of Healing' is used in this Act unless otherwise specifically defined, the same shall be understood and construed to mean and include any person not hereinafter excepted from the provisions of this Act who shall in any manner for any fee, gift, compensation or reward or in expectation thereof, engage in, or hold himself out to the public as being engaged in, the practice of medicine or surgery, the practice of osteopathy, the practice of chiropractic, the practice of any legalized method of healing or the diagnosis, analysis, treatment, correction or cure of any disease, injury, defect, deformity, infirmity, ailment or affliction of human beings or any condition or conditions incident to pregnancy or childbirth or examination into the fact, condition or cause of human health or disease, or who shall, for any fee, gift, compensation or reward or in expectation thereof, suggest, recommend or prescribe any medicine or any form of treatment, correction or cure therefor; also any person or persons, not hereinafter excepted from the provisions of this Act individually or collectively who maintains an office for the reception, examination, diagnosis or

treatment of any person for any disease, injury, defect, deformity or infirmity of body or mind, or who attaches the title of doctor, physician, surgeon, M.D., M.B., D.O., D.C., or any other word, abbreviation or title to his name indicating or designed to indicate that he is engaged in the practice of healing."

The law exempts Minnesota residents employed as follows from the Basic Science Act: Nurses, midwives, dentists, optometrists, chiropodists, barbers, cosmeticians, Christian Scientists, and other persons administering treatment or cures by exclusively mental or spiritual means, manufacturers or distributors of orthopedic appliances, drugs and poisons, and pharmacists, as long as they confine their activities within the scope of their respective licenses.

In order to qualify for the Basic Science examination, a candidate must be twenty-one years of age, a graduate of an acceptable Minnesota high school or its equivalent and be certified as to his or her moral character by two individuals. In 1955, the legislature passed an addition to these qualifications. Beginning January 1, 1965, the educational requirement will be two years of college work leading to a baccalaureate degree at the University of Minnesota or at an institution accredited to the University of Minnesota. The fee for taking these examinations is $25.00. In order to obtain a Basic Science Certificate, the candidate must pass each of the six examinations with a grade of 75% or better. Furthermore, the candidate must pass a minimum of four of the six examinations at one sitting. For one or two failures, the candidate must repeat these examinations and obtain the above grade, during the following calendar year only. The act requires that these examinations be given four times a year, on the first Tuesday of January, April, June and October, on the campus of the University of Minnesota. If a candidate fails three or more of the examinations, a new application and a new fee must be submitted in order to take the full schedule of examinations.

The Act also gives the Board the privilege of granting certificates without examination to individuals who have passed examinations in the Basic Sciences given by the National Board of Medical Examiners, and by legally qualified examining Boards. For such recognition of another board, the Act states that the standards of the other board must be the same as those of the Minnesota Basic Science Board, and that the other board must grant a like privilege to an individual who holds a Minnesota Basic Science Certificate on the basis of the successful passage of the examination (the N.B.M.E. is exempt from this last qualification). At present, the list of examining boards, in addi-

tion to the N.B.M.E., with whom reciprocity, in whole or part, exists, generally on an individual basis, reads as follows: Alaska, Arizona, Arkansas, Colorado, Indiana, Kansas, Kentucky, Michigan, Nebraska, Nevada, New Mexico, New York, North Carolina, Oklahoma, Oregon, South Dakota, Tennessee, Texas, Vermont, Virginia and Wisconsin. The fee for obtaining a Basic Science Certificate in this manner is $50.00.

In summary it might be noted that as of July 1, 1955, the Minnesota Basic Science Board has issued 13,199 certificates; 6840 have been granted on the basis of passing the board's written examination; 4032, on the basis of previous licensure (representing Minnesota residents who had a Minnesota license to practice an healing art at the time that the Basic Science Law was enacted); 1443 by reciprocity with the National Board of Medical Examiners; and 884 by reciprocity with the various state examining boards.

The Minnesota Basic Science Board: President – James S. McCartney, M.D., Professor of Pathology; Vice-President – R. George Hazzard, D.C.; Harold R. Tregilgas, M.D.; Carl Morrison, D.O.; Secretary-Treasurer – Raymond N. Bieter, M.D., Professor of Pharmacology.

Minnesota Medical Foundation

Health Forum

Plans for the Minnesota Medical Foundation Health Forum, previously announced in this BULLETIN, have progressed in good fashion. Public interest has been indicated by response to stories about the Forums which have appeared in the daily newspapers.

The program for the first Forum is as follows:

YOU AND YOUR HEALTH

Heart and Blood Pressure

	MINNEAPOLIS	ST. PAUL
Place:	Lyceum Theater	Theater Section, St. Paul Auditorium
Time:	Sunday, Jan. 29; 4:00 P.M.	Wednesday, Jan. 25; 8:00 P.M.
Chairman:	Dr. Robert E. Priest	Dr. A. E. Ritt
Moderator:	Dr. C. J. Watson	Dr. C. J. Watson
Panel Members:	Dr. Reuben A. Johnson Dr. Harold Miller Dr. Louis Tobian Dr. Richard L. Varco	Dr. John F. Briggs Dr. Joseph F. Borg Dr. Louis Tobian Dr. Richard L. Varco
Sponsors:	Hennepin County Medical Society Minneapolis Health Dept. Minneapolis Star	Ramsey County Medical Society St. Paul Health Department St. Paul Dispatch-Pioneer Press

and the

Minnesota Medical Foundation

Subject for the second Forum will be Miracle Drugs and for the third and final Forum, Cancer. Further information concerning the Health Forums may be obtained by writing Health Forum, 1342 Mayo Memorial, Minneapolis 14, Minnesota.

Medical School Activities

THE STUDENTS' CORNER

A Report on the Medical Students' Advisory Council

The Medical Students' Committee, which has come to be called the Medical Students' Advisory Council is the student representative body in the Medical School. It was formed for the purpose of advancing the interests and well-being of all medical students and of the University.

The members of the Student Council are the elected officers of the freshman, sophomore, junior, and senior classes. In addition three members are elected from and by the Council of the previous year to assure some continuity in the council from year to year. Thus it has fifteen student members. The Dean and Assistant Deans of the Medical School are ex-officio members of the Council. The Council meets monthly throughout the school year to conduct its business.

Any medical student can, through his representatives, bring any item of business to the attention of the Council. Some general areas of interest in the Council are student-faculty relationships, grading and ranking of medical students, competition between students, curriculum evaluation, and methods of testing. In the past the Council has been concerned with use of the honor system, a senior year "free period," and preceptorships.

One of the most important projects of the Council was a poll of student and faculty opinion on various aspects of medical education at the University of Minnesota Medical School. That survey was conducted in the sping of 1953, and the results were reported at a hospital staff meeting in 1954. This was, as far as is known, the only such survey that has been carried out in the Medical School. This survey revealed, among other things, that a majority of the students and faculty felt that the present grading system should be changed. It is interesting to note that at the present time a new grading system for the Medical School has been proposed and will probably soon be adopted.

At the present time one of the Council projects is the establishment of a group of medical students who would be available to answer questions that pre-medical students might have concerning the Medical School. Many medical students feel their pre-medical counsellors

had little information about the Medical School. It is hoped that an information bureau manned by medical students will provide useful information for students interested in medical school.

Another current project of the Council is the student-faculty coffee hour. The first of these coffee hours was held in 1954. The purpose of the coffee hours is to provide an informal opportunity for students and faculty to get together. Mr. Ray Amberg, Director of the University of Minnesota Hospitals, has thoughtfully provided funds for these coffee hours from income derived from automatic vending machines in the hospital. The Council currently organizes a coffee hour every other week during each school quarter.

The Council, as a representative group of students, is also of help to the faculty in sounding out student opinion. Not only are some reports of faculty committees read before the Council, but members of the Council also occasionally meet with some of the faculty committees. In this and other ways, the Student Council has been an organization useful to both students and faculty.

RALPH B. SWANSON
President
Medical Students' Advisory Council

Faculty News

On January 1, DR. N. L. GAULT, JR., assumed his duties as *Assistant Dean of the College of Medical Sciences,* a responsibility he will share with DR. WILLIAM F. MALONEY. Dr. Gault spent the fall months studying rheumatology and rehabilitation of the arthritic patient at the Hospital for Special Surgery, Cornell Medical Center; at Columbia University College of Physicians and Surgeons; and with the Study Group for Rheumatic Diseases, New York University Medical Center. This period of study was under the auspices of the National Foundation for Infantile Paralysis. An *Assistant Professor* in the Department of Medicine, Dr. Gault is in charge of the Collagen Disease Out-Patient Clinic.

DR. RICHARD T. SMITH, *Assistant Professor,* Department of Pediatrics, presented a paper at the annual meeting of the American Rheumatism Association in Bethesda, Maryland, December 9, 1955, entitled "Studies on a Heparin-Precipitable Fraction of Human Plasma."

Coming Events

January 30–February 1	Continuation Course in Emergency Surgery for General Physicians
February 2–4 . . .	Continuation Course in Mental Deficiency for General Physicians, Pediatricians, Obstetricians, and Child Psychiatrists
February 6–11 . . .	Continuation Course in Neurology and Neurosurgery for General Physicians and Specialists
February 8	J. B. JOHNSTON LECTURE; "The Measurement of Enzymes in Single Cell Bodies"; *Dr. Oliver H. Lowry,* Professor and Head, Department of Pharmacology, Washington University School of Medicine, St. Louis, Missouri; Mayo Memorial Auditorium; 8:15 P.M.
February 13–15 . .	Continuation Course in Internal Medicine for Internists
February 14	MINNESOTA PATHOLOGICAL SOCIETY LECTURE; "The Etiology of Hyperadrenalism"; *Dr. Joseph W. Jailer,* Associate Professor, Department of Medicine, College of Physicians and Surgeons, Columbia University, New York City; Mayo Memorial Auditorium; 8:00 P.M.
February 16–18 . .	Continuation Course in Cancer Detection for General Physicians
February 16	CLARENCE M. JACKSON LECTURE; "The Significance of the Sero-Flocculation Reaction"; *Dr. Harry S. Penn,* Associate Professor, Department of Radiology, University of California at Los Angeles Medical School, Los Angeles; Mayo Memorial Auditorium; 8:00 P.M.
February 27–29 . .	Continuation Course in Eye, Ear, Nose, and Throat for General Physicians

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 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.