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Diabetic Retinopathy

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I. DIABETIC RETINOPATHY

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It has been known for many years that diabetes mellitus can produce profound visual changes. Some of the most interesting lesions and most serious complications of diabetes are produced in the retina. With the use of insulin and better management of the diabetic, there has been an associated increase in length of life, and with this a definite increase in the incidence of diabetic retinopathy, making this retinopathy a serious problem of prime importance both to patient and doctor alike.

The earliest and most characteristically diagnostic diabetic lesions in the retina are the small punctate red spots found in the posterior poles of the eyes, usually near the macula and occurring in the presence of normal arterioles. Until the work of Ballantyne and Loewenstein[3] in 1943 these punctate red spots were all thought to be minute hemorrhages.[6] From their observations and also from the work of Friedenwald[13,14] in 1948 and Ashton[2] in 1949 we now know with absolute certainty that many of these "red spots" are capillary aneurysms. These capillary aneurysms are most often located in the inner nuclear layer of the retina. They arise on capillaries which connect the capillary net in the nerve fiber layer with the capillary net at the outer boundary of the inner nuclear layer. The size of the aneurysms may be as much as 10 to 15 times that of the parent capillary and varies from 30 microns to 90 microns in diameter.[3] The aneurysmal walls may allow blood to escape by diapedesis or actual rupture producing ophthalmoscopically larger, round deep hemorrhages. Some aneurysms undergo thrombosis which in turn leads to cicitrization and to the formation of a lesion viewed ophthalmoscopically as a round white nodule.[4,5]

A further development in the course of diabetic retinopathy is the appearance of small, "hard", irregularly-shaped yellowish-white exudates. These are usually in the central area of the retina, may occur singly or may coalesce into groups or clusters. If these "waxy" groups or clusters overlap the fovea, central vision is greatly interfered with. The above aneurysms, hemorrhages and exudates are what constitute the central punctate retinopathy of diabetes.[26,27]

In certain diabetics in addition to the hemorrhages or central punctate retinopathy and in the presence of normal arterioles, "soft" cotton-wool or "cotton-wool like" patches are sometimes observed. The cotton-wool patches in this type of diabetic retinopathy probably indicate a toxemia due to some complicating condition such as carbuncles, infected ulcers, gangrene or a urinary tract infection.[27] The "toxic" cotton-wool patches under these conditions and in the presence of normal retinal arterioles do not signify any coexisting hypertension. After removal of the complicating toxic process, these cotton-wool patches disappear.[27]

Another typical retinal finding in diabetes is that associated with venous changes in the visible veins.[1,5,15,21,26,27] Two main types of these changes occur: changes in the veins without proliferation of new vessels and changes in the veins characterized by new vessel proliferation.

In the non-proliferative type of diabetic venous disease probably the earliest visible diagnostic clue is an overfilling and increased tortuosity of the retinal veins.[5] This overfilling and tortuosity is not uniform and is limited to individual branches or to segments of branches. In certain cases this tortuosity becomes extreme, the veins being thrown into loops and coils.[5,21] In other veins nodular dilatations alternating with constrictions occur giving the appearance of beading. Yellowish-white exudate may occur along the wall of some of these veins giving them a sheathed appearance while others may appear to be obliterated completely in which case the vein appears white and smooth in contour peripheral to the thrombus.[15] Any of these venous lesions may be associated with extensive areas of hemorrhage. Diabetic venous changes when associated with numerous retinal hemorrhages are distinguished from central venous thrombosis or branch venous thrombosis by non-

uniform or erratic distribution, while in the central venous thrombosis all branches are distended and extensive hemorrhages always occur over the entire fundus.[5]

Since the venous changes appear to resemble the changes in the retinal arterioles in arteriolosclerosis, these venous changes have been referred to as retinal phlebosclerosis. Three main types of retinal phlebosclerosis have been described.[15] These are dependent upon whether the initiating process occurs within the lumen, within the wall or outside the wall of the vein. The changes occurring within the lumen are the intimal type and are seen after venous thrombosis and fibrosis have occurred. When the sclerotic process occurs within the wall of the vein it is known as the medial type and produces contour changes such as dilatations and constrictions of venous segments giving a beaded appearance. This medial type is the most characteristic type of diabetic venous disease.[15] In the adventitial type where changes occur secondary to processes outside the vein, a connective tissue sheathing of the vein occurs following subsidence of perivenous inflammation or edema.

Microscopically the veins in many areas show thickening and hyaline degeneration of their walls, endothelial proliferation and thromboses.[21]

In the proliferative type of diabetic venous disease the essential changes are the development of new vessels followed by the formation of delicate supporting connective tissue.[19] The development of this anastomotic network of new blood vessels is a compensatory mechanism which occurs secondary to stasis caused by degenerative vascular disease primarily on the venous side of the circulation in diabetes.[5,19]

Ophthalmoscopically diabetic retinitis proliferans, as this formation of new vessels is called, may appear as a more or less dense brush like mass of newly-formed blood vessels supported by a small amount of delicate connective tissue.[19] If the retinitis proliferans occurs in region of the optic nerve the newly formed network may project into the vitreous for a considerable distance. If the newly formed vessels arise over the region of the retina proper the internal limiting membrane must be perforated by the vessels before they enter the vitreous. In the early stages of diabetic retinitis proliferans, hemorrhages may be few or absent. In later stages hemorrhages occur from these newly formed vessels, become organized into strands giving a more substantial appearance to the supporting tissue and may even lead to retinal detachment.

In contrast with the above type of retinitis proliferans which is characteristic of diabetes, another type of retinitis proliferans exists in which the formation of connective tissue precedes the formation of new blood vessels.[19] In this type the primary cause of the changes is a traumatic or inflammatory alteration of the retinal vessels followed by hemorrhage from these vessels into the vitreous with subsequent organization and formation of dense connective tissue and very few new vessels.

If "soft" exudates or "cotton-wool patches" are observed ophthalmoscopically in addition to aneurysms or round, deep hemorrhages or in addition to the central punctate retinopathy of diabetes, one must always suspect a complicating hypertension. However, in order to insure a diagnosis of hypertension definite arteriolosclerosis must also be present and one is on much more certain ground if in addition to the above, focal arteriolar narrowings are also found.[27] If the above criteria are fulfilled we have then a mixed vascular retinopathy, that is diabetes and hypertension combined.[27]

In certain diabetic patients with hypertension, the ophthalmoscopic picture may be entirely that of hypertension including generalized and focal acteriolar narrowing, generalized arteriolar sclerosis, cotton-wool patches, superficial striate or flame shaped hemorrhages but without any diabetic retino-retinopathy. This picture will not re-

motely aid in the diagnosis of diabetes ophthalmoscopically.

From the observations on 49 patients with diabetic retinopathy seen in the Eye Clinic at the University Hospitals between January, 1949 and February, 1950, the following retinal lesions occurred.

Table I

INCIDENCE OF TYPES OF DIABETIC RETINOPATHY IN 49 PATIENTS

7	with microaneurysms only
2	with microaneurysms and hemorrhages
16	with central punctate retinopathy only without venous disease
4	with mixed vascular diabetic retinopathy only without venous disease
1	with microaneurysms only with venous disease
2	with microaneurysms and hemorrhages only with venous disease
11	with central punctate retinopathy only with venous disease
5	with mixed vascular diabetic retinopathy only with venous disease
1	with venous disease (this one was eliminated from any classification because nothing could be seen except the marked retinitis proliferans through the hazy media)
49	Total

* * * *

20	total number with venous disease (1 eliminated and not classified as noted above)
0	with venous disease alone
36	total number with exudates
0	with exudates only
4	with toxic cotton-wool patches
1	with retinal detachment
48	with microaneurysms (1 patient not classified as noted above)

Note: Non-proliferative and proliferative types of venous disease are grouped together as venous disease.

It is interesting to note that in 48 of the 49 cases microaneurysms were present, and in 7 cases were the only visible retinopathy. In the one case in which they were not observed, an accurate detailed view of the retina was impossible due to obscuring of the media by a dense retinitis proliferans.

These 49 cases were studied and tabulated in the hope that some definite sequence in the development of retinopathy might appear. However, from this small series at least, no definite sequence in the development of these lesions could be determined other than the observation that microaneurysms apparently always come first since out of all the different lesions, they were the only ones that occurred alone and that whatever type of retinopathy developed microaneurysms were also present. On the contrary, it appears as though two distinct main types of diabetic retinal disease may occur with any of the individual types of diabetic retinopathy we have previously described, a type with diabetic venous disease and a type without diabetic venous disease.

Table II shows two distinct main types of diabetic retinal disease, the left hand column indicating the number of cases in our series without venous disease, the right column the number of cases with venous disease. We realize that though this is a small series of cases, this further classification separating the venous from the non-venous retinal disease may be worthwhile for several reasons. For one thing venous disease may occur with nothing more than microaneurysms, or with only microaneurysms and small round hemorrhages, and need not necessarily occur after exudates have appeared or in the presence of other widespread diabetic retinopathy. In addition, it is a clinical impression from the study of these patients that any of the types of retinopathy with venous disease are likely to have more vitreous and preretinal hemorrhages and retinal detachment as compared with the same types of retinopathy without venous disease. Finally, the effect od diabetes on the retinal vascular system appears to be more pronounced on the venous rather than the arterial side of the circulation as evidenced by both

TABLE II

INCIDENCE OF TYPES OF DIABETIC RETINOPATHY IN 48 PATIENTS OCCURRING WITHOUT AND WITH COMPLICATING VENOUS DISEASE.

	Without Venous Disease	With Venous Disease
1.	Microaneurysms alone	Microaneurysms alone
	7	1
2.	Hemorrhages with Microaneurysms	Hemorrhages with Microaneurysms
	2	2
3.	Central Punctate Retinopathy	Central Punctate Retinopathy
	16	11
4.	Mixed Vascular Diabetic Retinopathy	Mixed Vascular Diabetic Retinopathy
	4	5

ophthalmoscopic and pathologic findings of retinal phlebosclerosis in the larger veins as well as the observations that the earliest visible changes are microaneurysms occurring on the venous end of the retinal capillary nets.

The average age of the 49 patients in this study was 54.1 years, the oldest being 78 years and the youngest 22 years. The average known duration of diabetes was 12.4 years, the longest being 26 years and the shortest one year. The sex incidence was 17 males and 32 females. The average blood pressure of the entire group was 157.3/89.9.

An interesting sidelight in this study was the grading of retinal arterioles in patients who had diabetic retinopathy with hypertension and without hypertension as compared with a random group of non-diabetic patients with and without hypertension. A person was placed in the non-hypertensive group if the diastolic blood pressure was 90 mm. of mercury or less and in the hypertensive group if the diastolic blood pressure was 100 mm. of mercury or greater. Those patients with diastolic blood pressures between 90 and 100 mm. of mercury were not included in this particular part of the study.

TABLE III

GRADING OF RETINAL ARTERIOLES OF PATIENTS WITHOUT HYPERTENSION AND WITHOUT DIABETES

	Generalized Sclerosis					Generalized Narrowing					Focal Narrowing				
Total Number	0	I	II	III	IV	0	I	II	III	IV	0	I	II	III	IV
26 cases	25	1				23	3				26				
			Average Age 50.5 yrs.			Average B.P.				129.2 / 78.2					

GRADING OF RETINAL ARTERIOLES OF PATIENTS WITHOUT HYPERTENSION AND WITH DIABETIC RETINOPATHY

	Generalized Sclerosis					Generalized Narrowing					Focal Narrowing				
Total Number	0	I	II	III	IV	0	I	II	III	IV	0	I	II	II	IV
26 cases	13	10	3			16	9	1			25	1			
			Average Age 57.6 yrs.			Average B.P.				142.8 / 78.6					
			Average Duration of Diabetes 13.5 yrs.												

From this table it would appear that the diabetes had a definite influence on the generalized sclerosis and the generalized narrowing of the arterioles in that these changes were more pronounced when compared with similar changes in the non-diabetic.

TABLE IV

GRADING OF RETINAL ARTERIOLES OF PATIENTS WITH DIABETIC RETINOPATHY AND WITH HYPERTENSION

	Generalized Sclerosis					Generalized Narrowing					Focal Narrowing				
Total Number	0	I	II	III	IV	0	I	II	III	IV	0	I	II	III	IV
13 cases		4	8	1			4	6	3		3	6	4		
			Average Age 48.5 yrs.			Average B.P.				196.7 / 114					
			Average Duration of Diabetes 10.8 yrs.												

GRADING OF RETINAL ARTERIOLES OF PATIENTS WITH HYPERTENSION AND WITHOUT DIABETES

	Generalized Sclerosis					Generalized Narrowing					Focal Narrowing				
Total Number	0	I	II	III	IV	0	I	II	III	IV	0	I	II	III	IV
13 cases	2	4	5	2			5	6	1	1	3	4	3	3	
			Average Age 57.7 yrs.			Average B.P.				208.7 / 124.6					

While we noted in Table III an acceleration of generalized arteriolosclerosis in the group with diabetic retinopathy and no hypertension, over the group without diabetes and without hypertension, Table IV shows an apparent further acceleration of generalized sclerosis and considerable focal arteriolar narrowing in the group with hypertension plus diabetic retinopathy over the group in Table III who had diabetic retinopathy but no hypertension. However, as can be seen from Table IV, there is very little difference in the arterioles between those with diabetic retinopathy and hypertension and those with hypertension and no diabetes.

Wagener in 1945[27] stated, "it has been my impression that there has been a gradual increase in the frequency of retinal complications -- in diabetes." He then went on to point out that the total incidence of diabetic retinopathy had increased from 8.3% in his 1921 series[25] to 17.7% in his 1934 series[26] and to 30.6% in his most recent series.[27] He also noted that occurrence of retinopathy among the younger age group of diabetic patients had increased definitely from an incidence of 0 in patients less than 40 years old in the 1921 series to 4.3% in the 1934 series to 12.8% in the 1945 series. Of this last group 8.3% of the patients were less than 30 years of age. Wagener also thinks that duration of the diabetes has much more influence in the development of retinopathy than age has. He pointed out that among patients less than 30 years of age who had had diabetes for more than 10 years 76% had retinopathy while among patients more than 30 years of age who had had diabetes for more than 10 years only 64% had retinopathy. He concludes from the above facts that the development of retinal lesions is dependent on some fault inherent in diabetes itself and not on extraneous vascular or infectious or deficiency factors that undoubtedly occur more frequently in the older age group.

Many different approaches to the treatment of diabetic retinopathy have been made.

A common observation throughout the literature has been the greatly increased capillary fragility as measured by the various skin capillary fragility tests in the diabetic patient with retinopathy. Typical of this finding is the work of Foxworthy[12] who subjected 85 non-diabetics and 69 diabetics without retinopathy and 44 with diabetic retinopathy to capillary fragility tests. The first petechiae in the non-diabetic group appeared in 4.9 minutes, in the diabetic group without retinopathy in 2.36 minutes, and in the group with retinopathy petechiae appeared first in 1.5 minutes. The average number of petechiae present at the end of 10 minutes were 14, 41 and 101 respectively. Also, according to the work of Rodriguez and Root,[23] 100% of 56 patients who had diabetic retinopathy had increased capillary fragility. They also felt that the incidence of increased capillary fragility was related to the duration of the diabetes more clearly than to the age of the patient.

With the evidence of increased capillary fragility in patients with diabetic retinopathy, an attempt has been made to reduce this fragility in the hope of thereby favorably affecting the retinopathy and to this end a number of substances have been tried, such as Vitamin P, ascorbic acid, hesperidin and rutin and various combinations of these like rutin and ascorbic acid.[8,9,17,23,24]

Various investigators have shown that rutin decreases capillary fragility but not to normal levels in diabetics with retinopathy. Despite some reduction in the general capillary fragility Donegan and Thomas[9] and Dolger[8] have found no significant improvement in the appearance of the retinopathy and no visual improvement despite therapy with large doses of rutin

This work is further borne out by our observations in the clinic of 18 patients with diabetic retinopathy who were on rutin and rutin with ascorbic acid for an average of 7.8 months, the longest being 2 years and the shortest 1 month. These patients showed no change in the

retinopathy and no visual improvement.

Further treatment of 2 patients in our group with severe retinitis proliferans by 8 x-ray treatments to the posterior regions of the globes over 19 days time was attempted. Marked visual improvement was attained on one, the other remained approximately the same as far as both vision and retinopathy were concerned.

The pathogenesis of the retinal lesions in diabetes are not well understood at the present time. Elwyn[10,11] believes that the hyperglycemia associated with diabetes influences the capillaries in some unknown manner producing dilatations of some of these terminal vessels in the retina. A chronic stasis occurs from this dilatation with repeated hemorrhages into the retina giving a chronic state of subnutrition and deficient oxygen supply with consequent appearance of hyaline and lipoids. This view is highly theoretic but indicates a view expressed by some which, if true, would demand very rigid control[22] of the hyperglycemia and glycosuria in treatment of diabetic retinopathy.

A different opinion as to the cause of the retinal hemorrhages in diabetes is suggested by Mosenthal[20] who believes they occur as results of hypoglycemic reactions and advises high enough levels of blood sugar and glycosuria short of polyuria to prevent such hypoglycemic reactions.

Ballantyne[5], in pointing out the development of the earliest visible lesion characteristic of diabetic retinopathy, namely, the capillary microaneurysm, offers a combination of 2 factors: "weakening of the resistance of the capillary walls and a relative increase of pressure within the vessel." In pathological specimens, he has found swelling of the endothelial cells with fat granule infiltration in the endothelium causing partial or complete blockage of the lumen. The damage endothelial cells are less resistant than normal cells and when there is complete blockage the capillary walls yield to the endovascular pressure.

Friedenwald[13] confirms Ballantyne's findings of small saccular aneurysms connected with the capillaries and notes in addition that these sacs are often incompletely lined with endothelium. This suggests that perhaps the first event is a leakage of blood through small breaks in the capillary walls that show little tendency to heal and that after the persistence of these tiny hemorrhages for some time there is a later enclosure of these petechiae by an outgrowth of endothelium from the capillary. If this explanation is correct, Friedenwald feels that the typical diabetic exudates could be explained by a leakage of plasma but not red cells into the retinal tissue spaces through still smaller breaks in the capillary walls, accounting for the high protein content observed in diabetic exudates.[13, 17]

The possibility has therefore been suggested that the retinal capillaries also are more fragile and permeable than normal, thus accounting for aneurysms, hemorrhages and exudates so characteristic of diabetic retinopathy.

In 1936, Kimmelstiel and Wilson in 8 cases[7] of diabetes described the deposition of a hyaline material in the intercapillary connective tissue of the glomeruli of the kidney. They called this intercapillary glomerulosclerosis.

Friedenwald[14] states that in its most outspoken form the lesion occurs almost exclusively in long standing diabetics and is very commonly associated with diabetic retinopathy. He adds that, in his own material, innumerable retinal capillary aneurysms were found in every case of Kimmelstiel-Wilson disease. Ashton[2] conforms the findings of Friedenwald as to the occurrence of retinal microaneurysms in every case of intercapillary sclerosis that he studied pathologically. Ophthalmoscopically, Kimmelstiel-Wilson disease may be represented by a fundus picture varying anywhere from a normal appearing fundus to

one showing massive exudates and extensive retinal and vitreous hemorrhages, retinitis proliferans and detachment of the retina.[2] Though intercapillary glomerulosclerosis occurs more or less regularly with the more advanced types of diabetic retinopathy, an absolute diagnosis cannot be made on the ophthalmoscopic picture but, according to Henderson[16,18] should be strongly suspected in patients who have diabetes mellitus of long standing associated with albuminuria, hypertension, renal insufficiency and diabetic retinopathy of an advanced type.

We would like to add in this connection that in compiling the statistics on our 49 patients with diabetic retinopathy, 3 cases were found to have notations by the medical department of a possible Kimmelstiel-Wilson disease. All 3 of these patients showed ophthalmoscopically a mixed vascular diabetic retinopathy with retinitis proliferans.

SUMMARY

The most characteristically diagnostic ophthalmoscopically visible lesions of diabetic retinopathy are the small punctate red spots occurring in the presence of normal retinal arterioles. These minute red spots were thought for years to be small hemorrhages but today we know with absolute certainty that many of them are capillary aneurysms.

Retinal changes are evidenced ophthalmoscopically by microaneurysms, hemorrhages, exudates, venous changes, proliferative or non-proliferative, with normal arterioles. When arteriolar changes, especially focal arteriolar narrowing, are superimposed, we have a mixed vascular diabetic retinopathy.

The retinal findings in 49 patients with diabetic retinopathy followed in our eye clinic for one year, were tabulated and discussed.

There appears to be a definite increase in the incidence of diabetic retinopathy and its occurrence apparently is more closely related to the duration of the disease than to the age of the person.

Capillary fragility is greatly increased in the diabetic with retinopathy and various attempts have been made to favorably influence the retinopathy by substances aimed at reducing this abnormal fragility. Results of this treatment have not so far been very promising.

The pathogenesis of diabetic retinopathy is not known at present but the capillary and larger vein changes may be an attempt on the part of the vascular system to furnish adequate nutrition to a tissue suffering from a basic metabolic fault causing poor nutrition and deficient oxygen supply.

Ophthalmoscopically, an absolute diagnosis of Kimmelstiel-Wilson disease cannot be made, but it should be suspected in patients with long standing diabetes mellitus associated with albuminuria, hypertension, renal insufficiency and diabetic retinopathy of an advanced type.

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II. MEDICAL SCHOOL NEWS

Coming Events

April 3 - Annual John W. Bell Tuberculosis Lecture (Hennepin County Medical Society) - "The Relationship of Sarcoidosis to Tuberculosis," Dr. Robert G. Bloch, University of Chicago, Auditorium of North American Life and Casualty Co. - 7:30 p.m.

April 10-12 - Continuation Course in Pediatrics for Specialists

April 17-19 - Continuation Course in Gynecology for General Physicians

April 20 - Phi Delta Epsilon Lectureship - "Regional Ileitis", Dr. Burrill B. Crohn, Columbia University, Museum of Natural History Auditorium - 8:00 p.m.

April 20-22 - Continuation Course in Cardiovascular Diseases for General Physicians

April 26 - Dr. A. C. Frazer, University of Birmingham, England, "The Mechanism of Fat Absorption," 15 Medical Science Amph. - 4:00 p.m.

April 26 - Annual George Chase Christian Lecture - "Cancer and Intermediary Metabolism of Steroid Hormones," Dr. Leo Samuels, University of Utah Medical School, 15 Medical Science Amph. - 8:00 p.m.

April 27 - Dr. A. C. Frazer - "The Normal and Abnormal Fat Absorption in Man," 15 Medical Science Amph. - 8:00 p.m.

* * *

Continuation Course in Pediatrics

Specialists in pediatrics will meet at the Center for Continuation Study on April 10-12 to attend a course devoted to metabolic and endocrine disorders in childhood. Distinguished visiting physicians who will participate as faculty members for the course include Dr. Daniel F. Darrow of the Department of Pediatrics, Yale University School of Medicine, and Dr. George M. Guest of Children's Hospital, Cincinnati. Dr. Darrow will present the subjects, "General Principles of Fluid Therapy" and "The Role of Potassium in Fluid Therapy." Dr. Guest will speak on the subjects, "The Management of Diabetes Mellitus without Dietary Restrictions in Infants and Children" and "Diabetic Coma -- Metabolic Derangements and Principles for Corrective Therapy." Dr. Irvine McQuarrie, Professor and Head of the Department of Pediatrics, is in charge of the course and will participate, together with other members of the staff of the University of Minnesota Medical School and the Mayo Foundation.

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Conference on Cardiovascular Disease

A new conference in Cardiovascular Disease will be added to the Medical School calendar beginning Wednesday, April 5. The conference, which will be held every two weeks alternating between the Veterans Administration Hospital and the University Hospital, will be an inter-departmental function inviting the participation of all physicians and staff members interested in this field. Anyone interested in presenting material should communicate with Dr. Morse Shapiro, Associate Professor of Medicine, Chairman of the conference. "Mitral Stenosis -- Hemodynamics and Prospects for Surgical Treatment," will be presented by Doctors Richard Ebert, Reuben Berman, and N. K. Jensen at the first conference on April 5.

III. UNIVERSITY OF MINNESOTA MEDICAL SCHOOL
CALENDAR OF EVENTS

April 2 - 8, 1950

No. 283

Sunday, April 2

9:00 - 10:00 Surgery Grand Rounds; Station 22, U. H.

10:30 - 11:00 Surgical Conference; Rm. M-109, U. H.

Monday, April 3

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; M-109, U. H.

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

11:00 - Pediatric Rounds; Erling Platou; Sta. I, Minneapolis General Hospital.

11:00 - 11:50 Physical Medicine Seminar; Arthritis; Ralph Worden; E-101, U. H.

11:00 - 11:50 Roentgenology-Medicine Conference; Veterans Hospital.

11:00 - 12:00 Cancer Clinic; K. Stenstrom and A. Kremen; Eustis Amphitheater, U. H.

12:00 - 1:00 Physiology Seminar; Quantitative Measurements of Pulmonary Edema; Allen Hemingway; 214 M. H.

12:15 - 1:20 Obstetrics and Gynecology Journal Club; Staff Dining Room, U. H.

12:30 - 1:20 Pathology Seminar; Hyaluronidase and Its Inhibitors; David Glick; 104 I. A.

12:30 - 1:30 Surgery Problem Case Conference; A. A. Zierold, C. Dennis and Staff; Small Classroom, Minneapolis General Hospital.

1:30 - 2:30 Surgery Grand Rounds; A. A. Zierold, C. Dennis and Staff; Minneapolis General Hospital.

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

4:00 - Public Health Seminar; Subject to be announced; 113 Medical Sciences.

4:00 - Medical-Surgical Conference; Main Conference Room, Bldg. I, Veterans Hospital.

4:00 - Pediatric Seminar; Chloromycetin; Albert Miller; 6th Floor West, Child Psychiatry, U. H.

5:00 - 5:50 Clinical Medical Pathologic Conference; Todd Amphitheater, U. H.

5:00 - 6:00 Urology-Roentgenology Conference; C. D. Creevy, O. J. Baggenstoss and Staffs; M-109, U. H.

Tuesday, April 4

8:00 - 9:00 Fracture Conference; Auditorium, Ancker Hospital.

8:30 - 10:20 Surgery Conference; Small Conference Room, Bldg. I, Veterans Hospital.

9:00 - 9:50 Roentgenology Pediatric Conference; L. G. Rigler, I. McQuarrie and Staffs; Todd Amphitheater, U. H.

10:30 - 11:50 Surgical Pathological Conference; Lyle Hay and E. T. Bell; Veterans Hospital.

11:00 - Contagion Rounds; Forrest Adams; Sta. L., General Hospital.

12:30 - Pediatric-Surgery Rounds; Drs. Stoesser, Wyatt, Chisholm, McNelson and Dennis; Sta. I, Minneapolis General Hospital.

12:30 - 1:20 Pathology Conference; Autopsies; J. R. Dawson and Staff; 102 I. A.

1:30 - 2:30 Pediatric Psychiatry Conference; R. A. Jensen and Staff; 6th Floor, West Wing, U. H.

1:00 - 2:30 X-ray Surgery Conference; Auditorium, Ancker Hospital.

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

3:15 - 4:20 Gynecology Chart Conference; J. L. McKelvey and Staff; Station 54, U. H.

3:30 - 4:20 Clinical Pathological Conference; Staff; Veterans Hospital.

4:00 - 5:00 Physiology-Surgery Conference; Eustis Amphitheater.

4:00 - 5:00 Pediatric Rounds on Wards; I. McQuarrie and Staff; U. H.

5:00 - 6:00 Porphyrin Seminar; C. J. Watson, Samuel Schwartz, et al; Powell Hall Amphitheater.

5:00 - 6:00 X-ray Conference; Presentation of cases by Ancker Hospital Staff; Doctors Aurelius, Peterson and Marshall; Todd Amphitheater, U. H.

Wednesday, April 5

8:00 - 8:50 Surgery Journal Club; O. H. Wangensteen and Staff; M-109, U. H.

8:00 - 9:00 Roentgenology-Surgical-Pathological Conference; L. B. Thomas and L. G. Rigler, Todd Amphitheater, U. H.

8:30 - 9:30 Clinico-Pathological Conference; Auditorium Ancker Hospital.

8:30 - 10:00 Orthopedic-Roentgenologic Conference; Edward T. Evans and Bernard O'Loughlin; Room 1AW, Veterans Hospital.

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

Wednesday, April 5 (Cont.)

11:00 - Pediatric Rounds; Erling Platou; Sta. I, General Hospital.

11:00 - 12:00 Pathology-Medicine-Surgery Conference; Surgery Case; O. H. Wangensteen, C. J. Watson and Staffs; Todd Amphitheater, U. H.

12:00 - 1:00 Radio-Isotope Seminar; Methods of Monitoring and Protection in Use of Isotopes and X-rays; Frank Loesser; 113 Medical Sciences.

12:00 - 1:00 Surgery Problem Conference; General Hospital.

12:15 - Staff Meeting; Main Classroom, General Hospital.

3:00 - Pediatric Rounds; C. J. Huenekens; Sta. I, General Hospital.

3:30 - 4:30 Journal Club; Surgery Office, Ancker Hospital.

4:00 - 5:00 Infectious Disease Rounds; Todd Amphitheater, University Hospitals.

5:00 - 5:50 Urology-Pathological Conference; C. D. Creevy and Staff; E-101, U. H.

Thursday, April 6

8:30 - 10:20 Surgery Grand Rounds; Lyle Hay and Staff; Veterans Hospital.

9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; M-109, U. H.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:30 - 11:50 Surgery-Radiology Conference; Daniel Fink and Lyle Hay; Veterans Hospital.

11:00 - 12:00 Cancer Clinic; K. Stenstrom and A. Kremen; Todd Amphitheater, U. H.

11:30 - Pathology Conference Clinic; Main Classroom; General Hospital.

11:30 - 12:30 Clinical Pathology Conference; Steven Barron, C. Dennis, George Fahr, A. V. Stoesser and Staffs; Large Classroom, Minneapolis General Hosp.

12:00 - 1:00 Physiological Chemistry Seminar; 214 M. H.

1:00 - 1:50 Fracture Conference; A. A. Zierold and Staff; Minneapolis General Hospital.

4:15 - 5:00 Bacteriology Seminar; Serological Tests for Tuberculosis; Ronald Howard, Mrs. E. A. Slater; 214 M. H.

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

5:00 - 6:00 X-ray Seminar; To be announced; Nils Westermark; Todd Amphitheater, U. H.

7:30 - 9:30 Pediatrics Cardiology Conference and Journal Club; Review of Current Literature 1st hour and Review of Patients 2nd hour; 206 Temporary West Hospital.

Friday, April 7 - Holiday

Saturday, April 8

7:45 - 8:50 Orthopedics Conference; Wallace H. Cole and Staff; M-109, U. H.

8:30 - 9:30 Surgery Conference; Auditorium, Ancker Hospital.

9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; E-221, U. H.

9:00 - 10:30 Pediatric Grand Rounds; I. McQuarrie and Staff; Eustis Amphitheater, U. H.

9:00 - 11:30 Neurology Conference; Disorders of Speech and Aphasia; Veterans Hospital Annex.

9:15 - 10:00 Surgery-Roentgenology Conference; F. Ruzicka, O. H. Wangensteen and Staff; Todd Amphitheater, U. H.

10:00 - 11:30 Surgery Conference; O. H. Wangensteen and Staff; Todd Amphitheater, U. H.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

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

11:00 - Contagion Rounds; Forrest Adams; Sta. L., General Hospital.