VOLUME III

Staff Meetings were held as usual each week during the regular school year. Because of a progressive increase in attendance, it was necessary to move the meeting place several times. The abstracts and case histories are the work of Bjarne Pearson, Rudolph Koucky (Citizen's Aid Society Fellows) and the Editor. The Bulletins were very well received and discussions were unusually good. Many visitors were present and the mail list continued to grow. The same plan of emphasizing malignancy proved popular. It is felt that we reach many people through our Bulletins. They serve as nuclei for public health talks and give to the Staff teaching outlines for students and graduate instruction. The hospital authorities provided the very tasty buffet luncheon each week without charge. Visitors are welcome at any time. Miss Gertrude Gunn, Record Librarian, made arrangements for all the meetings and took notes on the remarks made. Many of these were published the following week and added to the effectiveness of our message. At the final meeting by a rising vote, the Staff expressed its appreciation to the Citizen's Aid Society for financial assistance in preparing the Bulletin and providing funds for special fellows. Plans are under way for enlarging the scope of the meetings for next year.

William A. O'Brien, M. D., Editor.

VOL. III THURSDAY, OCTOBER 1, 1931 NO. 1

GENERAL STAFF MEETING
UNIVERSITY HOSPITALS
UNIVERSITY OF MINNESOTA

CONTENTS

I. ANNOUNCEMENTS

1. 1931-32: Looking into the future suggests that prospects for a successful year were never brighter. First and foremost, the appointment of Richard E. Scammon to the newly created position of Dean of Medical Sciences, rounds out our executive staff. Back from Chicago with a brand new sheen of administrative polish he has already made an auspicious start. Few men combine so many qualities of equal excellence; scientist, scholar, teacher, administrator, sociologist, economist, biometrician (to name but a few). Happy was the administrative choice in naming him and glad are we to pledge to him our loyalty, support, and cooperation. Through his inspiring leadership great things are possible. His work will be easier and more effective if we do our part.

2. Staff roster will not be printed for several weeks. To the new men we extend a hearty welcome and best wishes for the future. You have joined the University Hospitals Staff with all its privileges and obligations. This institution exists primarily for the care of the sick. Any other relationship between patient and physician is contrary to our ideals and purpose. At the same time our obligation to teach and advance knowledge must not be forgotten. Remember that many of the physicians who refer patients to us do not have the same opportunities to investigate them that we enjoy. Be scientifically charitable to them and remember that our relationships are exactly the same as if we were all in private practice. Evaluate carefully statements made by patients concerning previous opinions given by physicians and curb your tongue in their presence so that unfortunate mis-statements are not credited to our organization. You are expected to join in the weekly staff meeting and all other conferences of the institution. Give the best that is in you and you in turn will profit thereby. A service is just what you make it and many so-called bad assignments are frequently your fault. Complaints and suggestions are welcome at any time.

3. Wassermann reports are still unsatisfactory. The State Department of Health is authorized by law to do blood Wassermanns for the physicians of the state. In turn they ask our cooperation. We fail consistently to do this when we do not return a signed statement concerni the agreement of their report with our clinical-impression. This is the duty of the intern in charge of the patient. The blanks are to be found on the Wassermann report desk in the general laboratory. Look them over daily not only under the name of the physician but also under the patient's name. The admitting intern's name will be found on many who have gone into the house. Naturally, he does not know the condition of every patient he has admitted, and should not be expected to sign the report. The intern on the service should take care of this. The routine Wassermann is valuable but may be discontinued if we do not give better cooperation.

4. Breaking Departmental Technique is again before us for discussion and action. The increase in pediatric patients (many with acute communicable illness), tissue room in operating suite (no smoking - i.e., ethylene), possibility of operating room infections, taking ill patients to clinics from other men's services, etc., are all important matters. When we fail in our duty the student morale is weakened. Last year we had a nursing demonstration of contagious technique for physicians. It has been suggested that this would be a good idea to repeat. The other teaching hospitals in our group have rules and regulations which are respected; why not the University Hospitals? All of us have been offenders at one time or another, so the matter should be of concern to all.

5. Staff Meeting programs are tentatively arranged for [illegible] quarter. Malignant and non-malignant subjects will probably be discussed on alternate weeks. The Citizen's Aid Society has again financed this publication and each attendant at Staff

Meeting will be given his copy as in the past. In addition, they will be sent to other institutions and our University Hospitals alumni and friends. They are in no sense complete expositions of the subject under discussion, and unless they serve as a focus for further discussion, they are not worth the effort of getting them out. The desire of the Citizen's Aid Society for cancer education is commendable. Its vision in seeing the necessity for education of the profession (primarily) and the public (secondarily) is unusual. We are indeed grateful to them for the support of this principle and for their generosity in giving us the funds to make this publication possible. Ideas, themes for discussions, news, announcements, etc. are most welcome at any time.

II. ABSTRACT The Pathology of Diabetes Mellitus by Shields Warren, M. D., Pathologist to the New England Deaconess Hospital (Service of E. P. Joslin) Lea and Febiger, Philadelphia 1930, 1st Edition. Abstr. Pearson.

1. Note: Diabetes Mellitus commands our interest and attention. Its pathologic picture in the pancreas is still unfixed as a distinct entity, more victims are claimed by it yearly (in spite of insulin). Infection renders insulin impotent or nearly so, the arteriosclerotic complications grow in importance, gangrene is still too frequent, high fat, low carbohydrate insulin combinations are being questioned, the daily injection of a smaller dose of insulin rather than fixing administration of larger doses, near food intake is an interesting innovation, the future of the young diabetic is still in doubt. Those and many other features could be discussed. The present abstract will deal only with historical high lights, pathologic picture in diabetic and non-diabetic pancreases (control), cause of death and certain other phases.

2. Material: Joslin's report of 1294 diabetic deaths (Aug. 7, 1922 to date of publication 1930), 300 autopsied cases (259 pancreases available for study), and control material (Warren).

3. Historical Highlights. 1788, Cawley. Reported case of diabetes at autopsy, a pancreas full of calculi with scirrhous change in glands.

1889, von Mering and Minkowski. Removal of pancreas caused diabetes in experimental animals. Also demonstrated only one-eighth of pancrease sufficient to avert development of diabetes in animals.

1892, Hedon. Transplantation of remaining portions of partially resected pancreases with failure of development of diabetes as long as transplants remained in healthy condition demonstrating internal secretion (and not external) responsible for disturbance in carbohydrate metabolism.

1893, Laguesse. On anatomical grounds hazarded the opinion islands were organs of internal secretion, because of relationship of epithelium to rich vascular network that surrounds them.

1894, Hansemann. Collected 72 cases from literature and presented 54 new cases. (Chiefly gross pathological report). Theory of granular atrophy (interacinar fibrosis) and chief champion of acinar hypothesis.

1901, Opie. 1902, Ssoblew. Localized in islands pathological changes and explained some of difficulties in previous attempts at correlation.

1904, Sauerbeck. Championed insular hypothesis.

1907, Lane. 1911, Bensley. New stain for island cells probably discrediting Ssoblew's work (found complete absence of islands in 4 out of 15 cases).

1910, Weichselbaum. 1911, Heiberg. Claimed pancreatic changes present in every case of diabetes limited to islands in sufficient number of cases to prove insular hypothesis.

1909, 1911, Cecil. In series of 90 cases, came to same conclusion and later called attention to evidence of regeneration or hypertrophy in islands in diabetes (34 out of 100 cases).

1913, Allen. Pointed out every anatomical hypothesis of diabetes still requires assistance by assuming existence of a certain proportion of functional cases without known anatomical basis.

1914, Homans. Found disappearance of secretory granules in island cells of cats from which three-fourths of pancreas had been removed. In diabetic animals,

he noted hydropic degeneration of island cells, chiefly in "B" group. This gave rise to hope that single characteristic, universal diabetic lesion was to be discovered (not the case).

1900, Schulze. 1926, Ukai. And others, 1902, 1912. Extensive (but now known to be incomplete) atrophy of acinar tissue was unaccompanied by disturbance of carbohydrate metabolism.

1922, Banting. Insulin. Note it has never been produced from island tissue alone, always admixture of acinar tissue.

1927, Wilder. Striking case of hyperinsulinism due to carcinoma of islands of Langerhans which seemed to clinch truth of insular hypothesis.

1928, Thalhimer and Murphy. 1929, McClenahan and Norris. 1929, Howland. Demonstrated carcinoma and adenoma hyperinsulinism, also results of operative removal of carcinoma of island-cell.type.

1928, Finney. 1929, Allan. Operative removal of portion of whole pancreasefor functional hyperinsulinism.

Note: It was a case of pancreatic calculi which first called attention to the pancreas in diabetes; Moses Barron's report from our laboratory on case of pancreatic calculi which stimulated Banting to develop insulin.

4. Pancreas in Diabetes Mellitus.

Table 4 - Lesions in the Islands of Langerhans in 259 Diabetic Pancreases.

Age, Yrs.	Cases	Normal	S+	S++	S+++	H+	H++	H+++	Hypertrophy	Hydrodegeneration	Pyknotic nuclei	Hemorr.	Adenoma
0 to 10	10	2	0	0	0	1	0	0	0	2	2	0	0
11 to 20	23	10	4	0	0	0	0	0	0	1	0	0	0
21 to 30	20	7	3	2	1	0	1	0	2	2	1	0	0
31 to 40	21	9	3	3	0	0	1	0	0	3	0	1	0
41 to 50	34	9	3	6	1	0	5	7	4	2	0	0	0
51 to 60	63	15	11	5	1	1	15	14	7	2	1	0	0
61 to 70	63	12	6	6	3	5	17	14	5	2	0	0	1
71 to 80	19	2	6	1	1	1	0	6	2	1	1	1	0
81 +	2	1	0	1	0	0	0	0	0	0	0	0	0
?	4	2	0	1	1	0	0	1	0	0	1	0	0
Total	259	69	36	25	8	8	39	42	20	15	6	2	1

S = fibrosis or sclerosis. H = hyaline.

a. Hyaline change: Origin is either epithelial (intracellular), or mesoblastic (intercellular) (few show amyloid). Is it cause or effect of diabetes? Is it secondary replacement as a result of destruction of epithelium? Or, is it primary condition? In 97% of 89 cases, it occurred after 40. Hyaline changes are common in other parts of body (aging), but it may be seen in young individuals. Staining methods have attempted to prove its origin (Mallory's). If the result of diabetes, it should never be present in this particular location in absence of the disease. On the other hand, it has been found in non-diabetics. In carefully studied cases, definitely known to have diabetes over ten years, 50% showed hyalinization. Usually associated with uninvolved or nearly normal islands (also may be the seat of calcium deposits). Author believes it is result of intracellular substance (fibroblasts and possibly endothelial cells). Separates epithelium from blood supply by practically impermeable membrane, diabetes develops. Often

seen in mild diabetics.

b. Fibrosis. Next most frequent change after hyaline. Development of definite capsule with fibroblastic change throughout island. (27%) Tends to occur in older individuals. May be associated with arteriosclerosis of the pancreatic vessels and is practically always accompanied by interacinar or interlobular fibrosis. May be found with hyalinization.

c. Lymphocytic infiltration of islands may be seen in young persons. Associated with severe diabetes (?). Sometimes seen with endothelial leukocytes.

d. Hydropic degeneration. Chiefly sponsored by Allen. Questioned by author because of possibility of post-mortem change. Thought to be due to excessive functional strain. Sometimes seen in association with fulminating cases. (15 cases) Low figure may be result of treatment with Insulin (relieving functional strain).

e. Pyknotic Nuclei. (6 cases) usually unassociated with other conditions. Question as to postmortem change or improper fixation.

f. Hypertrophy of islands (not infrequently encountered). Simple increase in size without change in character or change in cells to columnar type with central nuclei. Rudimentary islands of latter type may be found (easily distinguished). (20 cases). Standard more than 400 micra in diameter. No correlation existed in cases studied with age, duration, severity, etc.

g. Hemorrhage. Probably a postmortem change or artefact. (2 cases).

h. Adenoma. (1)

i. Islands apparently normal. 69 (27%) showed normal islands. Considerable number occurred in insulin treated cases but a fair number in pre-insulin days, or in cases which received no or inadequate insulin. This is a most troublesome point in explaining pathology of diabetes.

j. Fatty infiltration. Increase in intracellular fat, not characteristic of diabetes. May be found in other diseases, (alcoholic intoxication), probably result rather than cause of diabetes (Wilder).

k. Quantitative changes.

1. Involving pancreas as a whole. Aside from insular changes (i.e. acinar cells). Fibrosis perhaps simplest and most frequently occurring change. (155 cases).

2. Lipomatosis. Pancreatic fat grossly related to normal body fat. 27% showed varying degrees of lipomatosis.

3. Arteriosclerosis. Of pancreatic vessels (15 cases only). Not as common as arteriosclerosis in spleen.

4. Pancreatitis. (6 cases) Diabetes developed after acute pancreatitis as result of destruction. More would have developed it if they lived? So-called subacute cases probably not true forms of pancreatitis (3 cases).

5. Abscesses. (4 cases of metastatic) from staphylococcus pyemia.

6. Calculi 3 out of 300 autopsies. Effect is same as liagation. Lesion is of much historical interest as 1 case reported by Barron (Minnesota) aroused Banting's interest and thus played a part in development of insulin.

7. Amyloidosis (2 cases).

8. Carcinoma. Average incidence (4% of all malignant tumors). Found in 32% of small series (37 cases of malignant disease in 3-1/2 years). Present series only 2 cases. Suggests possible relationship although selection of cases is possible.

9. Weight: Not significant because of normal variations? presence of fat, etc.

Comment: Hyalinization most frequent change. Fibrosis and normal next.

Control Studies:

Table 8 - Lesions of the Islands in 200 Non-Diabetic Pancreases.

Age, Yrs.	Cases	Fibrosis: Normal	Fibrosis: Slight	Fibrosis: Mod.	Fibrosis: Marked	Hyaline: Slight	Hyaline: Mod.	Hyaline: Marked	Hypertrophy	Mit-Pyk-osis	Pyknuc.	Hyd. degen.	Adenoma	Hemorrhage
0 to 10	6	6	0	0	0	0	0	0	0	0	0	0	0	0
11 to 20	2	2	0	0	0	0	0	0	0	0	0	0	0	0
21 to 30	3	3	0	0	0	0	0	0	0	0	0	0	0	0
31 to 40	10	9	0	0	0	0	0	0	0	0	0	0	0	0
41 to 50	34	31	0	0	0	0	1	0	0	0	1	0	1	0
51 to 60	63	54	3	0	0	0	0	1	1	2	1	0	0	1
61 to 70	52	40	5	2	1	0	1	0	1	1	0	1	0	0
71 to 80	28	20	2	1	0	0	1	0	3	0	0	1	0	0
81+	2	2	0	0	0	0	0	0	0	0	0	0	0	0
Total	200	167	10	4	1	0	3	1	5	3	2	2	1	1

Table 7 - Lesions of the Entire Pancreas in Non-Diabetics.

Age, Yrs.	Cases.	Interst. Panc.	Lipomatosis	Acute Pancrea.	Carcinoma	Metastatic tumors	Cysts	Calculi	Tuberculosis
0 to 10	6	0	0	0	0	0	0	0	0
11 to 20	2	0	0	0	0	0	0	0	0
21 to 30	3	0	0	0	0	0	0	0	0
31 to 40	10	3	0	0	0	0	0	1	0
41 to 50	34	3	5	2	0	1	0	0	0
51 to 60	63	23	10	0	1	6	1	0	0
61 to 70	52	17	8	2	0	6	0	0	1
71 to 80	28	10	4	1	0	1	1	0	0
81+	2	2	0	0	o	0	0	0	0
Total	200	58	27	5	1	14	2	1	1
Percent of total		29.0	13.5	2.5	0.5	7.0	1.0	0.5	0.5

Comment: Striking that any change found in diabetic pancreas may be found in non-diabetic organ (frequency only difference). Information from clinical studies and glycogen determinations of various organs only real evidence of disease.

5. Cause of Death in diabetes.

Cause of Death.	Banting Era total: Deaths.	Banting Era total: Per cent of all causes.
All causes	1294	100.0
1. (a) Primary coma	199	15.4
(b) Coma incidental to other causes	48	3.7
2. Cardio-renal-vascular diseases--total	597	46.1
Cardiac	273	21.1
Nephritis	57	4.4
Apoplexy	99	7.7
Arteriosclerosis--total	60	4.6
Arteriosclerosis with cardiac, renal or cerebral complications	38	2.9
Gangrene	108	8.3

	Causes	Deaths	Per Cent
3.	Infections--total	212	16.4
	Influenza and pneumonia	105	8.1
	Other respiratory infections	7	0.5
	Infections of the pharynx and tonsils	3	0.2
	Infections of the ear and mastoid	7	0.5
	Gall bladder disease	5	0.4
	Appendicitis	11	0.9
	Other infections of the digestive system	5	0.4
	Carbuncle	18	1.4
	Erysipelas	8	0.6
	Abscess of the skin	14	1.1
	Abscess of other organs	16	1.2
	All other infections	13	1.0
4.	Pulmonary tuberculosis	74	5.7
5.	Cancer	92	7.1
6.	Syphilis	1	0.1
7.	Other causes	119	9.2
	Inanition	6	0.5
	Acute intestinal obstruction	2	0.2
	Cirrhosis of the liver	10	0.8
	Diseases of the prostate	10	0.8
	Diseases of the thyroid gland	6	0.5
	Pregnancy	5	0.4
	Accidents	26	2.0
	Suicides	9	0.7
	Diabetes	13	1.0
	Other diseases and conditions	32	2.5

Note: In 300 autopsied cases uncomplicated, coma was cause of death in 53 cases; 38 others died of complicated coma induced by septic processes usually bronchopneumonia (23%) (not lobar), gangrene (11%), septicemia (10%). Is increased prevalence of arteriosclerosis due to disease or treatment? Always present after 5 years duration (older patients), but young patients may show it as well. Lipoid metabolism disturbance may result in intimal deposits (atheromatous plaques) (see Aschoff on Arteriosclerosis) Change most frequently seen in diabetics. In 300 cases 24% due to arteriosclerosis (many in series under 40). Heart is leading organ (coronary disease), extremities next, few cerebral (not many head posts). Low incidence of hypertension in group (argument against functional strain) (see Major, U. of Minnesota, who found it rather frequently). Only 37 of 300 case showed aorta free of arteriosclerosis. 55 of 300 showed gangrene (2 gas cases). Not always primary, frequently with coronary sclerosis. Gangrene usually moist and preventable! Arteriosclerosis occurs in young and old, intensified by disease, tends to intimal type, related to lipoid disturbance, seen also in pulmonary circulation, not the product of strain (hypertension). In pre-insulin days not so prominent because of shorter duration of disease. Believes internal ground substance is injured by variable sugar concentration and acidous; fat deposition is secondary (?). Well treated diabetics should have normal amount of arteriosclerosis for age. Infection causes 126 of 300 fatal cases. Pus plus insulin is inert mixture (suggestive only). Syphilis and tuberculosis were uncommon. Usual cause of death in children is coma (22 cases), with or without infection. Of series of 300 cases 8% were of 15 years duration or longer (one was 40 years). All but 4 showed severe arteriosclerosis. Insulin resistant cases (more than 200 units daily is standard) seen only once. May be end stage of hemachromatosis often with liver injury (lack of storage). Other interesting points were 28% of 300 cases with gall bladder infection or stone. Believes operation is indicated in diabetic patients (for beneficial effect on tolerance)

and not for possible pancreatitis change. Studied glyocogen distribution in various organs including skin (where it is usually decreased in amount).

Conclusions:

1. The pathological picture of diabetes in the pancreas is not constant.
2. The commonest causes of death are coma, infection and arteriosclerosis.
3. The latter is probably due to metabolic disturbance and not functional strain,(hypertension).
4. It is a premature development (aging), which may be prevented by proper management (well controlled cases).
5. Coma is often complicated by infection except in children (usually pneumonia).
6. Infection is still a serious condition as it seems to render insulin ineffective.
7. Gall bladder disease in diabetics should be treated surgically.
8. Insulin resistant cases (more than 200 units daily) are uncommon.
9. Gangrene is often due to carelessness on the part of patient and physician (education).
10. Coronary disease and complication is most frequent form of arteriosclerosis; extremities are next.

III. CASE REPORT:

DIABETES MELLITUS, ARTERIOSCLEROSIS, HYPERTENSION, GLAUCOMA.

Path. Pearson.

The case is that of a white male, 42 years of age, admitted to the University Hospitals 4-4-31 and died 6-10-31 (67 days).

Diabetes

1925 - Patient was found to be diabetic and was treated at a clinic. He was put on a diet and took 5 to 10 units of insulin daily until 4 months before admission. Patient had frequency of urniation, especially at night.

Vision

9- -30 - Patient noticed blurring of both eyes which began insidiously and went to a optometrist who found some difficulty in fitting him with the right glasses.

11- -30 - Patient became sick. He had stomach "flu" and noticed dimness of vision so he went to an eye specialist. The eye specialist examined his eyes and said he had hemorrhage of the retina and also found an albuminuria. He gave him some pills to take two times daily. Vision, however, became progressively worse so he had to quit his clerical work because he could not recognize figures.

No insulin.

1-10-31 - Patient went to a private hospital and saw a kidney specialist. He remained there for about ten days without any improvement. The doctor put him on a strict diet and cut out his insulin.

Edema

2-7-31 - Weakness began insidiously. Patient noticed that his feet were swollen at times, especially in the evening. He lost 15 lbs. of weight during the past year. He also noticed dyspnea and palpitation. Past history: Frequent sore throats ten years ago.

Hospital

4-4-31 - Admitted to University Hospitals. Physical examination reveals a well-developed, fairly well-nourished male whose vision is much impaired. He cannot read letters of ordinary size but, however, can distinguish light from dark.

Ophthalmoscopic examination

Pupils show slight reaction and marked edema of the discs obliterating the details. The peripheral portion of retina of right eye suggests a flat detachment. There is a grayish-white exudate in the macula. The blood vessels are irregular with definite sclerosis. Left eye shows marked neuro-retinitis. The discs are edematous with some capillaries at upper temporal margin. The blood vessels are sclerotic. There are many superficial hemorrhages. Diagnosis: Neuro-retinitis (cardiovascular-renal disease). B.P. 180/100. There is a soft systolic murmur in third left interspace just lateral to starnum. There is a slight ventricular enlargement. He was put on a diet containing carbohydrates 75, proteins 50 and fats 175. He was given 10 units of insulin daily. Pulse 99, Temp. 98.

Laboratory:

4-5-31 - Glucose test with 50 Gm. of glucose done in Dispensary gave the following values: .156 for the fasting; .309 1/2 hour later; .307 1-1/2 hour later. Wassermann is negative. Urine shows a trace of sugar. Blood shows Hb. 54, rbc's 2,750,000, wbc's 7,650, P 71, L 27 and M 1. Patient was given 10 units of insulin at 6:45 A.M. and 5 units at 5:00 P.M. Luminol gr. 1/4 t.i.d.

4-6-31 - Sugar .161, Creatinine 2.3. NPN 36.3. X-ray shows slight amount of thickening of the pleura at right apex. The lung parenchyma appears normal as also does the heart. Conclusion: Slight thickening of pleura in right apex. Electrocardiogram shows waves T_1 and T_{11} inverted (coronary).

Renal function.

4-7-31 - P.S.P.

1st spec.	1/2 hr.	7%	
2nd spec.	1 hr.	5%	Total
3rd spec.	1-1/2 hr.	5%	20%
4th spec.	2 hr.	3 %	

24 hr. specimen, 2575 cc., specific gravity 1.005, sugar 0 and albumin +

4-8-31 - 24 hour specimen, 1200 cc., specific gravity 1.010, sugar 0, albumen ++, numerous granular casts and few hyaline casts. Concentration and dilution test:

8 A.M.	80 cc.	1.014	
9 A.M.	40	1.010	
10 A.M.	75	1.006	
11 A.M.	115	1.005	(Specific gravity varies from 1.005 to 1.014)
12 A.M.	70	1.008	
3 P.M.	135	1.009	
6 P.M.	125	1.012	

4-10-31 - Basal metabolic rate - +1%. Stools show + for benzidene. Urine shows specific gravity 1.007, sugar 0, albumen +++, many granular casts. Output 1200 cc. and intake 2700 cc.

4-15-31 - Urine shows specific gravity 1.011, sugar 0, albumen +++ and many granular casts. Blood pressure 184/100.

Pain in eye.

4-18-31 - Patient complains of pain in right eye. Argyrol applied, 10% every 3 hours. Urine shows specific gravity 1.008, albumen +++ and granular casts. B.P. is now 184/102. The diet is changed to Carbohydrates 100, proteins 50 and fats 175. Patient continues, as before, with 15 units of insulin daily.

Glaucoma

4-20-31 - Patient still complains of pain in right eye. Eye consultation: Diagnosis - acute glaucoma. Advise - 1% pilocarpin, 1/2% eserine, 2 drops of each every 1/2 hour followed by hot compresses.

Nausea

4-23-31 - Patient complains of being nauseated, gastric distress, headache and pain in right eye. Rehberg creatinine clearance test - 18.1 cc. Urine - sugar ++ and albumen +++. B.P. is now 174/98. Pulse 108. Temperature 99.2.

4-24-31 - Patient feels sick and nauseated. The pulse is fast. Epistaxis of 100 cc. Has severe headache. Addition 10 units of insulin given at breakfast. Carbohydrates are decreased. Diet changed to carbodhydrates 75, proteins 50 and fats 150. Pyramidon gr. v given for headache.

Vomits

4-26-31 - Patient has emesis, 50 cc. of brownish fluid. The eye is still painful. Urine shows sugar + and albumen +. Blood sugar - .370. NPN - 77.0 mg. B.P.170/98. T 99. P 110.

Confusion

4-29-31 - Fluids are now forced. Patient seems confused. He thinks he is in Ireland. Temperature 99.4. Lumbar puncture is done - pressure increased on jugular compression, otherwise normal; 2 cells found; Nonne and Noguchi negative; Wassermann and colloidal gold negative.

Insulin increased

5-5-31 - Medical note: Blood sugar 288. NPN 66. Creatinine 2.3. Urine shows sugar ++++ and albumen ++. Patient is getting carbohydrates 50, proteins 25 and fats 50. Intake 1500 to 1600 daily. Insulin is increased to 35 units, 30 units and 35 units, 100 units in all, daily. The right eye tension is very hard. Mentally, patient is confused. Quantitative sugar 1.532 Gm. per 100 cc. of urine.

5-11-31 - Medical note: Urine shows sugar ++' in all specimens. Blood sugar .296. NPN 63. Temperature 99.6 daily. B.P. is now 160/84. The diet is now carbohydrates 50, proteins 25 and fats 50. Total of 155 units of insulin is now given. Blood - Hb. 48%, rbs'c 2,600,000 and wbc's 8,700.

5-20-31 - 165 units of insulin now given. Patient continually shows sugar in night and A.M. specimens. Blood - 48%, rbc's 2,600,000, wbc's 8,700.

Neurological consultation

Patient is fairly clear mentally today. Recalls history of his sickness in detail, occasionally hesitates over a doctor's name but remembers eventually. Blind in right eye. Can see light of ophthalmoscope in central field of left eye. Diminutions of hearing of right ear, apparently condition of deafness, however. Trunk and extremities negative, neurologically. Conclusions: practically negative, neurologically. A confused mental state would not be surprising in this case due to toxic status plus arteriosclerosis.

Insulin resistant?

6-3-31 - Medical note: Patient is getting 170 units of insulin per day with carbohydrates with a volume of only 105 grams daily. All of urine specimens still show +++ sugar. Will discontinue insulin.

Uremic coma?

6-8-31 - Blood chemistry - sugar .468. Medical note: Called to see patient. He had twitchings of hands and feet, severe epistaxis. Pulse is rapid and irregular. Patient is failing rapidly. B.P. 132/? Later B.P. was obtained, 220/106. 9 A.M.- caffeine gr. 7-1/2 given. Kussmaul type of breathing present. Perspiring some. Chest negative. Knee jerks absent. Babinski's positive on both sides. Abdominal reflexes absent. Triceps absent. Biceps 1+. Patient is comatose. Urine shows sugar ++++ and negative for diacetic and acetone. Given more caffeine.

Neurological consultation: Patient is in deep coma. Pulse and respirations rapid. Tongue moist. Left corner of mouth looks rather weak. Deep reflexes in arms exaggerated. Both arms falling limply. Abdominal reflexes absent. Knee and ankle jerks +3. Bilateral sustained ankle clonus. Babinski sluggishly positive on left, questionable on right. Does not react to painful stimulus except slight movement of the left leg. Incontinent. Spinal fluid reported under no increased pressure and was clear. No uremic odor to the breath. Conclusions: Possibly cerebral hemorrhage but localization is unusually bilateral. Suggest repeating spinal fluid after few hours to see if blood tinged. Uremia likely.

Exitus

6-10-31 - Patient is very much weaker. Has a sudden spasmodic contraction of the limbs, also involuntary. Appears to have typical Cheyne-Stokes respiration. Sodium caffeine benzoate gr. 7-1/2 given. 10 A.M. - 30 units of insulin given. Has twitching of muscles almost continuously. Hypodermoclysis 1000 cc. normal saline begun. 1 P.M. - 30 units of insulin given. 4 P.M. - 30 units of insulin given. 5:45 P.M. - Caffeine sodium benzoate gr. 7-1/2 given. 5:50 P.M. - patient expired.

Autopsy

The body is that of well-developed, fairly well-nourished, middle-aged, white male, measuring 175 cm. in length and weighing approximately 130#. Rigor is present. There is no edema nor cyanosis or jaundice. The pupils measure 3 mm. each in diameter and are regular.

Upon opening the PERITONEAL CAVITY it seems normal. The Peritoneum is smooth, moist, glistening and normal. The APPENDIX is subcecal and free.

The PLEURAL CAVITIES contain no fluid. There are firm, fibrous adhesions on left chest and also to diaphragm. Right lung is free from adhesions. The PERICARDIAL SAC contains a minimal amount of fluid.

The HEART weighs 420 Gm. The muscle is firm. The right valves are normal and free. The coronaries show very slight sclerosis. The lumen is patent throughout. The Root of the Aorta, the thoracic and part of abdominal aorta show numerous, raised, white patches of pearly arteriosclerosis, especially frequent around the small arteries in aorta.

The RIGHT LUNG weighs 850 Gm., the LEFT 340 Gm. Most of right lung, especially in lower portion, is very heavy and on cut section shows a very marked edema and a large amount of fluid exudes on the slightest pressure. The

lower portion of left lung shows slight edoma.

The SPLEEN weighs 190 Gm. and is normal except for three accessory spleens located at the hilus.

The LIVER weighs 140 Gm. and is normal except for slight cloudy swelling.

The GALL BLADDER and ducts are normal.

The GASTRO-INTESTINAL TRACT is normal in its entirety.

The PANCREAS weighs 75 Gm. and seems somewhat small. There is a great deal of fat about the head of the pancreas otherwise seems grossly normal.

The ADRENALS are normal.

The LEFT KIDNEY weighs 200 Gm., the RIGHT 175 Gm. The capsules of both kidneys strip easily revealing very finely pitted surfaces without a reddish tinge. The left kidney, however, shows a very large part of the surface to be of a light appearance. There is no evidence of abscess. The pelves and ureters are norman.

The BLADDER is normal.

The AORTA has been described above.

The organs of the neck are not examined.

Diagnosis:

1. Diabetes mellitus (clinical).
2. Hypertension (clinical).
3. Glaucoma (clinical).
4. Hypertensive kidney.
5. Hypertrophy of left ventricle.
6. Coronary sclerosis.
7. Edema of lungs.
8. Edema of pia-arachnoid.
9. Marked arteriosclerosis.
10. Uremia (clinical).
11. Cloudy swelling of liver and kidneys.
12. Accessory spleens.

HEAD. Upon opening the brain, the dura is noticed to be slightly dense. There is generalized edema of the pia-arachnoid. The brain is sectioned but no evidence of cerebral accident is shown.

Comment:

Sections of pancreas show no definite islands. There are a few structures which may be islands. Interacinar fibrosis and lipomatosis are moderate. Kidneys show marked hyalinization of glomeruli, atrophy, marked arteriosclerosis of medium sized vessels, slight arteriolosclerosis. Note intense picture of arteriosclerosis.

IV. CASE REPORT: DIABETES MELLITUS, ARTERIOSCLEROSIS, HYPERTENSION, GLAUCOMA.

Path. Randall

The case is that of a white male, 81 years of age, admitted to the University Hospitals 12-5-27 and discharged 1-14-28 (40 days): readmitted 6-15-28 and discharged 6-26-28 (11 days); readmitted 7-24-31 and died 9-10-31 (48 days).

BLIND

1925 - (About) - Patient's vision began to become impaired in the left eye. This gradually became worse and soon became blind in this eye.

11-15-27 - (About) - Patient had constant pain in left eye, lids became swollen, and eye closed completely.

Hospital

12-5-27 - Admission to University Hospitals. Physical examination revealed a white male, 77 years of age, with good nutrition and development, and shaking both upper extremities as with paralysis agitans.

Eyes - right - essentially negative, slight reaction to light; left - conjunctiva injected, shallow anterior chamber, no reaction to light, immature opacity of lens, increased intraocular tension; right 15/200, left blind. Chest - lungs- negative. Heart - systolic murmur at apex. Extremities - negative. Reflexes - paralysis agitans. Probable diagnosis: Chronic glaucoma. Paralysis agitans. Possible diabetes mellitus (has been on diabetic diet). Blood pressure 155/85. Laboratory: Urine - cloud of albumen, sugar negative, numerous wbc's, and mucous threads. Additional physical examination: Heart enlarged 10 cm. to left, sounds of fair quality, extrasystole (occasional). Lungs - emphysematous. Progress: Right fundus shows marked vascular changes (arteriosclerosis), a few lens opacities. Left eye - shows hemorrhage in anterior chamber, shallow anterior chamber, cornea not steamy, tension 2 +, cannot see fundus (grayish reflex) transilluminates clearly.

1-2-28 - Tension O.S. 60 incorrect); O.D. 30.

1-5-28 - Tension O.S. 38 O.D. 28.

1-8-28 - Tension O.S. 36. O.D. 28.

Operation:
1 - 9 - 28 Gold T - shaped foil inserted under conjunctival flap, through cyclo dialysis opening under sclera into edge of anterior chamber and fastened into place by conjunctival sutures. Local anesthesia.

Discharged.
1-14-28 -
6-15-28 - Since patient left Hospital, he has had almost constant pain in left eye. There had been a suture placed at the operation. He has been seen at regular intervals in the Dispensary since this time. The suture was removed today by a Staff physician.

Back.
6-15-28 - Readmission to University Hospitals. Past History: Some impairment of hearing for last two years. Has been told at various times within the past three years that there has been a trace of sugar in his urine. Urinates once or twice during night and has noticed burning on urination on several occasions in past few years. Physical examination: Blood pressure 192/90. Eyes - right - apparently negative to gross examination; left - there is a large haze over the cornea, pupils dilated somewhat, extreme conjunctivitis, eye very painful, pupils react to light very sluggishly. Heart - slight enlargement of left, systolic murmur heard over apex and mitral area, rate is slow and regular. Lungs - negative. Impression: Hypertension. Glaucoma. Arteriosclerosis. Progress: Gold T was removed.
6-19-28 - Tension - right eye 30; left eye 50. Urine - cloud of albumen, many rbc's and wbc's
6-20-28 - Blood sugar 0.236; creatinine 1.25; uric acid 1.849; urea nitrogen 21.46

Fields
6-23-28 - Vision 17/2, right; 0, left. Fields taken. Contraction is increasing. Diabetic diet of protein 56, fat 160, and carbohydrates 75. P.S.P. - intravenously at end of 1st hour 30%, 2nd hour 10%; total 40%.

Note
6-26-28 - Patient signed himself out at Hospital today. Apparently, he was dissatisfied with his diabetic diet.

Worse
7-24-31 - Readmitted to University Hospitals. Admission note by Fellow: Patient states that he has had diabetes for six years. He now presents a picture of dehydration, involuntary defecation, weakness, responds slowly to questions, face pulled slightly to right, heart slightly enlarged, spleen and liver not palpable, no edema. There is a swollen, red tenderness at anal ring which is draining; too tender to do rectal examination.

Left iris appears cloudy; pupil small, equal and regular; moderate tension. Urine - ± + + sugar, + + albumen, specific gravity 1.026, some wbc's and rbc's. Diagnosis: Diabetes mellitus, ischiorectal abscess, old glaucoma, dehydration. General condition poor. Do not believe patient has had apoplexy. Blood pressure 200/120. Will attempt to get sugar free, force fluids by mouth and subcutaneously. Have asked for surgical consultation and will ask for eye consultation immediately to find out whether abscess should be opened. Will keep on beck rest because of age (81) and poor condition.

Fistula.
Present complaints: Rectal fistula of two weeks duration. Diabetes for three years. Has been on diabetic diet since 1928. Has been constipated, excessively thirsty, and very weak. Referred to University Hospitals because of rectal condition. Past History: Headaches and dizzy spells, 1910 and 1911. Blind since 1926 due to glaucoma. Has upper and lower false plates. Has edema of feet and ankles. No abdominal pain. Jaundice in 1927. Difficulty in starting urination. Retention of urine. Some frequency. In 1911 had fits of anger then faint and get very weak afterward. Married for 60 years. 10 children living, 3 dead. Has not worked for fifteen years.

Physical examination: Patient is somewhat emaciated, 81 years of age, appearing weak, muttering a great deal and does not answer questions. Respirations are labored. Skin - there is a large, ulcerated, suppurating lesion on the left side of the rectum, polyp on upper anterior aspect of left thigh. Ears - hearing has diminished. Eyes - totally blind; pupils do not react to light, are irregular and unequal; mys-

tagmus; intra-ocular tension fields normal; conjunctiva and sclera are clear. Mouth - tongue is dry and furred; pharynx normal; Chest - very small chest excursion. Abdomen - liver not enlarged. Breath sounds are normal. Radial pulse is very feeble but regular. Heart is normal in size. Extremities - atrophy of muscles. Reflexes normal. Laboratory; Urine - 3+ sugar, 3+ albumen, acetone and diacetic 0, few granular and hyaline casts, occasional wbc's and rbc's. Blood - Hb. 80%, wbc's 9.800 P 79, L 17 and M 4. Blood sugar - .131, N.P.N. - 29.3, Van Slyke - 51 volume % CO_2. Stool - negative. Progress: Very tired, unable to help himself.

Surgical consultation:

7-25-31 - T 100 - 101. P 90 - 105. Abscess anterior, opened spontaneously. Finger inserted through opening reveals a dissecting cavity lined by soft friable tissue. Feces (?) seem to be discharging through opening. Suggest treatment as instituted already and add Dakin's irrigations with a syringe protected with a catheter tip.

Eye consultation: If patient complains, advise heat to both eyes. Otherwise, would advise waiting until diabetes is under control before giving any further eye treatment. Perspiring profusely. Pulse fairly regualr but slow. Respirations rapid. Incontinent. Involuntary defecation. Slightly stuporous. Continuous tremor of right hand. Insulin units X at 8 A.M., 10:50 A.M., and 5 P.M. Hot packs to rectum. Very tired and weak. Position changed frequently. Eats reluctantly. Hyperventilated, t.i.d. Diabetic diet. Fluids forced. 6 P.M. - 2000 cc. normal saline by hypodermoclysis. Abscess in rectum irrigated with Dakin's solution and hot packs applied. Dakin's irrigations to rectal abscess, q 2 h.

7-26-31 - Insulin units XV, t.i.d. Patient is stuporous. Involuntary defecations. Very drowsy. Takes fluids reluctantly. Drinks a great deal of water at night.

Surgical consultation:

7-27-31 - Few peri-rectal incisions made in left side of rectum. Abscess found to be dissecting peri-rectally on right side as well and connected on left with the rectum. Wound dissection done. Adequate drainage established. T 101 - 99. Abscess opened today by surgeon. Has eaten very little today. Takes fluids very well. Passed no urine. Bladder not distended. Coughing some. Insulin units XX, XV, and XX.

7-28-31 - T 99. P 100. Had insulin reaction this afternoon. Perspiring profusely. Seems comatose. Somewhat better after drinking orange juice. Mental condition poor. Put on serious. Units XXV, XV, and X of insulin.

7-29-31 - Stuporous. 2:45 P.M. - hands cold. 3 P.M. - given 50 cc. of orange juice. Quite stuporous. Takes fluids fairly well.

7-30-31 - Insulin units XV, X, and X. Continuous hot packs to rectum. Hyperventilated t.i.d.

7-31-31 - Extent of ischio-rectal absces has not increased. Adequate drainage. Exploration again this afternoon. A few locules broken down. Lesion has not advanced. Advise continuous hot packs and keep patient from being on the affected part. Patient seems somewhat worse today. Impossible to do p.S.P., dilution and concentration tests. Mineral oil oz. i q H.S Insulin units XX, X, and X. Urine has bee: sugar free since 7-27-31. The diabetic diet consists of carbohydrates 65, protein 52, and fat 127.

Neurological consultation:

8-5-31 - Patient stuporous. Cannot see fundi because of opacity of media. Hears fairly well. Possibly left side of mouth droops a little. Biceps and triceps jerks sluggish. Abdominal reflexes presen both sides. Could not elicit knee nor ankle jerks. Babinski's negative. Coarse tremor of hands at times. Conclusion: Evidence does not point to localized cerebral lesion. No doubt as to generalized C.N.S. arteriosclerosis. Blood pressure 140/60. Insulin units X, V, and X. Does not respond well. Somewhat irrational. Incontinent.

8-8-31 - Patient seems somewhat weaker. Insulin reaction last night. Perspiring profusely. Complains of being cold. Wound is quite clean. T 99. P 100.

Abscess

8-9-31 - Note by surgical Fellow: Indurated are on left posterior region of rectum incised still more widely to facilitate better drainage. Continue hot packs. Insulin units X at 6:30 A.M., V at 4:40 P.M. Still irrational and involuntary.

8-11-31 - Note by surgical Fellow: Wound is opened to its full extent. Drainage is entirely satisfactory. Do not feel that the abscess has any further bearing on patient's general condition. Continue treatment as before. T 99 - 100. Pulse 100. Respirations 20.

8-16-31 - Having involuntary defecations and urinations. General condition is poor. T 99 - 100. P 100.

8-20-31 - Appears slightly improved. Insulin units X, V.

8-22-31 - Appetite is improved. Enema given with good results.

Coronary?

8-25-31 - Complains of pain in chest. There is slught congestion at both bases. T and P normal. Respirations 18.

8-30-31 - Condition much the same. Bases still congested. T.P. and R. normal. Irrational at times. Somewhat stuporous at other times.

9-5-31 - Complains again of precordial pain. Relief obtained from allonal. Seems very tired.

9-7-31 - Involuntary. Condition seems slightly worse. Cheyne-Stokes respirations. Patient is restless at times. Involuntary. T 98, P 100 - 110, and R 20 - 30.

9 9 31 - This afternoon patient became stuporous and did not respond. Cheyne-Stokes respirations marked. Pulse very faint. Congestion has increased in bases. Given 500 cc. 20% glucoss, intravenously with 40 units of insulin, subcutaneously. Repeated urinalyses during this length of time have all been negative for sugar. Given caffeine sodium benzoate gr. 7½.

Exitus

9-10-31 - About 1 P.M., patient's respirations became labored and fluid appeared to collect in the lungs. He remained unconscious and expired at 8:50 A.M.

Autopsy

Well developed poorly nourished elderly male. There is a small pedunculated neurofibroma on the anterior surface of the left thigh. He has upper and lower false plates. The body is 5' 10" in length and weighs approximately 140#. Rigor is present. Hypostasis is purplish and posterior. There is no edema nor jaundice. There is very slight cyanosis. The pupils are regular and equal, measuring 3 mm. in diameter.

There is very slight increase in straw-colored fluid in the PERITONEAL CAVITY. The surfaces are smooth, moist and glistening. The right lobe of the liver extends about two finger- breadths below the right costal margin. The spleen is not enlarged The organs are in normal relationship to one another.

There is about 1500 cc. of fluid in both PLERUAL CAVITIES. The surfaces are smooth moist and glistening. ThePERICARDIAL SAC contains an increased amount of straw-colored fluid.

The HEART weighs 450 Gm. The right side is somewhat dilated and flabby. The left side is firm. About 2 cm. above the apex in the left heart, there is a thinned out area of the myocardium which measures about .5 cm, in thickness, normal measurement 2 cm. On section, this area shows definite fibrosis and myocardial infarcts. There is slight thickening of the mitral and aortic leaflets but other than this there is no epicardial or valvular defect. The ROOT OF THE AORTA is somewhat dilated. There is slight amount of arteriosclerosis The coronary vessels are diffusely thickened throughout and shows a very definite arteriosclerosis.

The RIGHT LUNG weighs 250 Gm., LEFT 300 Gm. There are crepitant throughout. No evidence of consolidation is present. They cut readly and on section show the surface to be pinkish-gray in color, no evidence of consolidation, congestion nor bronchopneumonia. On investigation of the pulmonary vessels, there is no evidence of arteriosclerosis, no evidence of emboli.

The SPLEEN weighs 150 Gm., is soft, cuts readily, and on section shows a pinkish-gray pulp which scrapes. The malpighian corpuscles are indistinct.

The LIVER weighs 1650 Gm. The surface is slughtly mottled and gray showing evidence of an old peri hepatitis. On section, a very typical picture of chronic passive congestion is seen.

The GALL-BLADDER is surrounded by adhesions. However, the foramen of Winslow is patent. There are no stones. The wall is only slightly thickened.

Gastro-Intestinal tract - normal

The PANCREAS is nearly replaced by fat. There is only a small amount of normal pancreatic tissue present. On section, the lobulations are shown to be indistinct. The lienal vessels which traverse through the pancrease are definitely sclerotic.

Each KIDNEY weighs 150 Gm. There is a diffuse, fine and coarse pitting present. They are reddish gray in color and on section the cortex and medulla are shown to be somewhat indistinct. The glomeruli are pale. There is a very definite fatty infiltration in the pelvis. The pelves are dilated.

The BLADDER contains about 200 cc. of straw-colored urine.

ThePROSTATE is slightly enlarged, partially obstructing the urethral outlet. Old,perirectal abscess present.

AORTA shows marked arteriosclerosis.

DIAGNOSES:

1. Diabetes Mellitus (clinical)
2. Fatty replacement of pancreas
3. Marked general arteriosclerosis.
4. Hypertension (clinical)
5. Hypertrophy of left ventricle
6. Coronary sclerosis
7. Myocardial scar (infarct)
8. Arteriolosclerotic kidneys
9. Chronic passive congestion of viscera
10. Pulmonary edema
11. Glaucoma (clinical)

COMMENT

Note same main diagnoses plus complicating infection. Islands show slight hyaline deposits. Pancreas is fatty and fiberous. Vessels show arteriolosclerosis (more marked) than first case and gross arteriosclerosis.