VOLUME XXVIII • NUMBER

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:

University of Minnesota Medical Bulletin

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VOLUME XXVIII *February 1, 1957* NUMBER 7

CONTENTS

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

Staff Meeting Report

Sex Determination from Nuclear Morphology*

Edgar L. Makowski, M.D.[1]

The concept of sex determination from nuclear cytology owes its origin to the observations of Barr and Bertram in 1949. A small body about one micron in diameter was noted adjacent to the nucleolus in the cells of some cats but was absent in others. This chromatin mass known as the "nucleolar satellite" migrated from the nucleolus toward the nuclear membrane in the recovery phase. Since it gave positive cytochemical tests for DNA, a chromosomal relationship was postulated. Significantly, this chromatin mass was found only in the neurons of *female* cats. Because of the constancy of this structure to the sex of the host, the mass was designated the "sex chromatin mass."

The sex chromatin mass is a planoconvex structure with its flattened surface adjacent to the nuclear membrane. The sex chromatin mass is found in nuclei of dog, mink, marten, ferret, racoon, skunk, goat, and deer and is present in all cells of these except the neuron. Nuclei in the rodent and rabbit contain multiple chromatin masses adjacent to the nucleolus so that a sex difference is not determinable cytologically. The chromatin mass is a stable body and is unaltered by experimental variations in sex hormone milieu.

Moore *et al* studied skin specimens from normal human subjects. In the female specimens they were able to visualize the sex chromatin mass in 52 to 85 per cent of nuclei with an average incidence of 69 per cent. A similar mass, smaller in size, was found in male specimens in 1 to 14 per cent of nuclei with an average incidence of 5 per cent. Davidson and Smith described a morphological sex difference in the neutrophils of human blood smears. They noted in the female a distinct appendage, the "drumstick", projecting from a nuclear lobe of the mature neutrophil. More than one "drumstick" is never found in the same cell. The incidence in the female is at least 6 "drumsticks" per 500 neutrophils. In males, these authors failed to demonstrate any

* This is an abstract of a report given at the Staff Meeting of the University of Minnesota Hospitals on January 18, 1957. A copy of the complete report, including all tables and references, may be obtained by writing to the Editor, UNIVERSITY OF MINNESOTA MEDICAL BULLETIN, 1342 Mayo Memorial, Minneapolis 14.

[1] Medical Fellow, Department of Obstetrics and Gynecology

nuclear appendages in 500 neutrophil nuclei. Briggs and Kupperman recently studied the usefulness of the blood smear in determining the chromosomal sex. They modified the above criteria in 15 to 87 cases with endocrinopathies because the incidence of "drumsticks" was below 6 in presumably known females.

Exfoliative cytology was first applied in this connection to the buccal mucosa by Marberger, Boccabella, and Nelson in 1955. This study included normal anatomical males and females in various age groups. The incidence of the sex chromatin body in the buccal mucosal smear of females was 20 to 79 per cent of 100 nuclei examined, with a mean of 45.6 per cent. The incidence in males was 0 to 4 per cent, with a mean of 0.6 per cent. This technical concept is also applicable to amniotic cellular debris, since the cells in amniotic fluid originate only from the integument, amnion, or mucosa of the fetus.

Methods and Results

Amniotic fluid was obtained from 44 pregnant women by direct aspiration of the amniotic sac with a needle and syringe. The fluid was centrifuged for 15 minutes and the sediment thinly spread on a slide treated with egg albumen. The smear was immediately immersed in equal parts of 95 per cent ethyl ether and ethyl alcohol for 2 to 24 hours. The fixed smears were then passed through 70 per cent and 50 per cent ethyl alcohol and distilled water for five minutes each. They were then stained for 8 minutes in 1 per cent cresyl violet and differentiated in 95 per cent ethyl alcohol for 2 to 3 seconds. The stained smears were rinsed in absolute ethyl alcohol until nuclear detail was clear on examination under the high dry objective of the microscope. They were then mounted in Permount.

The mounted smears were studied under the oil-immersion objective. Many nuclei were unsuitable for this study because of pyknosis, hypochromasia, and fragmentation. Only vesicular nuclei with intact nuclear membranes were counted. The anatomic sex of the new born infant was established on physical examination of the external genitalia.

Table I. Incidence of Sex Chromatin Body in Amniotic Fluid Cell Nuclei

	Observer 1			*Observer 2*		
	No.	Range (%)	Mean (%)	No.	Range (%)	Mean (%)
Male	20	0-17	9	6	6-22	13
Females	24	49-78	61	6	42-70	54

Results are summarized in table I. Note that there is no overlap between the maximum counts on male fetuses and the minimum on females. The means are separated by a gap 4 to 6 times the mean for male fetuses. Since there are no erroneous identifications of anatomic sex in the group, the differences are highly significant.

Buccal mucosal smears were obtained from 21 patients with gonadal aberrations. The mucosa was scraped with a sterile tongue blade and the scrapings thinly spread on a slide treated with egg albumen. The fixation, staining, and mounting of these smears was as that described above.

Only well stained vesicular nuclei with intact nuclear membranes were studied. One hundred such nuclei were counted.

A control series of buccal mucosal smears was obtained from 9 males and 8 females. In the specimens from males, the incidence of the sex chromatin mass ranged from 0 to 5 per cent. In smears from normal females, it ranged from 20 to 58 per cent.

An amniocentesis was performed on a pregnant patient at 36 weeks gestation who previously delivered two female infants having adrenogenital syndrome. Fifty-six per cent of the cells in amniotic fluid contained the sex chromatin mass. The mother again delivered a female pseudohermaphrodite. A buccal mucosal smear obtained from the infant showed 48 per cent of the cells containing the sex chromatin mass.

Two cases of female pseudohermaphroditism due to adrenal hyperplasia and one case of male pseudohermaphroditism have been studied. The chromosomal sex patterns in the female pseudohermaphroditis and in the male pseudohermaphrodite were female and male respectively.

Buccal smears have been studied in 13 patients with gonadal dysgenesis. Table II summarizes the pertinent data pertaining to this group. 12 of these patients had a male chromosome pattern and one a female pattern. The diagnosis of gonadal dysgenesis was confirmed by exploratory laparotomy in two cases. One of these individuals had elevated blood pressure. Three cases had coarctation of the aorta, two cases had osteoporosis, and four cases had lymphedema of the extremities.

Buccal mucosal smears were obtained from five patients with Klinefelter's syndrome. Three of these patients had a male chromatin pattern and two a female pattern. Physical examination on the two

patients with female chromatin pattern showed bilateral gynecomastia, male hair distribution, normal penis, palpable prostatic tissue, and atrophic testes in the scrotal sac. Testicular biopsy of one patient showed hyaline structures which may represent completely atrophic tubules. A few nests of small cells with granular cytoplasm which may represent atrophic Leydig cells were seen. The physical examination and testicular biopsy of the three patients with a male chromatin pattern did not appreciably differ from those of the two patients with a female chromatin pattern. Six ovarian dermoid cysts which were studied showed a female chromosomal pattern. The shape and the size of the chromatin body was studied in five cases of cervical squamous cell carcinoma. The average diameter was one micron with no appreciable alteration in shape from that seen in non-malignant cells.

Table II. Pertinent Findings in 13 Cases of Gonadal Dysgenesis

Patient	Age in yr.	Ht. in inch.	Cubitus valgus	Nuchal webbing	Coarctation of aorta	FSH MU/24 hr.	Incidence of Chromatin Body
------	37	57	−	+	−	96	0%
------	21	55	−	−	−	−	20%
--------	19	58	+	+	+	−	0%
--------	19	57	+	−	+	64-128	2%
-------	18	53	+	+	−	−	0%
--------	18	56	+	−	−	24	2%
--------	17	56	+	−	−	192	5%
--------	16	57	+	+	−	16-32	0%
-------	3	37	+	+	+	48	1%
-------	2	31	+	+	−	−	2%
-------	2	−	+	+	−	−	2%
-------	3/12	22	−	+	+	6	4%
--------	1/12	19	−	+	−	−	5%

Discussion

The genetic sex in mammals is determined at the moment of fertilization. It depends upon whether an X or a Y sperm unites with the ovum. The genetic sex determining factors are contained partly in the sex chromosomes and partly in the autosomes. The careful studies of Bridges with *Drosophila* and Goldschmidt with the gypsy moth, *Lymantria dispar,* showed that the simple presence of sex chromosomes (XX or XY) is insufficient to explain sex determination in these insects. The definitive sex is the result of a balance of genetic determinants which are always present in the same individual. These genes

are balanced in regard to each other in such a way that a preponderance of femaleness over maleness leads to a female offspring and *vice versa.* Probably this balance theory of sex determination is true for man also. A fruit fly with two X chromosomes but three of each set of autosomes is not a female but an intersex. This indicates that the autosomes evidently contain certain male-determining genes while the X chromosomes contain certain female-determining genes.

The phenotypic sex, or the sex which is determined by visible primary and secondary sex characters, is known to depend on hormones and other environmental factors, and is experimentally reversible. Experimental evidence exists indicating that it is not the sexual genotype which is responsible for the specific differentiation of secondary sex characters but rather that the embryonic ovary or testis controls by hormonal means their alternate differentiation. This dependence on outside influence applies even to the germ cells themselves. An XX primordial germ cell typically develops into an egg in some cases, not because it has two X chromosomes but because it finds itself in the cortical part of a gonad and an XY primordial germ cell develops into a sperm in some cases, not in response to its own chromosomal constitution, but as directed by its medullary location in a gonad.

Somewhere in normal development the genetic constitution is decisive, apparently when the neutral gonad is initially developed. If the somatic cells of the gonad are XX, then the germ cells located in the cortical layers proliferate more than those in the medulla while the opposite is true when the gonadal cells are XY. The sexual genotype presumably exerts its influence directly at this stage only, and the further control of suitable sexual development is under various hormonal influences.

Sex chromosomes have heterochromatic response, or a complex staining pattern. It has been assumed that the heterochromatic portions of the two X chromosomes in the female cells unite to form this visible sex chromatin mass. The Y chromosomes of male cells are small, thus the sex chromatin mass in male nuclei is too minute to be detectable by light microscopy. In a few of the male nuclei there is a visible sex chromatin mass which may be an abnormal chromosomal complex such as XXY.

The term hermaphroditism is frequently used to refer to the various imperfect phenotypes which may more accurately be labeled intersexual. One of the most practical classifications of ambisexual development has been formulated by Wilkins as follows:

A. Gonadal dysgenesis
B. Intersexuality
   1. True hermaphroditism
   2. Male pseudohermaphroditism
   3. Female pseudohermaphroditism without adrenal disorder
C. Female pseudohermaphroditism due to virilizing adrenal hyperplasia

In most human intersexes, it has not been possible to establish with certainty whether the phenotype is XX or XY. The greater similarity of an intersex to a female, for instance, than to a male, is no criterion by which to judge its genetic XX or XY nature. There are developmental considerations which suggest that perhaps most human intersexes are XX in constitution which have, under various modifications of the femaleness-maleness balance system, developed into the many grades of weak, medium, and strong types of intersexes. There is, however, evidence that a specific human intersex type consists of XY individuals. Several reported pedigrees show that this type of intersexuality is transmitted by normal females who are heterozygous for an allele which in XY individuals results in the intersexual condition.

Grumbach *et al* have advocated the use of the term *gonadal dysgenesis* instead of the more commonly used term *ovarian agenesis* for conditions in which a mature gonad is absent and the anatomic sex is female. The gonads on microscopic examination may show rudimentary mesonephric elements which in reality represent dysgenesis and not agenesis.

The stigmata of gonadal dysgenesis are in varying frequency, normal infantile female external genitalia, absence of secondary sexual characteristics, primary amenorrhea, infertility, short stature, lymph edema of distal portions of the extremities, high urinary titers of gonadotropin, decreased urinary excretion of 17-ketosteroids, hypertension, and multiple congenital anomalies such as nuchal webbing, cubitus valgus, coarctation of the aorta, broadening of the chest, late union of epiphyses, and osteoporosis.

According to present embryological concepts in gonadal dysgensis, the germinal epithelium of the fetal testis is affected by some deleterious agent before the ninth week of embryonic life. The male characteristics are suppressed and in the absence of fetal testicular secretion, the embryo becomese feminized with more or less complete female genital tracts and external genitalia. The syndrome of gonadal dysgenesis has a predominantly male chromosomal sex ratio. Sixty cases

of gonadal dysgenesis have been reported of which 40 were chromosomal males and 20 were chromosomal females. Grunbach *et al* suggest that, "the fetal testis embryologically differentiates before the ovary . . . the male gonad, particularly its germinal elements, may be more susceptible to damage from some unknown cause in early intrauterine life than the fetal ovary." The occurrence of congenital anomalies in gonadal dysgenesis has been ascribed to mutant genes or the influence of an injurious environment.

The sex of ambisexual individuals should ideally be decided soon after birth. The psychosexual development of an ambisexual infant is likely to be more dependent on the psychological sex than on the type of gonad or the chromosomal sex. Any alteration of the infant's gender after three years of age is considered precarious to the infant's psychosexual development since at this time a natural stirring of sexual feeling develops. The degree of devlopment of the external genitalia in intersexuals should be the determining factor. Patients with female pseudohermaphroditism due to the adrenogenital syndrome should be reared as females and placed on cortisone therapy to suppress virilization and ACTH elaboration from the anterior pituitary gland. In some of the ambisexuals, substitutional sex hormone therapy and perineal plastic operations are indicated.

Staff Meeting Report

The Increasing Incidence of Unexplained Liver Necrosis*†

Joel G. Brunson, M.D.,[1] Philip L. Eckman, B.A.,[2] and John B. Campbell, B.A.[3]

Focal areas of necrosis may be found in the liver in a number of infections and toxic diseases accompanied by prolonged shock, notably bactermia caused by Gram-negative bacilli. Similarly, blotchy areas of hemorrhagic liver necrosis are not uncommonly seen and are characteristic of such conditions as eclampsia and carbon-tetrachloride poisoning.

Pale areas of ischemic hepatic necrosis, on the other hand, are of relatively rare occurrence and are thought to represent infarcts. Pass, in 1935, reported 22 cases in which pale infarcts of the liver were associated with polyarteritis. He reported 30 additional cases in which pale infarcts were associated with embolism, thrombosis, or hypoplasia of the hepatic artery. Lund, Stewart, and Lieber, in 1935, reported 7 instances of hepatic infarction associated with embolic or thrombotic occlusion of the hepatic arterial system. Woolling, Baggenstoss, and Weir, in 1951, in a review of over 18,000 consecutive autopsies at the Mayo Clinic, found only 54 instances of liver infarction. Of these, 10 were associated with hepatic artery occlusion, 11 with portal vein occlusion, and 16 with combined occlusions of the portal vein, hepatic artery, or hepatic veins. In 17 instances no vascular occlusion was demonstrated.

A review of current autopsy material from the University Hospitals disclosed an apparent increase in the incidence of unexplained liver

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* This is an abstract of a report given at the Staff Meeting of the University of Minnesota Hospitals on January 25, 1957. A copy of the complete report, including all tables and references, may be obtained by writing to the Editor, UNIVERSITY OF MINNESOTA MEDICAL BULLETIN, 1342 Mayo Memorial, Minneapolis 14.

† These studies were supported in part by grants from the Minnesota Heart Association, the U. S. Public Health Service (H-2540), and the Graduate School Research Fund of the University of Minnesota.

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necrosis. To evaluate this impression, a thorough review of a larger number of autopsies was undertaken.

Materials and Methods

3,229 autopsy protocols of patients examined at the University of Minnesota Hospitals morgue from 1946 through 1955 were reviewed and analyzed for gross and microscopic evidence of liver necrosis. All deaths which occurred during these years were included in the survey, except still births and infants with multiple congenital defects who died shortly after birth.

In the preliminary survey, every case of liver necrosis was included and the microscopic slides examined. Following this examination and in conjunction with a study of the clinical and autopsy records, cases were excluded in which necrosis was associated with eclampsia, cirrhosis, "subacute yellow atrophy," intrahepatic neoplasms, chemical poisoning, abscess formation, or vascular disease, such as polyarteritis. Instances of focal necrosis associated with Gram-negative bacilli bacteremia, shock, or congestive heart failure also were eliminated from further consideration. The remaining cases, which are the subject of this report, include instances of pale, ischemic liver necrosis (liver infarcts) or hemorrhagic necrosis involving two or more contiguous liver labules. This type and degree of necrosis will be referred to as liver necrosis in the remainder of this report.

Results

As shown in table I, a striking increase in the incidence of liver necrosis has occurred in the years 1953-1955. Of the 62 cases collected over the ten-year period 1946-1955, 45, or 72%, occurred in the latter three years. Of the total number, 43 occurred in patients on whom some surgical procedure had been performed, an incidence of approximately 69%. It is also of interest that in approximately 40% of the total cases, some degree of jaundice was observed. In 33 patients, liver necrosis followed abdominal surgery in which opportunity for damage to the hepatic vascular system was present, but in the remainder this factor was not important. The latter group included patients with a variety of conditions including myocardial infarction (4 cases), bacterial endocarditis (2 cases), carcinoma of the pancreas, pancreatitis, pulmonary embolism, gastric ulcer, and granulocytic leukemia (1 each).

Morphologic features of the lesions: The gross characteristics of the lesions, derived from descriptions in the autopsy protocols, are sum-

marized in Table II. Those lesions described as "pale" consisted of single or multiple areas of yellowish-gray infarct, usually surrounded by a zone of hemorrhage. These were described as being triangular or irregular in shape, slightly firmer than the surrounding liver parenchyma, and varying in size from a few millimeters to areas as large as 10 centimeters in diameter.

TABLE I
SUMMARY OF CASES

YEAR	Number of autopsies reviewed	Number of cases of liver necrosis	Sex		Service			Jaundice	
			Male	Female	Medicine	Surgery	Pediatrics	Present	Absent
1946	302	2	2	0	2	0	0	2	0
1947	254	0	-	-	-	-	-	-	-
1948	277	1	1	0	0	1	0	0	1
1949	265	2	2	0	1	1	0	2	0
1950	323	3	2	1	1	2	0	1	2
1951	340	3	0	3	0	2	1	1	2
1952	346	6	5	1	2	4	0	2	4
1953	435	14	9	5	2	12	0	4	10
1954	365	14	8	6	5	9	0	4	10
1955	322	17	12	4	3	12	2	8	9
TOTALS	3,229	62	42	20	16	43	3	24	38

The lesions classified as "hemorrhagic" consisted of multiple areas of reddish to purple parenchymal discoloration averaging approximately 1 to 3 centimeters in diameter. In these areas, the lobular pattern of the liver was described as "prominent or accentuated," and the remainder of the liver flabby or extremely soft in consistency. Eighty per cent of these lesions involved both lobes of the liver.

In 16 instances the liver was described only as having a pronounced nutmeg appearance or as being softer or more flabby in consistency than normal.

TABLE II
SUMMARY OF GROSS CHARACTERISTICS

Number of cases	Pale		Hemorrhagic		Not stated or described as "nutmeg" or "flabby"
	Single	Multiple	Localized	Diffuse	
62 (69 gross alterations)	8	25	4	16	16
	48%		29%		23%

On microscopic examination, two types of lesions were observed. In 59% of cases, areas of ischemic or coagulative necrosis were seen, and in 24%, areas of necrosis associated with hemorrhage. In 16%, both types of lesions were observed.

Microscopically, the pale lesions appeared as typical areas of ischemic necrosis or infarction. In these lesions the architectural pattern of the liver was preserved, but there was necrosis of all elements which was manifested by pyknotic nuclei, karyolysis and karyorhexis, and homogeneous, deeply acidophilic cytoplasm. Inflammatory cells, nuclear

debris, and a varying degree of hemorrhage surrounded these areas of necrosis. In many instances scattered, smaller areas of ischemic necrosis were present in the adjacent liver parenchyma.

In some lesions, there was little or no inflammatory reaction about the periphery and no surrounding hemorrhage. In others, the liver cells in the infarcted area showed extensive calcification. Proliferating fibrous tissues was present in and about the areas of infarction in some instances, and occasionally bile duct proliferation was observed within and around the area of necrosis. In one case, the degree of connective tissue proliferation and the numerous bile ducts produced a picture which simulated post necrotic cirrhosis, but the remainder of the liver appeared normal. This appeared to be an organizing infarct, and its morphologic features suggested that it had been present for a considerable length of time prior to patient's death.

Microscopic examination in other cases disclosed numerous scattered areas of coagulation necrosis of the liver cords which involved at least two lobules of the liver. A neutrophilic cellular reaction was usually present at the periphery of these lesions, but hemorrhage was not a prominent feature.

Microscopic examination in some instances showed the presence of blotchy, confluent areas of hemorrhage and necrosis with complete disruption of the arrangement of the liver cords, often involving several lobules. These lesions in general appeared to destroy more completely the architectural pattern of the liver than did the previously described types, and bore a striking resemblance to the changes which occur in the liver in eclampsia.

Discussion

This survey indicates that there has been a definite, marked increase in the incidence of hepatic necrosis, with respect both to classic, localized, pale type of infarcts and the confluent, diffuse areas of ischemic and hemorrhagic necrosis. It is also obvious from this survey that the most striking increase occurred in the years 1953 through 1955. With this rise, many instances have appeared in which no anatomic basis for the infarction has been demonstrated. In 52 of these 62 cases, or approximately 84%, no cause was evident at the time of post mortem examination to explain the presence of these lesions, in contrast with the series reported by Woolling, Baggenstoss, and Weir in which, in 17 of 54 cases, or 31%, no vascular occlusion or trauma was demon-

strated. Several possible factors which may be involved in the production of these lesions warrant discussion.

Since the advent of the antibiotics, there has been an increase in the incidence of Gram-negative bacteremia. One of the prominent clinical features associated with this condition is profound shock and cardiac failure. In only 8 cases in this series, however, was Gram-negative bacteremia present. Furthermore, according to other reports the hepatic lesions which occur in Gram-negative bacteremia and shock are more often scattered, focal areas of necrosis without predilection for any particular part of the lobule. Our own observations in 19 consecutive cases of death due to Gram-negative bacteremia and shock at the University Hospitals in the years 1950 to 1955 confirm these reported findings.

Likewise, the presence of shock from other causes must be considered. In 39 of these cases (63%) shock, ranging from a few hours to several days in duration, had been present. The factor of shock alone, however, appears to be of little importance, since it has been shown that the hepatic lesions in this condition are characterized by regular, centrilobular hemorrhage and necrosis.

Of particular interest, however, is the possible role of the vasopressor amines in the pathogenesis of the hepatic lesions. Recent studies have shown that the intravenous administration of any of the sympathomimetic amines to dogs may be associated with the development of diffuse hepatic necrosis. Whether such lesions may follow the administration of these agents to humans is, of course, a matter of speculation. Of the patients in this series, 48 (77%) were treated with vasopressor agents. Similarly the precipitous increase in the incidence of liver necrosis coincides with the general increase in the use of these substances in patients in shock. Although no definite correlation has as yet been obtained between dosage and extent of liver necrosis, preliminary data indicate that high dosages of the pressor amines are associated with more severe and more extense liver lesions. It is possible also that the administration of these substances, by prolongation of life after a period of shock, may allow hepatic lesions to develop which otherwise would not become manifest.

Editorial

Physiologic Periodicity

For more than a hundred years scientists have observed with interest striking differences between day and night blood levels and rates of excretion of a number of physiologically important substances. In most instances, the practical significance of these observations was not apparent. Recently, however, investigators have found evidence of a 24 hour cycle of adrenal cortical activity and this finding has reawakened interest in physiologic periodicity in general. Blood levels of adrenocortical hormone rise in the early morning hours to a peak between 6 and 9 A. M., fall thereafter to reach a low point at midnight and then begin to rise again at about 3 A. M. The rate of urinary excretion follows to some extent this same type of cyclic pattern. Though serum concentrations of electrolytes remain remarkably constant, their rates of excretion also follow a cyclic rhythm which appears related to that of the adrenal cortex. For example, the urinary excretion of sodium, potassium, bicarbonate, uric acid and water is described markedly at night and rises sharply in the early morning hours.

These studies seem to be approaching at least three practical goals. First, they may provide an explanation for certain puzzling occurrences such as the increased incidence of attacks of bronchial asthma and cardiac dyspnea at night and the periodicity of gouty attacks and convulsive seizures. Secondly, they may result in improved experimental design, notably in the testing of new therapeutic agents. In the past, baseline determinations often have been obtained without regard for physiologic periodicity. For example, the design of an experiment may provide for baseline observations during the morning hours, then, after introduction of the test agent, measurement of its effects in the afternoon. Clearly, such a design may lead the investigator to assign undue significance to changes which were merely the expression of a diurnal variation, a part of the body's homeostatic physiology.

Finally, in these rhythmic variations, nature is providing us with an experiment of unique investigative value. Thus the effects of varying blood levels of hormones may be assessed at "physiologic" concentrations without the artefacts often produced by exogenous administration, such as inhibition of endogenous production of hormone.

Medical School Activities

Faculty News

DR. C. WALTON LILLEHEI, *Professor,* Department of Surgery, and DR. RICHARD A. DE WALL, *Research Fellow* of the American Heart Association, Department of Surgery, were presented the AAAS - Ida B. Gould Memorial Award for Research on Cardiovascular Problems at the recent annual meeting of the American Association for Advancement of Science in New York. This was the first presentation of this award of $1,000, and it honored the pioneering developments of Doctors Lillehei and De Wall in the techniques of intracardiac Surgery.

DR. LEO G. RIGLER, *Professor and Head,* Department of Radiology, will address the staffs of the Veterans Administration Hospital and the University of Michigan Hospital and the members of the Washtenaw Medical Society on January 28 on the subject "The Acute Abdomen."

DR. CHARLES M. NICE, JR., *Assistant Professor,* Department of Radiology, visited important radiological centers in Europe during October and November, 1956.

DR. ARNOLDS VEINBERG has been appointed *Clinical Instructor* of Radiology in the Radiation Therapy Section.

DR. JEROME T. SYVERTON, *Professor and Head,* Department of Bacteriology and Immunology, served as Chairman of the first meeting of the Conference on Cellular Biology, Nucleic Acids, and Viruses sponsored by the New York Academy of Sciences, January 3 to 10, 1957. Dr. Syverton also presented a paper at this conference entitled "Comparative Studies of Normal and Malignant Cells in Continuous Culture."

DR. ROBERT A. GOOD, *Professor,* Department of Pediatrics, will participate in a continuation course in Pediatrics at the University of Kansas Medical School, March 11-13, 1957, and will speak on the subjects "Disturbances in Renal Function in Childhood" and "Disturbances in Globulin Formation." Dr. Good will also give one of the principal addresses at the spring session of the American Academy of Pediatrics in Washington, D. C., in March on the subject "Experiments of Nature."

Alumni Association

Dr. Edward M. Gans Honored

DR. EDWARD M. GANS, '05, Harlowton, Montana, was recently selected by the House of Delegates of the American Medical Association to wear its gold medal and bear the title of general practitioner of the year. Dr. Gans was born in St. Cloud, Minnesota, in 1875. After graduation from St. Cloud Teachers College, he taught for three years and then enrolled in the University of Minnesota Medical School on the urging of a friend. Upon graduation, he took up the general practice of medicine in Eveleth, Minnesota, and later moved to Montana where he has since practiced continuously. He is remembered here by former fellow students and friends as a tall, lean, friendly individual. One stated, "His life has been medicine, and he loves it."

We take pleasure in congratulating Dr. Gans in this honor bestowed on him. In bearing this honor, he is the arch-type of the general practitioner, skillful, patient, and devoted to the responsibilities his patients place on him.

Alumni News

DR. E. S. MURPHY, Missoula, Montana, was recently installed as president of the Montana Medical Association. DR. JOHN A. LAYNE, '34, Great Falls, was elected 1957-58 president of the association.

DR. RICHARD J. KREBSBACH, '54, Hawthorne, California, is *Assistant Medical Director* of Northrop Aircraft Corporation.

DR. SAM F. SEELEY, '26, *Brigadier General,* Medical Corps, United States Army, is stationed at the Valley Forge Hospital, Phoenixville, Pennsylvania.

DR. WILLIAM H. A. WATSON, '46, St. Paul, Minnesota, is *Speaker* of the House of Delegates of the Minnesota Chapter, American Academy of General Practice.

DR. CARL A. PETERSON, '42, is *Assistant Clinical Professor* of Pathology, Stanford University Medical School, Palo Alto, California.

Minnesota Medical Foundation

The George A. Macpherson Scholarships

The scholarship program for medical students sponsored by the Minnesota Medical Foundation has been commented upon in the pages of the BULLETIN from time to time. It is a worthy project, and it has received excellent support from individuals and medical organizations. Thus far, the Foundation has had to depend upon annual contributions for these scholarships. The scholarship program must be on a sounder financial basis. The officers have looked forward to establishing an endowment scholarship fund, the income of which will be utilized for scholarships. Therefore, it is with grateful appreciation, as a step towarad that goal, announcement of the George A. Macpherson Scholarships is made.

Mr. George A. Macpherson, a citizen of St. Paul, was a railroad supply and steel broker, who was associated with Mr. James J. Hill when the latter was building the Great Northern Railway. Mr. Macpherson had lived for 60 years of his life at the Minnesota Club in St. Paul. He passed away March 14, 1956, at the age of 88 years. The Trustees of his Estate in The First Trust Company of St. Paul adopted the following resolution recently:

> "To the Minnesota Medical Foundation, two scholarships in the amount of $500.00 each, one for a freshman medical student and the other for a senior medical student, said scholarships to be awarded annually commencing with the school year 1957 and continuing until further action by the Trustees, said scholarships to be known as the 'George A. Macpherson Scholarships.'"

New Members

Last fall copies of the BULLETIN were sent to all physicians in Minnesota and all alumni of the University of Minnesota Medical School. As a result of this mailing, membership in the Foundation has been increased by the addition of 102 new members.

Postgraduate Education

Anesthesiology for General Physicians

The University of Minnesota announces a continuation course in Anesthesiology for General Physicians which will be held at the Center for Continuation Study from February 11 to 13, 1957. Anesthetic techniques suitable for use in the smaller community hospitals will be stressed. Guest speakers will include DOCTORS WILLIAM K. HAMILTON, *Associate Professor* of Anesthesiology, State University of Iowa College of Medicine, Iowa City; and WILLIAM A. O'BRIEN, III, *Anesthesiologist,* Reno, Nevada. The program will be presented under the direction of DR. F. H. VAN BERGEN, *Associate Professor and Head,* Department of Anesthesiology, and the remainder of the faculty will be drawn from the faculties of the University of Minnesota Medical School and the Mayo Foundation.

Neurology for General Physicians and Specialists

The University of Minnesota will present a continuation course in Neurology for General Physicians and Specialists at the Center for Continuation Study on the University of Minnesota Campus from February 11 to 16, 1957. Emphasis will be placed on the management of the more commonly-met neurological disorders. Faculty for the course will include DOCTORS FRANCIS FORSTER, *Dean* of the Medical School and *Professor* of Neurology, Georgetown University School of Medicine, Washington, D. C.; ADOLPH SAHS, *Professor,* Department of Neurology, State University of Iowa College of Medicine, Iowa City; and HENRY T. WYCIS, *Clinical Professor,* Department of Neurosurgery, Temple University School of Medicine, Philadelphia. The course will be presented under the direction of DR. A. B. BAKER, *Professor and Director,* Division of Neurology, and DR. WILLIAM T. PEYTON, *Professor and Director,* Division of Neurosurgery.

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

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

February 7 ——— GEORGE E. FAHR LECTURE; "Alveolar Function in Pulmonary Emphysema;" *Dr. Richard V. Ebert,* Professor and Head, Department of Medicine, University of Arkansas Medical Center, Little Rock, Arkansas; Mayo Memorial Auditorium; 8:15 p.m.

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

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

February 13 ——— J. B. JOHNSTON LECTURESHIP; "Human Stereotaxic Surgery and its Applications;" *Dr. Henry T. Wycis,* Temple University Hospital, Philadelphia; Mayo Memorial Auditorium; 8:15 p.m.

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

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

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

WEEKLY CONFERENCES OF GENERAL INTEREST

Physicians Welcome

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

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