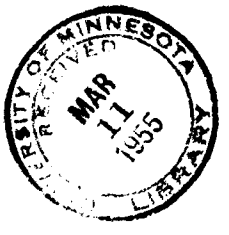
Bulletin of the

University of Minnesota Hospitals
and
Minnesota Medical Foundation



RIBONUCLEIC ACID

Volume XXVI | Friday, March 11, 1955 | Number 20

BULLETIN OF THE
UNIVERSITY OF MINNESOTA HOSPITALS
and
MINNESOTA MEDICAL FOUNDATION

Volume XXVI | Friday, March 11, 1955 | Number 20

CONTENTS

Published weekly during the school year, October to June, inclusive.

The Bulletin is sent to members of the Minnesota Medical Foundation. Annual membership fee - $10.00.

Address communications to: Staff Bulletin, 1342 Mayo Memorial, University of Minnesota, Minneapolis 14, Minn.

I. THE INTRACELLULAR DISTRIBUTION, METABOLIC ACTIVITY, AND POSSIBLE FUNCTION OF RIBONUCLEIC ACID

Cyrus P. Barnum, Ph. D.

Nucleic acids have long been suspected of being intimately involved in two of the most fundamental reactions in which cells are engaged; namely, self duplication and protein synthesis. The evidence on which such suspicions were based was, for some time, largely circumstantial. For example, it has long been known that large amounts of DNA (desoxyribonucleic acid) occur on the chromosomes and that cells which are rapidly producing protein contain large amounts of RNA (ribonucleic acid). In the last 20 years our knowledge of nucleic acid distribution and metabolism has increased markedly, and, while present theories of its functions are still speculative, our speculations are now given more support by many experimental observations. I would like to discuss today some of our present knowledge concerning RNA--its intracellular distribution, its metabolic activity, and some possibilities concerning its function.

One of the techniques that has contributed much to our knowledge is that of differential centrifugation applied to homogenates of various tissues. For the initiation and development of this technique we owe a great deal to Dr. R. R. Bensley and his students,[1] among them Dr. Arnold Lazarow. The particular usefulness of this technique is that it allows one to isolate certain cellular constituents in amounts sufficient for chemical and enzymatic analysis.

Table 1 gives some data on the chemical composition of various cellular fractions isolated from normal mouse liver[2,3,4] and from a transplantable mouse mammary carcinoma.[5]

We are not going to concern ourselves here with the mitochondrial fraction since it is not, to the best of our knowledge at present, concerned directly with those aspects of nucleic acid metabolism which we shall be discussing. Furthermore, the homogenizing fluid employed in these experiments--physiological saline-- was chosen to give the best yields of the smaller cytoplasmic particulates but does not give the best preparations of mitochondria. A mitochondrial fraction, prepared by these methods,

Table 1

Percentage of Cellular Protein, RNA, and Phospholipid found in various Cell Fractions of Normal Mouse Liver and Mouse Mammary Carcinoma

	Sedimentation	Size	Liver			Tumor		
			Prot.	RNA	P.L.	Prot.	RNA	P.L.
Nuclei	4' 1400 g		6	6	2	38	11	14
Mitochondria	25' 2000 g		17	12	30	10	7	40
Microsomes	90' 20,000 g	50-150 mμ	14	51	52	6	38	37
Ultramicrosomes	60' 100,000 g	10-30 mμ	4	19	7	6	29	5
Supernate			59	12	9	40	14	4

(These percentage values are based on the total amount of a given constituent recovered in the 5 cellular fractions.)

may be seen under the electron microscope to be contaminated by material that resembles aggregates of microsomes and, therefore, at least some of the RNA observed in this fraction is probably of microsomal origin.

Inspection of Table 1 will reveal that most of the phospholipid and RNA are associated with the particulate fractions of the cytoplasm whereas much of the protein is non-sedimentable at 100,000 g and is therefore presumably molecularly dispersed in the cytoplasm. Included in Table 1 are some estimates of particle size as seen in the electron microscope.

This view of the distribution of various compounds among the several cellular fractions does not give a picture of the composition of any particular fraction. The major constituents of these fractions are protein, nucleic acid and phospholipid. In Table 2 each fraction is characterized by recording a given constituent as a percentage of the sum of protein, nucleic acid and phospholipid in that fraction.

Inspection of Table 2 makes it apparent that the microsomes are rather rich in both RNA and phospholipid and might be visualized as lipoprotein-nucleoprotein complexes. The ultramicrosomes are

Table 2

Percentage Composition of various Cellular Fractions from Mouse Liver and Mouse Mammary Carcinoma

	Liver				Tumor			
	Prot.	DNA	RNA	P.L.	Prot.	DNA	RNA	P.L.
Nuclei	66	27	3.5	3.5	75	21	2	2
Mitochondria	76	--	3	21	73	--	5	22
Microsomes	57	--	10	33	56	--	24	20
Ultramicrosomes	68	--	15	17	67	--	29	4
Supernate	97	--	1	2	96	--	3	1

even richer in RNA but contain less phospholipid. We have a number of observations on a microsome fraction isolated from lactating mammary glands of mice which indicate a composition intermediate to that found for this same fraction from liver and mammary carcinoma. The mammary gland microsomes contain about 57% protein, 17% RNA, and 26% phospholipid. Chantrenne[6] and Petermann, et al,[7] have analyzed several sedimentable fractions of small granules from various tissues and find them to be comparably rich in RNA.

The pertinent question that must be raised at this point is whether these submicroscopic particles, obtained by differential centrifugation after rather violent disruption of cell membranes, bear any resemblance to what may have existed within the intact cell. In the past few years electron microscopic technique has advanced to an extent that permits excellent resolution of what is assumed to be submicroscopic cellular organization.[8-10] One cannot immediately say to what extent the structures so visualized are artifacts but it seems probable that they come closer to giving a true picture of the intact cell than what is seen after homogenization. The electron microscope studies reveal a network of cytoplasmic canaliculi that Porter[8] and Palade[9] refer to as endoplasmic reticulum. In apposition to the

outer aspects, or membranes, of these canaliculi are numerous small, dense particles.[9] Similar small particles may be seen free in the matrix between canaliculi and also appear in abundance in nucleoli.[8] Palade finds that most of these small granules fall in the size range 10-15 mμ. In acinar cells of various glands the intracellular distribution of basophilia, indicative of concentrations of cytoplasmic RNA, coincides with the distribution of endoplasmic reticulum and associated small granules. However, other cells that show an intense basophilia have a poorly developed reticulum but do have a high concentration of small granules. Palade finds this situation to occur in embryonic cells and in many rapidly proliferating cells in the adult, such as the epithelial cells of intestinal crypts. He therefore concludes that cytoplasmic RNA is better correlated with the small granules than with the reticulum.

It may be seen then that the electron-microscope reveals particles, presumably rich in RNA, which are comparable in size to the RNA-rich ultramicrosomes that can be isolated after rupture of the cell membrane. Slautterback[11] has recently examined a microsome fraction in the electron microscope and finds it to contain small particles, averaging about 22 mμ in diameter, associated with larger irregular vesicles which could easily represent fragments of reticulum. At the present stage of our knowledge I feel that a satisfactory hypothesis would be that microsomes, as isolated after cellular disruption, consist of fragments of reticulum and associated small granules whereas ultramicrosomes represent a more or less pure fraction of these small granules as visualized in intact cells.

The next question I would like to raise is whether or not there is any justification for considering that the RNA isolated along with nuclei or microsomes is any different from the RNA associated with ultramicrosomes or that found in the supernate. The RNA from these various fractions can be isolated in pure form and analyzed for its content of various purines and pyrimidines. On this basis there is some evidence that nuclear RNA differs slightly from cytoplasmic RNA. However, a much more dramatic difference between the RNA found in the various fractions can be seen if one administers an isotope to an animal and measures the rate at which this is incorporated into the RNA of each fraction. Figure 1 shows the specific activity-time curves for the phosphorus of various fractions from mouse liver. These curves were obtained by sacrificing mice at various times after administration of P^{32} (radiophosphorus). It may be seen that the nuclear RNA incorporates P^{32} at an extremely rapid rate compared to microsomal RNA. Not shown in Figure 1 are the specific activity-time curves for the RNA from ultramicrosomes and from the supernatant fraction. At one hour after administration of P^{32} the specific activities of the RNA from these two fractions are respectively about 3 and 10 times the specific activity of microsomal RNA, but the supernatant RNA, which shows the highest activity of any cytoplasmic RNA, still has only about 9% of the specific activity of nuclear RNA. We have been unable to observe any significant difference between the specific activities of mitochondrial and microsomal RNA, which is an additional reason for believing that the RNA found in the mitochondrial fraction may be due to microsomal contamination. These observations do permit us to say that in normal liver tissue there are at least four metabolically distinct RNA fractions derived from nuclei, microsomes, ultramicrosomes and the cytoplasmic supernate. We cannot evaluate the homogeneity within any given fraction and it could be that more metabolically distinct fractions exist.

How are we to explain these differences in microsomal and ultramicrosomal RNA if we adopt the view emerging from electron microscope studies that the particulate RNA of the cytoplasm is associated with the small particles described by Palade and Porter? At the moment a possible explanation might be that those particles which are closely associated with the reticulum may spin down with fragments of the reticulum as a microsome fraction while others become the ultramicrosome fraction. If P^{32} were

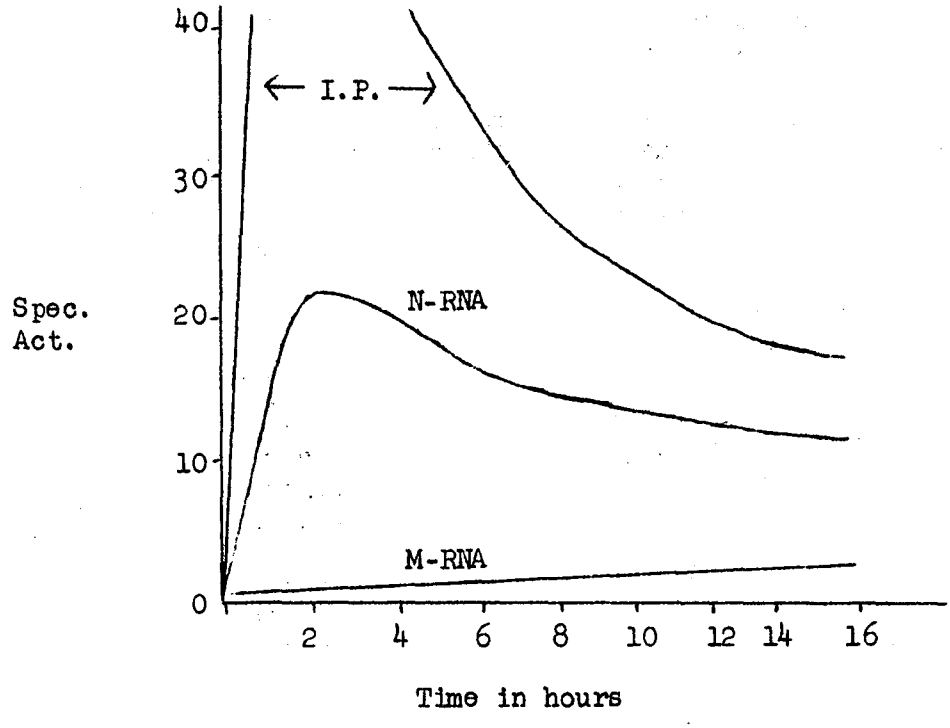


Figure 1. Specific activities of inorganic phosphorus, nuclear RNA and microsomal RNA separated from mouse liver tissue at various times after injection of mice with P^{32}.

incorporated first into the RNA of free particles and these particles subsequently equilibrated with those associated with the reticulum then we would expect to see the kind of differences that are observed.

Pertinent to this discussion is the fact that in the tumor tissue studied, in sharp contrast to the liver, there is no metabolic distinction between the RNA of the ultramicrosomes and the microsomes. One is tempted to speculate that in tumor tissue, or at least in this particular mammary carcinoma, the cytoplasmic organization at a submicroscopic level is such that there is no distinction between various RNA-rich particles. This speculation obtained strong support very recently from the work of Howatson and Ham.[12] They have made an electron microscopic study of two rat liver tumors, one of which they feel clearly originated from parenchymal tissue. When compared to a normal liver cell these tumor cells contained a comparable abundance of small granules but very little in the way of organized reticular structures. The small granules were rather uniformly distributed throughout the tumor cells, an observation in keeping with the diffuse basophilia seen in such cells.

This lack of metabolic distinction between microsomes and ultramicrosomes as seen in our mammary carcinoma cannot be due solely to the rapid growth rate of the tissue since Mrs. Jardetzky, in my laboratory, has obtained evidence that the metabolic distinction is present in rapidly regenerating mouse liver just as it is in normal liver.

Next I would like to call attention to our recent knowledge concerning the relationship between RNA and protein synthesis. A number of workers during the past several years have studied the

incorporation of labeled amino acids into the proteins associated with various intracellular fractions. In general, these investigators have separated out a nuclear fraction, a mitochondrial fraction and a microsomal fraction but have not obtained an ultramicrosomal fraction and therefore what they report as supernate probably still contains some of the RNA-rich small granules along with the large amount of non-sedimentable protein. All investigators agree that of the fractions isolated the microsomal protein shows the most rapid incorporation of the labeled amino acid. Figure 2 is taken from a recent paper by Keller, Zamecnik and Loftfield[13] and very nicely illustrates this point.

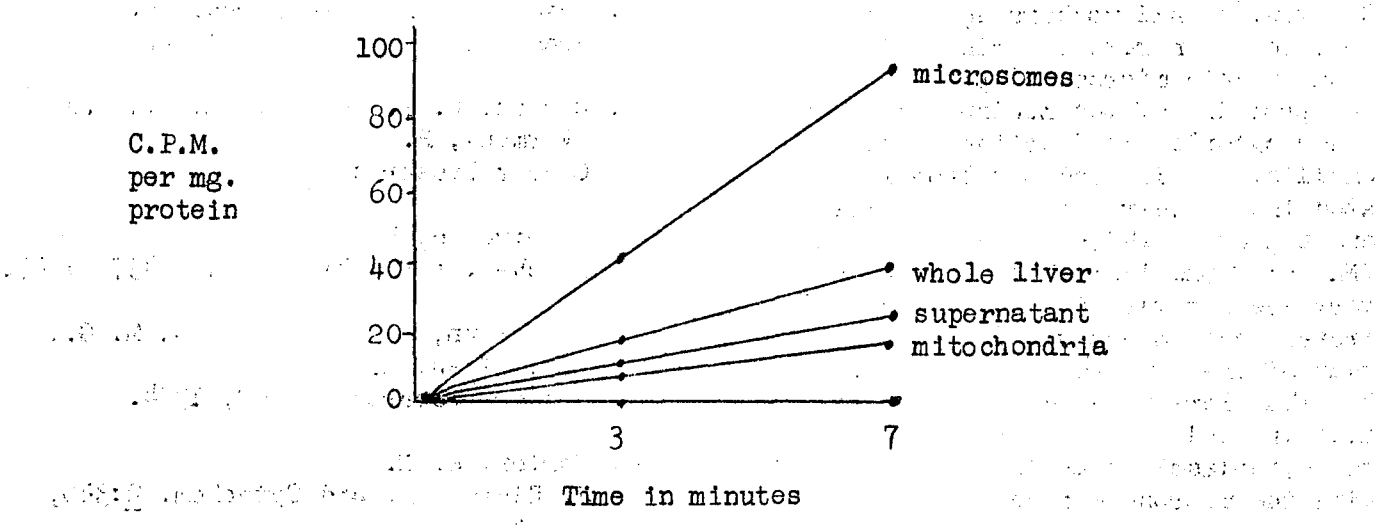


Figure 2. 50 μ moles DL-valine-1-C^{14}, containing 7.68 X 10^5 cpm/mg., injected intravenously into a 150 gm. rat at 0 time. (Copied from paper by Keller, Zamecnik and Loftfield[13].)

From these data they have calculated that at least 70% of the valine incorporated went into the protein of the microsome fraction.

Another study demonstrating a relationship between RNA and protein synthesis is that by Allfrey, Daly and Mirsky.[14] These workers studied the incorporation of N^{15} labeled glycine into the proteins of pancreas, liver and kidney of the mouse. They point out that in terms of net production of protein the pancreas shows the greatest activity, the liver somewhat less, and the kidney very little. The concentration of RNA is highest in pancreas, next in liver, and least in kidney. They isolated a microsome fraction from each of these tissues and found that the RNA content as a percentage of the lipid-free dry weight of the microsome fraction was 24% for pancreas, 11% for liver, and 6.8% for kidney.

They next administered a single large dose of N^{15}-glycine and after 30 minutes found that the atoms percent N^{15} in the microsomal proteins of pancreas, liver and kidney were 0.183, 0.107 and 0.046 respectively. Thus they concluded that the incorporation of labeled glycine was rather directly correlated with the microsomal content of RNA. A further observation of particular interest here was that if they incubated a microsomal fraction with ribonuclease, and then subjected it to the same centrifugal treatment used in preparing the microsomes, about 20% of the protein did not sediment and this protein had more than twice the atom percent N^{15} of the whole microsomal protein. This points to the probability that the most active fraction

of protein is that which is intimately associated with the RNA and highlights the need for a careful examination of the ultramicrosome fraction with a view to ascertaining the rate of incorporation of amino acids into its protein.

An intriguing corollary to the observation that the RNA-associated protein of microsomes shows greater activity than the total microsomal protein has come from Davidson's laboratory in Glasgow.[15] All workers agree that the incorporation rate of amino acids is greater into microsomal protein than into the proteins of the nucleus or of any other cytoplasmic fraction. However, Smellie, McIndoe and Davidson fractionated the nuclear protein into histone and a protein which accompanied nuclear RNA and found that while histone had a very low activity the RNA-associated protein had an activity even greater than that of their microsomal protein. Remember that Porter has observed small granules in nucleoli that appear similar to the cytoplasmic granules seen associated with the microsome fraction.

The point is certainly not yet unequivocally proven but it seems plausible to suggest that these small granules seen in either the nucleus or the cytoplasm, and presumably rich in RNA, are the sites of most active protein synthesis. This would seem to rather clearly implicate RNA as being present when proteins are synthesized and might be interpreted to suggest that there were as many different kinds of RNA molecules in the cell as there are different proteins. In this area, however, we have no experimental evidence to fall back on nor do we have any picture as to how RNA may carry out this probable function of facilitating protein synthesis.

In conclusion I would like to acknowledge with deep appreciation the close collaboration of Dr. Robert Huseby, Dr. Halvor Vermund and Mrs. Christine Jardetzky in the accumulation of the original data presented in this paper.

REFERENCES

1. Biological Symposia, Vol. X, 1943. "Frontiers in Cytochemistry."

2. Barnum, C. P., and Huseby, R. A. Arch. Biochem. 19:17, 1948.

3. Barnum, C. P., Nash, C. W., Jennings, E., Nygaard, O., and Vermund, H. Arch. Biochem. 25:376, 1950.

4. Huseby, R. A., and Barnum, C. P. Arch. Biochem. 26:187, 1950.

5. Barnum, C. P., Huseby, R. A., and Vermund, H. Cancer Research 13:880, 1953.

6. Chantrenne, H. Biochem.et Biophys, Acta 1:437, 1947.

7. Petermann, M. L., Hamilton, M. G., and Mizen, N. A. Cancer Research 14:360, 1954.

8. Porter, K. R. J. Histochem. and Cytochem. 2:346, 1954.

9. Palade, G. E. J.Biophys.Biochem.Cytology 1:59,1955.

10. Sjöstrand, F. S. and Hanson, V. Expt'l Cell Research 7:393, 1954.

11. Slautterback, D. B. Expt'l Cell Research 5:173, 1953.

12. Howatson, A. F. and Ham, A. W. Cancer Research 15:62, 1955.

13. Keller, E. B., Zamecnik, P. C., and Loftfield, R. B. J.Histochem.and Cytochem. 2:378,1954.

14. Allfrey, V., Daly, M. M., and Mirsky, A. E. J. Gen'l. Physiol. 37:157, 1953.

15. Smellie, R. M. S., McIndoe, W. M., and Davidson, J. N. Biochem.et Biophys.Acta 11:559, 1953.

II. MEDICAL SCHOOL NEWS

Coming Events

March 11	Special Lecture; "Studies on the Pathogenesis of Renal Hypertension;" Dr. Michael A. Floyer, Assistant Director of the Medical Unit, London Hospital; Todd Amphitheater, U. H.; 4:00 p.m.
March 16	Family Doctors' Day; Division of Urology; Hospital Dining Room; 12:15 p.m.
March 16	Society for Experimental Biology and Medicine Meeting; Owre Amphitheater; 8:00 p.m.
March 21 - 23	Continuation Course in Cardiovascular Diseases for General Physicians
March 31 - April 2	Continuation Course in Emergency Surgery for General Physicians

* * *

Faculty News

Dr. John A. Anderson, Professor and Head, Department of Pediatrics, took part in the 66th Annual Session of the Mid-South Postgraduate Medical Assembly which was presented in Memphis from February 8 to 11. He discussed "The Value of Laboratory Tests in the Diagnosis of Rheumatic Fever" and "The Nephrosis-Nephritis Problem." Following this meeting, Dr. Anderson returned via Tuscon, Arizona, where he was joined by his family for the return trip to Minneapolis.

Dr. Jerome T. Syverton, Professor and Head, Department of Bacteriology and Immunology, served as Visiting Professor of Cancer Education and Research at the University of California in Los Angeles from February 16 to 25. During his stay at the California institution, he presented a series of four lectures.

Dr. J. A. Myers, Professor, School of Public Health, and consultant in chest diseases for the Students' Health Service, will deliver a series of lectures on diseases of the lung at a postgraduate course for chest physicians which will be held in Puerto Rico between March 10 and 17.

Dr. H. D. Lamb, of the Mental Hygiene Department of the Students' Health Service, will spend the spring quarter on leave in England and France. He will present a paper on "Some Aspects of Psychosomatic Medicine in a Large Students' Health Service" at the University of Bordeaux.

Miss Lorraine Gonyea, Instructor in Medical Technology, has been granted a Fulbright student grant and will study with Dr. Paul Owren at the University of Oslo, Norway, for one year. She will begin in July, 1955.

* * *

Publications of the Medical School Faculty

Campbell, Berry and Ryzen, Maria: The Nuclear Anatomy of the Diencephalon of Sorex Cinereus. J. Comp. Neur., 99: 1, 1953.

Campbell, Berry and Petersen, W. E.: Milk "Let-Down" and the Orgasm in the Human Female. Human Biology, 25: 165, 1953.

III.

UNIVERSITY OF MINNESOTA MEDICAL SCHOOL
WEEKLY CALENDAR OF EVENTS

Physicians Welcome

March 14 - 19, 1955

Monday, March 14

Medical School and University Hospitals

9:00 - 9:50 Roentgenology-Medicine Conference; L. G. Rigler, C. J. Watson and Staff; Todd Amphitheater, U. H.

9:00 - 10:50 Obstetrics and Gynecology Conference; J. L. McKelvey and Staff; W-612, U. H.

10:00 - 12:00 Neurology Rounds; A. B. Baker and Staff; Station 50, U. H.

11:30 - 12:30 Physical Medicine and Rehabilitation Staff Seminar; Subject to be announced; R. S. Blanchard; Heart Hospital Theater.

11:30 - Tumor Conference; Doctors Hitchcock, Zimmermann, and Stenstrom; Todd Amphitheater, U. H.

12:15 - Obstetrics and Gynecology Journal Club; Staff Dining Room, U. H.

1:00 - 2:00 Roentgenology-Surgical-Pathological Conference; Paul Lober and L. G. Rigler; Todd Amphitheater, U. H.

1:30 - 2:30 Pediatric-Neurological Rounds; R. Jensen, A. B. Baker, and Staff; U.H.

1:30 - 3:30 Dermatology Hospital Rounds; H. E. Michelson and Staff; Dermatology-Histopathology Room, C-394 Mayo Memorial.

4:00 - 6:00 Anesthesiology Conference; F. H. Van Bergen and Staff; Todd Amphitheater, U. H.

4:30 - Pediatric-Medicine Infectious Disease Rounds; Station 33, U. H.

5:00 - 6:00 Urology-Roentgenology Conference; C. D. Creevy, O. J. Baggenstoss, and Staff; Eustis Amphitheater.

Ancker Hospital

8:00 - 9:00 Pediatric Contagion Rounds; Richard Lein; Contagion 5.

8:30 - 10:30 Medical and Surgical Chest Conference; Dr. Gehlen and Staff; Auditorium

9:30 - 12:00 Visiting Staff Rounds.

10:00 - 12:00 Surgery Grand Ward Rounds; Begin Floor E4.

11:00 - 12:00 Pediatric Rounds; Harry Orme; Contagion 1.

12:30 - 2:30 Surgery Out-Patient Clinic; Room 8.

2:00 - 3:00 Routine EKG Interpretation; Dr. Sommers and House Staff; Medical Record Library.

2:30 - 3:00 Discussion of Problem Case; Auditorium.

3:00 - 4:00 Surgery Journal Club; Classroom.

3:00 - 4:00 Lectures on Electrocardiography; Ben Sommers; Auditorium.

4:00 - 5:00 Medical Clerk Journal Club; Auditorium.

Monday, March 14 (Cont.)

Minneapolis General Hospital

10:30 - 12:00 Medicine Rounds; Thomas Lowry; Station 31.

11:00 - Pediatric Case Discussions; Erling Platou; Station 4.

10:30 - Orthopedic and Fracture Rounds; Drs. John Moe and O. J. Campbell; Station 20.

12:30 - Surgery Grand Rounds; O.J. Campbell; Station 21.

1:30 - 2:30 Tuberculosis Conference; J. A. Myers; Station 8.

2:00 - Pediatrics Rounds; William Krivit; Stations 4, 5, & 6.

Veterans Administration Hospital

9:30 - Infectious Disease Rounds; Drs. Hall, Zinnemann, and J. Brown.

1:30 - Cardiac Conference; Drs. Smith, Berman, Hoseth, Simonson, Tamlyn, and Farquhar; Conference Room, Bldg. I; Rounds immediately following conference.

Tuesday, March 15

Medical School and University Hospitals

9:00 - 9:50 Roentgenology-Pediatric Conference; Samuel Feinberg, John A. Anderson and Staffs; Eustis Amphitheater, U. H.

12:30 - 1:20 Pathology Conference; Autopsies; J. R. Dawson and Staff; 104 Jackson Hall.

3:30 - General Physiology Seminar; 323 Zoology Building.

3:30 - Pediatric Seminar; Tetanus; Dr. Schulz; 1450 Mayo Memorial.

4:00 - 5:00 Pediatric Rounds on Wards; John A. Anderson and Staff; U. H.

4:00 - 5:00 Physiology-Surgery Conference; Todd Amphitheater, U. H.

4:30 - 5:30 Clinical-Medical-Pathological Conference; Todd Amphitheater, U. H.

5:00 - 6:00 X-ray Conference; Presentation of Cases from Minneapolis General Hospital; Drs. Lipschultz and Paciotti; Eustis Amphitheater, U. H.

Ancker Hospital

8:00 - 9:00 Pediatric Rounds; Dale Cumming; Contagion 1.

9:00 - 10:30 Visiting Staff Rounds.

9:00 - 12:00 Practical Diagnostic Clinic; Harry Orme; Out-Patient Department.

11:00 - 12:00 Medical X-ray Conference; J. R. Aurelius; Auditorium.

2:30 - 4:00 Routine EKG Interpretations; Resident Staff.

4:00 - 5:00 Medical-Pathological Conference; W. F. Mazzitello, Auditorium.

Minneapolis General Hospital

9:30 - Pediatric Rounds; Elizabeth Lowry and A. Bridge; Station 5.

9:30 - 10:30 Obstetrics and Gynecology Staff Rounds; William P. Sadler and Staff; 301 Harrington Hall.

Tuesday, March 15 (Cont.)

Minneapolis General Hospital (Cont.)

10:00 - Psychiatry Grand Rounds; R. W. Anderson, Station 3.

11:30 - 12:30 Neurology-Neurosurgery Conference; Classroom, Station 8.

12:30 - 2:30 Dermatology Rounds on Clinic; Carl W. Laymon and Staff.

12:30 - ECG Conference; Boyd Thomes and Staff; 302 Harrington Hall.

1:00 - Tumor Clinic; Drs. Eder, Coe, and Lipschultz; Classroom.

3:30 - Pediatric-Psychiatry Rounds; Station 4.

Veterans Administration Hospital

7:30 - Anesthesiology Conference; Surgical Conference Room, Bldg. 43.

8:30 - Hematology Rounds; Drs. Hagen and Wexler.

8:30 - Surgery Journal Club; Conference Room, Bldg. I.

9:30 - Surgery-Pathology Conference; Conference Room, Bldg. I.

10:30 - Surgery-Tumor Conference; D. Ferguson and J. Jorgens.

1:00 - Review of Pathology, Pulmonary Tuberculosis; Conference Room, Bldg. I.

1:30 - Combined Medical-Surgical Chest Conference; Conference Room, Bldg. I.

2:00 - 2:50 Dermatology and Syphilology Conference; H. E. Michelson and Staff; Bldg. III.

4:00 - Thoracic Surgical Problems; Conference Room, Bldg. I.

5:00 - Fluid Balance Conference; Conference Room, Bldg. I.

5:30 - Physiology Seminar; Surgical Conference Room, Bldg. 43.

Wednesday, March 16

Medical School and University Hospitals

11:00 - 12:00 Pathology-Medicine-Surgery-Pediatrics Conference; Todd Amphitheater, U. H.

12:15 p.m. Family Doctors' Day; Division of Urology; Hospital Dining Room.

1:00 - 2:00 Dermatology Clinical Seminar; F. W. Lynch; 300 North Clinic.

1:30 - 3:00 Pediatrics Allergy Clinic; Albert V. Stoesser and Lloyd Nelson; W-211, U. H.

3:30 - 4:30 Dermatology-Pharmacology Seminar; 3rd Floor Conference Room, Heart Hospital.

4:30 - 5:50 Dermatology-Infectious Disease Seminar; 3rd Floor, Conference Room, Heart Hospital.

5:00 - 6:00 Radiology Residents Lectures; Retrospectroscope; Leo G. Rigler; Todd Amphitheater, U. H.

5:00 - 5:50 Urological-Pathological Conference; C. D. Creevy and Staff; A503, Mayo Memorial.

5:10 - 6:10 Endocrine Seminar; ACTH and Cortical Steroids in Relation to Infectious Diseases; Wesley W. Spink; 271 Lyon Laboratories.

Wednesday, March 16 (Cont.)

Medical School and University Hospitals (Cont.)

5:30 - 7:30 Dermatology Journal Club and Discussion Group; Hospital Dining Room.

7:30 - 9:30 Dermatology Seminar; Review of Interesting Slides of the Week; Robert W. Goltz; Todd Amphitheater, U. H.

*8:00 p.m. Society for Experimental Biology and Medicine Meeting; Owre Amphitheater.

Ancker Hospital

8:30 - 9:30 Clinico-Pathological Conference; J. Noble; Auditorium.

11:00 - 12:00 Pediatric and Contagion Rounds; Harry Orme; Contagion 1.

11:00 - 12:00 Medicine Resident Rounds; W. F. Mazzitello.

3:30 - 4:30 Pediatric-Surgery Conference; Harry Orme and I. D. Baronofsky; Auditorium.

Minneapolis General Hospital

10:30 - 12:00 Medicine Rounds; Thomas Lowry and Staff; Station 11.

11:00-- Pediatric Rounds; Erling Platou and Richard Raile; Station 6.

12:00 - Surgery-Physiology Conference; O. J. Campbell and E. B. Brown; Classroom.

12:30 - Pediatrics Staff Meeting; Classroom, Station 4.

Veterans Administration Hospital

8:30 - 10:00 Orthopedic X-ray Conference; E. T. Evans and Staff; Surgical Conference Room, Bldg. 43.

8:30 - 12:00 Neurology Rehabilitation and Case Conference; A. B. Baker.

9:00 - Gastro-Intestinal Rounds; Drs. Wilson, Zieve, Ferguson, Brakel, Swenson, Nesbitt and Sadoff.

10:30 - Psychosomatic Conference; C. K. Aldrich; 7th Floor, Bldg. 43.

12:30 - Medical Journal Club; Doctors' Dining Room.

12:30 - X-ray Conference; J. Jorgens; Conference Room, Bldg. I.

1:30 - 3:00 Metabolic Disease Conference; Drs. Flink and Williams.

3:30 - Urology Pathology Slide Conference; Dr. Gleason; Conference Room, Bldg. I.

7:00 - Lectures in Basic Science of Orthopedics; Conference Room, Bldg. I.

Thursday, March 17

Medical School and University Hospitals

9:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; Room 3.148 Mayo Memorial.

11:00 - 12:00 Cancer Clinic; K. Stenstrom, B. Zimmermann; Todd Amphitheater, U. H.

---

* Indicates special meeting. All other meetings occur regularly each week at the same time on the same day. Meeting place may vary from week to week for some conferences.

Thursday, March 17 (Cont.)

Medical School and University Hospitals (Cont.)

12:30 - 1:55 Physiology Seminar 210; Transport; Selected Topics in Permeability; Nathan Lifson; 214 Millard Hall.

1:30 - 4:00 Cardiology X-ray Conference; Heart Hospital Theatre.

4:00 - 5:00 Anesthesiology Seminar; F. H. Van Bergen and Staff; Room 100, Mayo Memorial.

5:00 - 6:00 Radiology Seminar; Therapy of Carcinomas with Unknown Primaries; Heino Alari; Eustis Amphitheater, U. H.

7:30 - 9:30 Physiology 211 Seminar; Selected Topics in Heart and Circulation: Hemodynamics; M. B. Visscher and Robert Evans; 271 Lyon Laboratories.

Ancker Hospital

8:00 - 9:00 Pediatric Clinical Staff Conference; Contagion Classroom.

9:00 - 10:00 Pediatric Contagion Rounds; Alexander Stewart, Contagion 5.

9:30 - 10:30 Medical Grand Rounds; Auditorium; Visiting Staff Rounds immediately following Grand Rounds.

11:00 - 12:00 Pediatric X-ray Conference.

11:00 - 12:00 Medicine Resident Rounds; W. F. Mazzitello.

2:00 - 3:00 Routine ECG Interpretation; Ben Sommers; Medical Record Library.

Minneapolis General Hospital

9:30 - Neurology Rounds; Heinz Bruhl; Station 4.

9:30 - Pediatric Contagion Rounds; R. B. Raile; Station 4.

10:00 - Psychiatry Grand Rounds; R. W. Anderson and Staff; Station 3.

11:30 - 12:30 Clinical Pathological Conference; John I. Coe; Classroom.

12:30 - 2:30 Dermatology Rounds and Clinic; Carl W. Laymon and Staff.

1:00 - Fracture X-ray Conference; Drs. Campbell and Moe; Classroom.

1:00 - House Staff Conference; Station 4.

Veterans Administration Hospital

8:00 - Experimental Surgery Laboratory Meeting; Conference Room, Bldg. I.

8:30 - Hematology Rounds; Drs. Hagen and Doe.

9:00 - Surgery Grand Rounds; Conference Room, Bldg. I.

9:00 - Surgery Ward Rounds; D. Ferguson and Staff; Ward 11.

11:00 - Surgery-Roentgen Conference; J. Jorgens; Conference Room, Bldg. I.

1:00 - Infectious Disease Conference; Conference Room, Bldg. I. (Rounds immediately following conference.)

4:00 - 5:00 Medical-Surgical Conference; Conference Room, Bldg. I.

Friday, March 18

Medical School and University Hospitals

8:00 - 10:00 Neurology Grand Rounds; A. B. Baker and Staff; Station 50, U. H.

9:00 - 9:50 Medicine Grand Rounds; C. J. Watson and Staff; Todd Amphitheater, U. H.

10:30 - 11:50 Medicine Rounds; C. J. Watson and Staff; Todd Amphitheater, U. H.

11:00 - 12:00 Vascular Rounds; Davitt Felder and Staff Members from the Departments of Medicine, Surgery, Physical Medicine, and Dermatology; Eustis Amphitheater, U. H.

11:45 - 12:50 University of Minnesota Hospitals Medical Staff Meeting; Serum Lipids in Acne Vulgaris; Gordon Vaughn; Powell Hall Amphitheater.

1:00 - 2:50 Neurosurgery-Roentgenology Conference; W. T. Peyton, Harold O. Peterson and Staff; Todd Amphitheater, U. H.

1:00 - 2:00 Physiology Seminar 212; Selected Topics in Respiration: Respiratory and Circulatory Effects of Hypothermia; E. B. Brown; 214 Millard Hall.

1:30 - 2:30 Dermatology Grand Rounds; Presentation of Cases from Grouped Hospitals (University, Ancker, General and Veterans) and Private Offices; H. E. Michelson and Staff; Eustis Amphitheater, U. H.

2:30 - 4:00 Dermatology Hospital Rounds; H. E. Michelson and Staff; Begin at Dermatological Histopathology Room, C-394 Mayo Memorial.

3:00 - 4:00 Neuropathological Conference; F. Tichy; Todd Amphitheater, U. H.

3:30 - 4:30 Dermatology-Physiology Seminar; 3rd Floor Conference Room, Heart Hospital.

4:00 - 5:00 Physiology Seminar 213; Selected Topics in Advanced Neurophysiology; Role of the Vestibular Apparatus and the Cerebellum in the Extrapyramidal Motor Activity; Werner Koella; 129 Millard Hall.

4:30 - 5:20 Ophthalmology Ward Rounds; Erling W. Hanson and Staff; E-534, U. H.

5:00 - Urological Seminar and X-ray Conference; A503, Mayo Memorial.

Ancker Hospital

8:00 - 9:00 Pediatric Rounds; Charles Steinberg; Contagion 1.

10:30 - 11:30 Pediatric Contagion Rounds; Richard Smith; Contagion 1.

11:00 - 12:00 Contagion Rounds; Harry Orme; Contagion 5.

2:00 - 3:00 Routine EKG Interpretation; Resident Staff.

3:00 - 4:00 Medical-Surgical-Pathological Conference; Auditorium.

4:00 - 5:00 Medical Journal Club; Conference Room, E5.

4:00 - 5:00 X-ray Surgery Conference; Auditorium.

Minneapolis General Hospital

10:00 - Otolaryngology Conference; Robert A. Priest, Large Classroom.

10:30 - Pediatric Surgical Conference; Tague Chisholm and B. Spencer; Classroom, Station 4.

12:00 - Surgery-Pathology Conference; Drs. Campbell and Coe; Classroom.

1:00 - 3:00 Clinical-Medical Conference; Thomas Lowry; Classroom, Station 8.

Friday, March 18 (Cont.)

Veterans Administration Hospital

10:30 - 11:20 Medicine Grand Rounds; Conference Room, Bldg. I.

11:00 - 12:30 Psychiatry Case Conference; Werner Simon; Psychiatry Department, VA Hospital Annex.

12:30 - Urology X-ray Conference; X-ray Department.

1:00 - CPC Conference; Conference Room, Bldg. I.

2:00 - Pathology Slide Conference; E. T. Bell; Conference Room, Bldg. I.

Saturday, March 19

Medical School and University Hospitals

7:45 - 8:50 Orthopedic X-ray Conference; W. H. Cole and Staff; M-109, U. H.

9:00 - 9:30 Pediatric Grand Rounds; Eustis Amphitheater, U. H.

9:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; Heart Hospital Amphitheater.

9:15 - 10:00 Surgery-Roentgenology Conference; Alexander R. Margulis, Owen H. Wangensteen and Staff; Todd Amphitheater, U. H.

10:00 - 11:30 Surgery Conference; Todd Amphitheater, U. H.

10:00 - 12:50 Obstetrics and Gynecology Rounds; J. L. McKelvey and Staff; Station 44, U. H.

10:00 - 12:00 Otolaryngology Seminar on Current Literature; L. R. Boies and Staff; Todd Memorial Room, A-675, Mayo Memorial.

Ancker Hospital

8:30 - 9:30 Surgery Conference; Auditorium.

9:30 - 11:00 Medicine Grand Ward Rounds; W. F. Mazzitello.

11:00 - 12:00 Medical Clerk Case Conference; W. F. Mazzitello.

Minneapolis General Hospital

8:00 - Urology Staff Conference; T. H. Sweetser; Main Classroom.

9:00 - Psychiatry Grand Rounds; R. W. Anderson; Station 3.

9:30 - Pediatrics Rounds on all Stations; R. B. Raile.

11:00 - 12:00 Medical X-ray Conference; O. Lipschultz, Thomas Lowry and Staff; Main Classroom.

Veterans Administration Hospital

8:00 - Proctology Rounds; W. C. Bernstein and Staff; Bldg. III.

8:30 - Medical X-ray Conference; Conference Room, Bldg. I.