I. ANNOUNCEMENTS:

1. Meeting Time Changed

to 12 noon in order to get out of way announcements which can be read by those arriving late, new arrangement permitting more time for prolonged discussion without running over usual closing time. Your special attention is called to the large number of vacant seats in the front of the room which could be occupied by those "who arrive late and stand at the back."

2. Shoot

commanded squat, red-haired, affable, Major William Guy Guthrie, Medical Corps United States Army in command of Medical Reserve Corps, Training Center, University of Minnesota Medical School. Eight long and short, dark and fair, dignified and otherwise, members of our staff fired hither and thither (frequently thither) at the targets in the University Armory last Thursday afternoon. When the bombardment had ceased, the flags of Sweden (Stenstrom), Norway (Hilleboe), Czecho-Slovakia (Shimonek) floated idly in the breeze symbolizing excellency in marksmanship. Mighty bear hunter, Surgical Fellow Mead with various and sundry aid by the entire Military Department managed to secure a number of fair hits. Mighty deer hunter Surgeon ---------- (name deleted because he is apparently a very truthful fellow) made all wonder who really shot the game he so proudly returned with a few weeks ago. Major Guthrie in his modest way scored only a few bull's eyes in order to encourage the trembling tyros. All interested, see Major Guthrie at once about weekly shoot every Thursday afternoon until further notice.

3. William J. Mayo.

The following abstract from an editorial by Dr. William J. Mayo, published in a prospectus for Surgery, Gynecology and Obstetrics with International Abstract of Surgery, is of interest.

"In the process of the physician's education after graduation, clinical trips play an important part. These trips should be made for the purpose of investigating and studying the achievements of others. Time should not be consumed in the observation of inferior work. Attendance at Medical meetings is helpful, because opportunities are afforded for the exchange of views and for better understanding of the personalities of forceful men of the medical world who are contributing to progress.

Above all, familiarity with the contents of medical journals is essential. Every practitioner of medicine should charge himself with the obligation of devoting at least an hour a day to their study, and should pay the debt. If for any reason he misses a day or two he should make up the time, but if on any one day he is able to read for a number of hours, he should credit himself with only the single hour. The man who follows this course will, almost unconsciously, become well informed in medical matters, and if he has the power to apply and correlate this knowledge with his own experience, he will become a leading member of the medical profession. Many men, in speaking of an original conception of a disease, an original method of treatment, or an original operation, have informed me that the idea came to them in the attempt to correlate their own experiences with those reported by writers of articles in medical journals.

To the physician, patients represent medicine in practice; books on medicine represent stabilized medical opinion; and the medical journals -- the very breath he breathes -- represent medicine in the making."

Comment:

It is interesting that in our weekly attempts to correlate our experience with that of others we usually use medical journals, less frequently testbooks.

4. Western Surgical Association

met at Madison, Wisconsin, Dec. 9 and 10, 1932, under presidency of Harry P. Ritchie, Associate Professor of Surgery. Excellent meeting, spirited papers, outstanding clinics. Long (8 years) secretary of the group, Plastic Surgeon Ritchie was this year honored with the

presidency. Surgeon O. H. Wangensteen took active part in discussions, Pathological Fellow Wallace Ritchie (son) beamed from obscure position in room.

5. Pool Table.

Hospital Director Halbert Louis Dunn comes forth with suggestion that we buy a pool table for the interne's quarters. Backed by a $5.00 bill, his words ring true. The $5.00 bill will be held until January 1st at which time he hopes others will contribute the necessary 95 additional dollars to purchase table. Please make contributions directly to his office.

6. Committee on Costs of Medical Care.

Recommendations:

(1) The Committee recommends that medical service, both preventive and therapeutic, should be furnished largely by organized groups of physicians, dentists, nurses, pharmacists and other associated personnel. Such groups should be organized, preferably around a hospital, for rendering complete home, office and hospital care. The form of organization should encourage the maintenance of high standards and the development or preservation of a personal relation between patient and physician.

(2) The Committee recommends the extension of all basic public health services--whether provided by governmental or non-governmental agencies--so that they will be available to the entire population according to its needs. This extension requires primarily increased financial support for official health departments and full-time trained health officers whose tenure is dependent only upon professional and administrative competence.

(3) The Committee recommends that the costs of medical care be placed on a group payment basis, through the use of insurance, through the use of taxation, or through the use of both methods. This is not meant to preclude the continuation of medical service provided on an individual fee basis for those who prefer the present method. Cash benefits, i.e., compensation for wage-loss due to illness, if and when provided, should be separate from medical services.

(4) The Committee recommends that the study, evaluation and coordination of medical service be considered important functions for every state and local community, that agencies be formed to exercise these functions, and that the coordination of rural with urban services receive special care.

(5) In the field of professional education the Committee makes the following recommendation: (a) That the training of physicians give increasing emphasis to the teaching of health and the prevention of disease; that more effective efforts be made to provide trained health officers; that the social aspects of medical practice receive greater attention; that specialties be restricted to those specially qualified; and that postgraduate educational opportunities be increased; (b) that dental students receive a broader educational background; (c) that pharmaceutical education place more stress on the pharmacist's responsibilities and opportunities for public service; (d) that nursing education be thoroughly remoulded to provide well-educated and well-qualified registered nurses; (e) that less thoroughly trained but competent nursing aids or attendants be provided; (f) that adequate training for nurse-midwives be provided; and (g) that opportunities be offered for the systematic training of hospital and clinic administrators.

Haven Emerson, M.D., Professor of Public Health Administration and Director of the Institute of Public Health, College of Physicians and Surgeons, Columbia University, New York, writing in the December issue of the Survey Graphic has this to say in regard to the minority report.

"A half dozen physicians, more imbued than the rest of the medical members of the Committee with the present excellencies of private family practice, present a minority report which rings with resentment, and over-

flows with ambitions and unverified* claims of accomplishment and promises of future progress. Stung with even the gentlest implications of medical inertia and lack of effective leadership, and registering radical opposition to the first three recommendations of the Committee, they object to the proposed medical service center as a probable creator of medical hierarchies, obstruction to free competition, cause of greater cost to patients, and destroyer of the personal relationship between patient and physician.

They offer seven recommendations of their own for good measure and advice:

(1) That government competition in the practice of medicine be discontinued and that its activities be restricted (a) to the care of the indigent and of those patients with disease which can be cared for only in governmental institutions; (b) to the promotion of public health; (c) to the support of the medical departments of the Army and Navy, Coast and Geodetic Survey, and other government services which cannot because of their nature or location be served by the general medical profession; and (d) to the care of veterans suffering from bona fide service-connected disabilities and disease, except in the case of tuberculosis and nervous and mental disease.

(2) That government care of the indigent be expanded with the ultimate object of relieving the medical profession of this burden.

(3) That the study, evaluation and coordination of medical service be considered important functions for every state and local community, that agencies be formed to exercise these functions, and that the coordination of rural with urban services receive special attention. (Agrees with the Committee's recommendation.)

(4) That united attempts be made to restore the general practitioner to the central place in medical practice.

(5) That the corporate practice of medicine, financed through intermediary agencies be vigorously and persistently opposed as being economically wasteful, inimical to a continued and sustained high quality of medical care, or unfair exploitation of the medical profession.

(6) That methods be given careful trial which can rightly be fitted into our present institutions and agencies without interfering with the fundamentals or medical practice.

(7) The development by state or county medical societies of plans for medical care."

7. Minnesota's Answer:

Note that recommendation No. 4 of the majority report agrees with No. 3 of the minority report. Health leaders in Minnesota have called a preliminary meeting to discuss the report and the problems it hopes to solve. Represented will be the following Organizations: County, State and National Organized Medicine, Administrative Public Health, Practicing Physicians and Public Health, Medical Education, National Organized Dentistry, Organized State and National Hospitals, Sociology and Economics. Names: E. A. Meyerding (M.S.M.A.), F. S. Chapin (Sociology), C. E. Rudolph, (Dentistry), Clin West (A.M.A.), E. H. Cary (A.M.A.), respectively Secretary and President of the National Organization, C. B. Wright (A.M.A.), M. S. Henderson (M.S.M.A.), N. C. Pearce (M.S.M.A.), R. E. Scammon (Medical Education), F. E. Harrington, (Public Health). J. A. Thabes, Sr. (Public Health), A. M. Colvin (Hospital), H. M. Johnson, L. R. Critchfield, George Earl, Theodore Sweetser (Committee for M.S.M.A.). Place: Nicollet Hotel. Date: Sunday, December 18th, 1932, 2:30 P.M. and 7 P.M. Recess for Sunday supper with no special arrangements for meal. Admission: State membership card or special card to be obtained at Director Dunn's office. Note: No other method of admission. All the members of our staff, including the internes and fellows, should make a special effort to attend and hear the discussions. All medical men's wives are being paged by telephone to excuse them for the day and send them to the meeting. This is an unusual opportunity for all to hear this matter discussed, and it is the desire of the administra-

tion of the Medical School that all medical students, internes, fellows and supervisory staff attend at least part of the program.

II. ABSTRACT:

NEPHROSIS.

References;

Note: Partial list of Minnesota's contributions to the problem of "Nephrosis."

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2. Epstein, A. A. "Thyroid Therapy and Thyroid Tolerance in Chronic Nephrosis", J.A.M.A. 87:913-918, (Sept. 18), '26.
3. Epstein, A. A. "Further Observations on the Nature and Treatment of Chronic Nephrosis", A.J.Med.Sc., 163:167-186, '22.
4. Wilbur, D. L. and Brown, G. E. "The Blood in Lipoid Nephrosis with Special Reference to the Absence of Anemia", Arch. Int. Med. 45:611-623, (Apr.) '30. (Mayo)
5. Kumpf, A. E. "The Blood Proteins", Arch. Path., 11:335-379, (Mar.) '31. (Minn.)
6. Kumpf, A. E. "Experimental Edema and Lipemia Produced by Repeated Bleeding", Arch. Path., 13:425-432, (Mar.) '32. (Minn.)
7. Leiter, L. "Nephrosis", Medicine, 10:135-242, (May) '31 (No. 2).
8. Rigler, L. G. and Rypins, H. "Chronic Nephrosis", Minn. Med., 419-423, (June) '24. (Minn.)
9. Elwyn, H. "The Pathogenesis of Lipoid Nephrosis", Arch. Int. Med. 38:346-359, '26.
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11. Bell, E. T. "Nephritis and Nephrosis", Cal. and West. Med., 34:---'31. (Minn.)
12. Bell, E. T. "The Relation of Lipoid Nephrosis to Nephritis", Ann. Int. Med., 6:167-182 (Aug.) '32. (Minn.)
13. Thompson, W. H., Ziegler, M. and McQuarrie, I. "A Comparative Study of the Inorganic Metabolism in Nephrosis and in Edema of Undetermined Origin." A.J. of Dis. of Child. 44:651 (Sept.) '32. (Abstract in Society Transactions). (Minn.)
14. Weech, A. A., Snelling, C. E. and Goeetsch, E. "The Relation between Plasma Protein, Plasma Specific Gravity and Edema in Dogs, etc.," A.J. of Dis. of Child, 44:657, (Sept.) '32. (Abstract in Society Transactions.)
15. Hartman, A. F. and Senn, M. J. Studies in Edema, with Particular Reference to the Therapeutic Value of Acacia, A.J. of Dis. of Child, 44:673 (Sept.) '32. (Abstract in Society Transactions.)
16. Thompson, W. H., Ziegler, M. and McQuarrie, I. Effects of Pituitary Antidiuresis on Non-Cardiac Edema, Proc. of Soc. for Exper. Biol. & Med., 30:16-17, 1932. (Minn.)

1. General Statement:

(From Leiter). "Nephrosis" began its existence in medical nomenclature as a point of view. Original views in regard to parenchymatous disease of the kidney proved inadequate. Became desirable to adopt term for those changes which did not appear to be inflammatory change. Term "nephrosis" coined for these "degenerative" changes in contrast to "nephritis" which remained to indicate inflammatory changes. Soon after establishment of term, it was received with enthusiasm. "Nephrosis" became a disease entity. However, as data accumulated, more and more confusion arose as to the exact boundaries and distinctive criteria for this "entity". Such terms as "pure nephrosis", "mixed nephrosis", "nephrotic tendencies" arose. In addition, theories of pathogenesis incompatible with each other have been advanced.

It seems that "nephrosis" has come to stay, but the flurry concerning its "entity" has been overenthusiastic and at present the term must be carefully defined and delimited.

2. Definition.

Nephrosis (chronic lipoid nephrosis) is a chronic disease characterized clinically by edema and albuminuria without hypertension or uremia; and pathologically by lipoid and necrotic degeneration in the kidney tubules probably secondary to proliferative changes in glomeruli:

3. Classification of Nephrosis:

(Bell). In following classification subgroups have very little in common. Pathogenesis of each is widely separated but microscopic picture is somewhat similar.

A. Acute
   - Due to infections
   - Due to chemical poisons

B. Chronic
   - Eclampsia
   - Amyloidosis
   - Lipoid

The nephrosis of infections is the most common kidney change at autopsy. Chemical nephrosis is rarely seen clinically except in corrosive sublimate poisoning. Eclampsia has been previously discussed (Univ. Minn. Staff Meeting Bull. Vol. III, #28,(Apr. 14) 1932.

Change was shown to be primarily in glomeruli and could be demonstrated by special stains.

Amyloidosis is not a true kidney disease. Amyloid deposits are present in other parts of body and kidney changes are part of a systemic condition.

None of these forms of "nephrosis" are kidney disease entities. In all the kidney condition is part of systemic change.

Lipoid nephrosis. (All further reference will be to this type of nephrosis.

4. History:

Müller 1905 - Proposed term "nephrosis" to signify degenerative disease of kidney.

Munk 1913 - added adjective "lipoid" and applied new term to cases of chronic parenchymatous nephritis that showed no hypertension or uremia and which at autopsy had large fatty kidneys.

Epstein 1912 - began studies of lipoid nephrosis, first as an investigation of edema and later proposed his hypothyroid and metabolic theory of pathogenesis and popularized Eppinger's high protein diet.

Volhard and Fahr 1914 - adopted lipoid nephrosis as disease entity differing from chronic parenchymatous nephritis.

Many Ingestigators 1914-1929 Period of accumulation of data and of investigation which created more confusion as to exact demarcation between nephrosis and chronic parenchymatous nephritis.

Bell 1929 - published first of papers showing that micro-pathological picture of nephrosis does not differ from cases of chronic glomerulonephritis.

Bell 1932 - Is lipoid nephrosis a form of chronic glomerulonephritis?

5. Clinical Description: General:

Disease begins insidiously in child or young adult with edema which rapidly becomes generalized. With this, there may be malaise, anorexia, headache, backache or gastro-intestinal distress. Physician is consulted. A high grade albuminuria without other significant urinary changes is found. There is no anemia, blood pressure is normal, the plasma protein is low, especially albumin. Globulin and fibrinogen are elevated (comparatively?) Cholesterol is high.

Some form of treatment is given. After a time perhaps because of treatment but usually spontaneously the edema melts away and the patient resumes activity retaining a little albumin in the urine. Following an insignificant cold, the cycle is repeated. One, two or several cycles may be passed. No hypertension or uremia appears. The length of life is variable. Sometimes the patient recovers entirely. (Follow-up may change this idea?). More often during one of the edematous stages, the abdomen becomes slightly tender with perhaps a little fever. Patient goes rapidly downhill. Death takes place quietly with infection (peritonitis, et etc.).

At autopsy edema and large fatty kidneys without other findings except terminal infection is found. Microscopically, (by hematoxylin and eosin stains) nothing but fatty and retro-

grade degenerative changes with dilatation in the kidney tubules is found. The glomeruli appear normal (Note: Difference with special stains).

Clinical Description in Detail: Incidence:

Schlager	- 300 cases nephritis	-6
Eppinger	- "many thousand"	-4
Kollat		rare
Fahr	- entire experience	-8
Bell	- 3300 autopsies	-0
McElroy	- 600 cases nephritis	-19
Bright	- never saw a case	
Weigert	- "hunted all his life for a pure case"	

Leiter estimates 1 - 5% of all bilateral non-suppurative kidney disease are lipoid nephrosis.

Age: Leiter: 26 collected cases.

1 decade	9
2 "	8
3 "	7
4 "	1
5 "	1

Bell: Age corresponds to age of glomerulonephritis.

Sex: No significant difference.

Etiological Factor: Most authors are satisfied to say that no known etiological factor or relationship exists.

Leiter: Greatest proportion fall into group of unknown etiology. Infectious diseases play only role of immediate exciting factor on a soil already prepared. Syphilis appears to be common agent (?). Munk was greatest exponent of syphilis as factor but in his latter works he gave up this view (and nearly everyone else).

Bell: In 38 collected cases found infectious process preceding onset of disease in 14 (37%). Note: our cases today.

Infection is a definite factor in producing excerbations during course of disease and in terminal picture. Cause or effect?

Edema: "Without edema, there is no nephrosis". It is presenting symptom. Dependent type, resembling cardiac edema except that it involves face. Characterised further by stubborn persistence, lack of response to usual diuretics and by termination with sudden, spontaneous (?) diuresis. May however persist for years without remission. Aggravated chiefly by infections, also by high salt and fluid intake.

Albuminuria: "There is no edema without albuminuria". Albuminuria precedes edema but is not presenting symptom for obvious reasons. Persists after edema, subsides to a minimum and is only sign that cure has not occurred. Degree of albuminuria rarely reached by other forms of nephropathy. Up to 60 grams per liter reported; usually 20 - 30 grams per liter. High concentration found during severe edema. Total output varies from 5 - 50 grams. During edema, free stages of albuminuria may disappear for a time and reappear as a precursor of a relapse.

Other Urinary Changes: Total quantity of urine is scanty (500 c.c.) turbid, dirty brown, acid and has a high specific gravity (highest recorded is 1.060). Anuria does not occur.

Gross Hematuria: has never been observed. Red cells in sediment are found in small numbers (may be found in normal urine - Addis) but never with regularity or in high concentration. If found in great numbers, the diagnosis of "mixed nephrosis" or "nephrotic glomerulonephritis" is to be considered.

Fat: as free droplets or as doubly refractive droplets is characteristic but is found in other nephropathies. Ordinary fat, staining with Sudan III, may also be found.

Cardiovascular System: It is said "neither early nor late in clinical course of uncomplicated nephrosis is an increase in blood pressure ever found." All associated changes in eyegrounds, peripheral vessels, heart size, etc. are said to be absent. Hypertension is due to obstruction in capillary bed of

demonstrated thickening of the endothelial membrane of the glomeruli differing from glomerulonephritis in degree only. In 2 cases, the thickening was patchy or slight, in 5 it was generalized and marked. This author has never observed in any kidney disease, tubular degeneration without a preceding glomerular defect.

In nephrosis, the tubular degeneration is secondary to the glomerular lesion exactly as in glomerulonephritis. The degree of injury to the glomeruli is much less in nephrosis. Therefore, "pure nephrosis" is unassociated with obstruction to the flow of blood in the kidney and hypertension is not manifested. Nitrogen retention and kidney function are dependent primarily on the degree of glomerular damage and show no change in nephrosis because of the slight glomerular change. The more severe glomerular changes show proprotionate disturbances of blood pressure, kidney function, and nitrogen retention (and are then called mixed nephrosis and nephrotic glomerulonephritis).

On this basis, the following position is given to nephrosis in the classification of glomerulonephritis:

Glomerulonephritis
- A. Focal
  - a. Embolic
  - b. Benign hemorrhagic
- B. Diffuse
  - a. Acute
  - b. Subacute
  - c. Chronic
    1. With contracted kidney.
    2. Without contracted kidney (lipoid nephrosis).

Note: Not all nephritics with edema have a nephrotic component. (Bell).

7. The Pathogenesis of Nephrosis:

General: Several attempts have been made to explain the pathogenesis of nephrosis on the basis of some uniform concept. This has involved assumption of a primary renal lesion, a primary general systemic or metabolic disturbance or combinations thereof. Analysis of the changes in urine, blood and tissue fluids may be considered individually before any comprehensive theory of genesis as a whole is considered.

Albuminuria: 85-95% of the urinary protein is albumin and the remainder is globulin. By precipitin tests and optical rotatory powers this urinary protein is proven to be identical with serum protein, i.e., it is not a protein foreign to the blood serum. The loss of albumin lowers the albumin-globulin ratio in the blood.

These changes (loss of blood protein thru the urine) are not specific for nephrosis. They also occur in glomerulonephritis. The albumin-globulin ratio in the latter disease is from 2 to 10 (normal 5 to 22). The passage of the protein into the urine is a filtration process through injured glomeruli. (Note: Aglomerular fish do not develop albuminuria). In chronic glomerulonephritis, progressive fibrosis incident to greater glomerular injury prevents the passage of albumin and as further shrinking takes place less albumin is passed. The difference in albuminuria between nephrosis and chronic nephritis may be due to the degree of fibrosis of the glomeruli.

Serum proteins: Classical work dates to Epstein (1912). The findings are reviewed by Leiter as "monotonously uniform". There is notable diminution of total proteins especially of the albumin, so that reversal of the globulin-albumin ratio occurs. There is nothing specific however in these changes. They occur in many conditions. The following table is compiled from Kumpf.

(Given in percentages. Refractometric method of determination.)

Condition	Total Protein	Albumin	Globulin	Ratio
Normal	7.36	5.20	2.16	2.52
Nephrosis	5.93	1.97	3.96	0.49
Glomerulonephritis				
Acute	5.67	3.05	2.67	1.34
Chronic	5.60	2.61	2.99	0.96
Amyloidosis	2.16	0.20	1.96	0.10
Hypertension with uremia	6.40	4.29	2.11	2.37
Mercuric chloride poisoning	6.11	3.46	2.65	1.30

ondition	Total Protein	Albumin	Globulin	Ratio
obar pneumonia	5.74	2.47	3.28	0.81
cute infections	6.21	3.34	4.17	1.14
eart disease with edema	5.70	3.09	2.61	1.65
clampsia	7.03	4.71	2.32	2.23
eficiency edema	3.36	0.66	2.70	0.19
tarvation edema	4.83	3.00	1.83	1.80
arcinoma	6.06	3.51	2.53	1.58
ultiple myeloma	13.27	3.87	9.40	0.41

Roughly the loss of serum protein is ccounted for by the urine excretion plus that in the edema fluid). The reersal of the ratio has no particular ignificance. The globulin molecule is arger and is not filtered through the lomerulus as readily as the albumin. loreover, globulin is restored by the body ore rapidly.

dema: Epstein contributed explanation of edema (based upon Starling's eachings). He stated that as a result of he albuminuria the plasma proteins were educed to such a level that the colloid smotic pressure of the plasma was insufficient to balance the hydrostatic pressure n the capillaries. These pressures have been measured. There is about 2.5 to 4.5 m. water pressure for each gram % protein lepending upon the Albumin-globulin ratio. he larger globulin molecule has less ower of raising the pressure. Globulin l gram % = 1.95 cm. Albumin 1 gram% = 7.50 m.

The osmotic pressure of serum therefore is a sum of the pressures of total globulin and total albumin. This is advanced because some workers have found no relation between edema and the total protein of the serum. A high globulin fraction sufficient to give a high total protein may still result in edema if the active albumin fraction is low.

The protein content of the edema fluid is almost nil, proving that the tissue has no "increased affinity for fluid."

In general, it may be stated that when the serum protein falls below 5% (dependent on the proportion of globulin and albumin), edema results because of the fall in osmotic pressure. This is true not only in nephrosis but holds true for any condition in which the proteins are diminished--starvation, bleeding, infection, etc.

Edema: Weech in a more recent review (Sept. 1932) again points out the relation between edema and the fall of blood protein, particularly fall of the albumin fraction. In dogs, he found that edema was always present when the concentration of the albumin was less than 1 gram per 100 c.c. Emphasis however is laid in this paper and in the discussion of it by others that occasional variations do occur. It is pointed out that influences other than albumin concentration may modify this tendency to edema, such as chlorides. (See also Bell).

Lipoid Metabolism: Like the serum protein, the observations on blood lipoids are very uniform:

1. There is a marked increase of the lipoids of the serum when the patient is edematous.

2. There is practically no lipoid in the edema fluid. This lipoid is chiefly cholesterol. The lipoids in the kidney tubules are cholesterol esters. There apparently is a relation between the protein level and the degree of cholesterinemia. With low serum protein there is a high fat content. It is unknown whether this is a protective mechanism or a disturbance of transfer of fat from the blood to the tissues. (The fat is more unsaturated than normal.) In general the fat disturbance appears to be a phenomena dependent on the protein disturbance and its significance is unknown. The phenomena is found in any condition associated with protein loss (i.E. acute nephritis.)

Basal Metabolic Rate: Aub and DuBois (1917) and later Epstein and Lande found basal rates lowered to -40% in nephrosis. Eppinger and then Epstein found that these patients tolerate enormous doses of thyroid (as much as 4 grams daily) without symptoms of hyperthyroidism or (Platt) excreting any thyroxin in the urine.

On this basis, Epstein believed that there was a "relative hypothyroidism" and advocated the use of thyroid extract.

Low basal rates however occur as an incident secondary to undernutrition, inactivity, other forms of edema and possibly other factors."

Leiter: "On the whole, little has been added to the understanding of the nature of nephrosis by the demonstration of the moderately reduced basal metabolism."

General Theories of Pathogenesis:

Munk: General metabolic disorder consisting of a shift of the plasma colloids toward the course euglobulin fractions. The albuminuria is a protective mechanism ridding the body of a foreign protein and edema is the result of increased hydration of the altered colloids.

Volhard and Fahr: Extrarenal disease with vascular capillary damage causing edema with albuminuria of tubular origin due to increased permeability of the capillaries and epithelial degeneration.

Aschoff and Lohlein: presented about the same views with a definite tendency toward some glomerular change which however they could not demonstrate.

Epstein: believes that nephrosis is a full-fledged metabolic disease due to disturbance in protein utilization. The albuminuria is due to excretion of a protein which the body cannot utilize just as in diabetes there is excretion of sugar. He calls nephrosis a "Albuminuric diabetes." Edema is secondary to the low protein level. Lipemia is thought to be a manifestation of thyroid dysfunction. The kidney damage is secondary to the excretion of protein.

Bell: This author emphasizes that no clinical or pathological feature of nephrosis differs from glomerulonephritis except in degree. Microscopic changes in the glomeruli identical with those of very mild glomerulonephritis are found. The course of events are (1) glomerular injury by some toxic substance probably of bacterial origin, (2) albuminuria, (3) tubular degeneration secondary to the glomerular injury, (4) edema when the serum proteins fall below 5% due to lowered osmotic pressure and, (5) associated lipemia dependent on the protein level. When the glomerular injury is of slight degree, nephrosis develops. When greater, there is thickening of the endothelium and proliferation and charactierstic nephritis develops. When there is moderate reaction, mixed nephrosis results.

The other theories are various modifications or combinations of the theories outlined.

8. Treatment:

Leiter's review of the entire field leads him to discard all the forms of "specific" treatment. He states that the treatment should be such as to "do no harm." Withholding proteins, salt and fluid he feels is harmful. Adequate protein should be given to counterbalance the loss in urine. High protein may increase the albuminuria (Berglund).

Rest in bed, moderate restriction of salt and water and diuretics are used for edema. The saline diuretics seem to have little effect, urea, acid-forming diuretics and the mercurial compounds may be safely used.

Removal of infections are of value.

Decapsulation; artificial increase of colloid in the blood by acacia, transfusion, etc: thyroid treatment, all appear to have no significant value.

Epstein: This author on the basis of his "relative hypothyroid" and "diabetes albuminuricus" theories advocates thyroid extract on thyroxin in conjunction with a high protein diet. A protein intake of 2 - 3 grams per kilo is given. To this, thyroid extract is added if immediate improvement does not take place. 1/2 to 1 grain t.i.d. is given. This is rapidly increased to 15 grains. If no results are obtained, the dose is increased to 30 grains. If this fails, thyroxin 5 - 10 mgms. intravenously is used at 8 - 10 day intervals.

"Experience convinces me that uncomplicated cases and occasionally others are susceptible of complete care by the intelligent and persistent use of the high protein diet and thyroid therapy."

Some of the more recent attitudes regarding treatment of edema and nephrosis presented at the Forty-Fourth Annual Meeting of American Pediatric Society at Rochester in May 1932. Thompson, Ziegler and McQuarrie presented the results of their studies in edema in several types of cases. It was shown that changes in diet, variation of sodium chloride intake, water intake, raising of total serum protein by blood transfusion showed somewhat variable reactions. In all such cases protein and chloride was lost in proportion to the loss of body water. The occurrence of spontaneous diuresis in which the patient would unload many pounds of water, stimulated interest in the possible endocrine factors of water control. To patients parathormone and pitressin were given. Response to parathormone was variable. Response to pitressin however produced definite diuresis. One patient showed a drop in body weight of almost 1/5 the original due to water excretion. During the period of pitressin administration, sodium chloride was excreted in excessive amount and following withdrawal of pitressin there was rapid increase of water excretion. When the effect of the pitressin wore off, the cycle is again repeated with a still further drop of body weight. Accompanying this change in edema and body weight, there was a fairly marked increase in the albumin of blood and the simultaneous decrease in the globulin fraction in one case of nephrosis. No ill effects resulted from the procedure. It was felt that the further studies might prove the usefulness of these procedures. Hartmann and Senn again show that the diminution of edema is preceded by an increase in the blood protein, particularly the albumin, and a corresponding increase of osmotic or "oncotic pressure." In the more severe types of nephrosis when the plasma albumin cannot be brought to and maintained at level sufficiently high to prevent edema, the intravenous administration of acacia has proven of value in maintaining the normal plasma pressure. Their experience indicates the most satisfactory method of an administering of acacia for this purpose is to give a 30% solution to produce a plasma acacia concentration of about 2% (1 gram of acacia per kilogram of ideal body weight) and to repeat the administration when the diuretic effect has ceased. It was also felt by this method the tendency toward ascites and therefore the danger of fatal peritonitis lessened. The dangers however resulting from use of acacia (intravenously) are pointed out. It is felt that these are due to stale solutions or those not sufficiently refined. The reaction consists of fever, chills, fall in blood pressure, cyanosis, respiratory difficulty and occasional fatal outcome.

Impressions:

1. "Nephrosis" has been coined to describe so-called degenerative lesions of the kidney. Acute nephrosis is common and due to infections and poisons
2. Chronic nephrosis includes such things as eclampsia, amyloidosis and lipoid nephrosis.
3. None of these conditions are related.
4. The name "nephrosis" was first suggested by Müller in 1905. (Later called lipoid nephrosis). Volhard and Fahr adopted the "disease" as a clinical entity.
5. Disease is characterized by edema, albuminuria, loss of blood protein, high serum cholesterol and a cyclic course usually terminated by an intercurrent infection.
6. In "pure" cases, hypertension, retention of nitrogenous products and impaired kidney function is absent.
7. The disease is rare. At most 1 - 5% of all true nephritis is nephrosis. The age corresponds to that of glomerulonephritis. There are no sex differences in lipoid nephrosis.
8. Most cases have an unknown etiology. About 35% are preceded by infections which may prepare the soil. (Bell).
9. The edema is primarily of the dependent type, is extreme, usually becomes generalized and has sudden characteristic remissions.
10. Albuminuria precedes the edema, exceeds that seen in other nephropathies, averages 20 - 30 grams per L during acute stages and persists in slight amounts during remissions. The urine otherwise is concentrated and shows a few casts, lipoid bodies and only a few rare red cells.
11. Anemia does not occur.

12. Non-protein nitrogen rise is not observed in the so-called pure cases and kidney function is normal.

13. Grossly, the kidney shows only fatty degeneration and swelling. Microscopically, there are various forms of degenerative changes with lipoid deposits in the convoluted tubules without glomerular changes demonstrable by ordinary stains. By azo-carmine stain, thickening of the glomeruli similar to glomerulonephritis can be demonstrated. On the basis of these findings, the pathological classification of nephrosis can be "chronic glomerulonephritis without contracted kidney."

14. About 90% of the urine protein is albumin and 10% globulin. These are derived from serum and are identical with serum protein.

15. There is a sharp drop of serum protein chiefly the albumin with reversal of the ratio. This occurs in numerous other conditions, commonly other nephritis.

16. Edema is due to lowered osmotic pressure of the blood resulting from loss of the albumin and less of the globulin. Total albumin content rather than total protein content governs osmotic pressure because of the small size of these molecules.

17. High serum lipoids chiefly cholesterols appear to be associated with a low protein level. Its relation is unknown. Unsaturation and failure to anchor in the tissues appears to be a factor.

18. A low basal metabolic rate is found in nephrosis but is also found in a wide variety of similar conditions of edema or malnutrition.

19. Three main theories of genesis exist - European, Epstein and American headed by Bell. The European theory suggests that the disease is a systemic metabolic one with an associated or secondary tubular lesion. Epstein's theory states that there is a protein metabolic disturbance with hypothyroidism. Bell's theory is that nephrosis is a mild form of chronic glomerulonephritis.

20. The treatment appears to be entirely symptomatic. Epstein's high protein and thyroid therapy does not appear to be specific. Repeated courses of pitressin appear to be effective in reducing edema.

Abstract by Koucky.

III. CASE REPORT

LIPOID NEPHROSIS. TERMINAL PERITONITIS.

Path. Koucky.

The case is that of a white, female child, 9 years of age, admitted to University Hospitals 8-1-30 and discharged 12-24-30 (145 days); readmitted 7-6-31 and discharged 10-27-31 (113 days); readmitted 5-6-32 and expired 8-12-32 (98 days). Total stay - 356 days.

Colds

4- -30- Developed a cold from which she recovered in short time.

5- -30 - Developed another cold which was more severe and apparently became chronic. Was irritable and inactive. Extreme pallor observed (edema?).

Burning, Oliguria, Edema

5-20-30 - Complained of burning on urination. Had nocturia once or twice a night.

6-1-30 - Mother observed marked diminution in amount of urine which child passed.

6-8-30 - Edema began in legs and spread quite rapidly to remainder of body. There was also ascites. Backache and malaise, accompanied these symptoms.

Admitted

8-1-30 - Admitted to University Hospitals. Admission findings: Generalized edema of face, eyelids, extremities, abdomen, and marked pallor. Throat - moderately enlarged tonsils. Lungs - slight dullness at both bases. Abdomen - distended apparently with fluid. Skin - fine pinpoint size rash over back and legs. Weight - 76 lbs. Past history: Colic at age of 3months, diarrhea at 6 months, measles and pneumonia at 3 years, influenza or "cold" in April and May 1930.

Special examinations

8-11-30 - X-ray of sinuses - negative.
11-1-30 - Electrocardiogram -Tachycardia, sino-auricular in type. Auricular extrasystoles. 11-24-30 - Electrocardiogram - Auricular extrasystoles (numerous). Sinus Arhythmia.

Laboratory:

Urine - During this admission, approximately 150 urine examinations were done. Total amount and specific gravity - variable. Minimal 24 hr. specimen - 40 c.c., maximum 1476 c.c., usual - between 150 and 300 c.c. Specific gravity of 24 hr. specimen - ranged from 1.002 to 1.040, usually between 1.027 and 1.030. Sugar-absent in all specimens. Reaction - usually acid but occasionally alkaline. Albumin - absent to 4+, average about 3+; quantitative (when done) ranged from 0 to 3.5 grams per liter. Sediment - usually negative, for short periods of time showed hyaline casts, and in like manner for a few days in a stretch showed occasional wbc's and rbc's, granular casts rarely observed. Blood - On admission, Hb. 97%, wbc's 14,200, Pmn's 55%, L 37%, E 8%. On this admission, the only other hemoglobin reading was 93%. Blood Wasserman - negative. Only a few white blood count readings were reported, these were all normal average (9,500). Blood urea nitrogen - (admission) - 15.4, N.P.N. 48.0. 10-21-30 this dropped to 25; 10-29-30 - 34.2; last examination before discharge - 31. Cholesterol - 8-4-30 - .452; 9-11-30 - 1.025; 10-28-30 - 583.0. Blood chlorides - 8-13-30 - 420.7; 8-20-30 - 462.0; 9-11-30 - .374. Total blood protein - 8-5-30 - 4.53; 9-11-30 - 5.38; 10-7-30 - 5.44; 10-8-30 - 6.05. Albumin - 10-7-30 - 4.65; 12-10-30-1.77; 12-22-30 - 4.4.
Globulin - 10-7-30 - 1.4.
Phosphorus - 11-17-30 - 5.04.
Calcium - 11-17-30 - 8.8

Clinical progress

Tried on various diets. Diet maintained over longest period was 100 grams casein, 110 grams egg yolk, 120 grams cane sugar, 400 grams water, 5 grams yeast.

Discharged - Better

12-24-30 - Condition very much improved. Edema has practically subsided. Weight - 63-1/4 lbs. Greatest (while in hospital) 78 lbs. Sent home with diet containing 500 c.c. water and a high protein intake. Last blood examination showed N.P.N. (before discharge) 27.3, total protein 4.4, albumin 1.77. Urine still showed albumin (bad prognosis!)

Readmitted (6 mo. later).

7-6-31 - Readmission note: Has been doing well but had "colds". Contracted another severe "cold". Soon after onset of "cold" edema reappeared which subsided with bed rest. Has been in bed almost continuously since May 1930 when she contracted "cold". Output of urine measured while at home and averaged 24 ounces. Since onset of "cold" amount varied from 10 to 16 ounces; on the two days prior to admission to 8 ounces. Restlessness occasionally present. Otherwise had no other symptoms. Examination shows edema and pallor as before. Blood pressure 110/60.
Special examinations: X-rays of maxillary sinuses and legs are of no significance.
Laboratory: Urine: During earlier part of stay, output ranged around 500 cc. During latter part, ranged between 1000 and 2000 cc. Maximum output 2500 cc. Specific gravity - quite constantly around 1.030, minimum 1.012, maximum 1.040. Reaction - usually acid, frequently alkaline. Sugar - observed at no time. Albumin - grading dropped from 4+ to 2+., occasionally 3+ and 1+. Sediment - early, casts were constant chiefly granular; later absent; few wbc's from time to time; occasional rbc's. Albumin-(quantitative) 7-21-31 - 8.2 grams, 7-28-31 - .6 grams, 7-29-31 - 2.4 grams, 8-4-31 - 3.1 grams, 8-13-31 - 1.5 grams, 8-14-31 - 1.5 grams, 8-15-31 - 4.5 grams, 8-17-31 - 5.0 grams, 8-18-31 - 4.5 grams 8-25-31 - 3.8 grams, 10-18-31 - 1.8 grams
Blood - 7-6-31 - Hb. 113%, wbc's 10,850, L 56%, M 1%, B 1%, Pmn's 42%. 7-13-31 - Hb. 92%. 7-22-31 - Hb. 75%. N.P.N. 7-7-31 - 31.0. P.S.P. 7-8-31 - 1st half hour 25%, 2nd half hour 15%, third half hour 5%, 4th half hour 2.5%. Total 57.5%. 8-3-31 - 1st half hour 20%, 2nd half hour 15%, 3rd half hour 10%, 4th half hour - no specimen. Total 45%. Protein - 7-6-31 - 4.78; 9-16-31-4.81, 10-2-31 - 4.93. Globulin - 9-16-31 - 3.3, 10-2-31 - 3.82.
Albumin - 9-16-31 - 1.51, 10-8-31 - 1.11
Cholesterol - 7-6-31 - 945.0.

Treatment - Better

Restricted fluids. Intake from 200 to 275 cc. Urea gr. xx, 4 times a day. Thyroid extract gr. i, 5 times

a day. Diet - carbohydrate 127, protein 100, fat 100. Later this was changed to - carbohydrates 75, protein 100, fat 125. On admission, weighed 3107 kg., on discharge 26.194 kg. Edema down remarkably. Very much improved. Discharged to return to Out-Patient Department.

Readmitted. (7 mo.)

5-6-32 - "Cold" - Since discharge in Oct. 1931, felt quite well. In December, contracted severe "cold". Diet cut down following this (in Out-Patient Department). Unable to be in school because of increasing edema. Referred back to hospital. Physical examination - negative except for very marked generalized edema and pallor.

Clinical course - Peritonitis.

Expired during this admission. General condition not controlled by rest and therapy as on previous admissions. Shortly before death edema became worse. Three days before death, developed pain in abdomen. Cultures of ascitic fluid showed streptococcus. Expired of peritonitis secondary to nephrosis.

Treatment

Diet during this admission - carbohydrate 115, fat 60, protein 90. K. I. gr. ii twice a day. Thyroid extract gr. 1/4, 4 times a day. Ammonium chloride gr. xx, 3 times daily. Just prior to death, sedatives and stimulants.
On admission, weighed 40.45 kg. 7-30-32- dropped to 36.985 kg. Thereafter, slowly rose until at time of death when it was 41.587 kg. Urine output ranged between 140 and 330 cc.

Laboratory

Urine: Specific gravity - 1.035, 1,044, only 2 readings reported. Albumin (quantitative): Amt. per liter extremely variable. Shortly after admission, measured 25 gm. per liter or total output of 5 gm. 5-25-32 - Dropped to 9 gm. per liter or total output of 2.385 gm. Thereafter, output ranged from 16, 14 to 6 gm. per liter, with daily output from 2 to 5 gm. In the last 14 days of patient's life, total albumin in urine was fairly constant at 4 or 5 gm. per liter. Blood: Hbg. on admission again elevated (95) but after stay dropped to 68 and then to 56. N.P.N. - 5-8-32 - 23.4; 6-2-32 - 80.4; 6-8-32 - 72.6; 6-28-32 - 50.4; 7-9-32 - 34.5; 7-23-32 - 90.8; 8-10-32 - 44.5; total protein - 5-9-32 - 3.77; 6-2-32 - 3.2; 6-8-32 - 3.5; 7-9-32 - 4.47; 7-23-32 - 5.94. Albumin - 5-9-32 - .606; 7-9-32 - .87. Globulin - 5-9-32 - 3.164; 7-9-32 - 3.6. Cholesterol - 5-9-32 - 254; 6-2-32 - 1750 (?); 6-8-32 - 616.6; 7-23-32 - 766.6. CO_2 combining power - 6-11-32 - 21 vol. %.

Exitus

2:00 A.M. - Awoke with severe pain in lower quadrants of abdomen. Temperature 101. Pulse 110. Respirations 36. Throat seemed to be reddened. Later in day, abdomen aspirated - 750 cc. of slightly opalescent fluid obtained. Smears of this and cultures showed a short chain streptococcus. Progress from then on - progressively downhill. 8-12-32 - Comatose. Temperature 99.4. Pulse 110. Respirations 28. 11:15 A.M. Expired.

Summary of blood pressure readings:

A consistent record of blood pressure readings not made through stay. Record of 4 blood pressure readings noted. 11-17-30 - B.P.88/30, (1st admission) 7-7-31 - B.P. 110/60, 8-28-31 - B.P. 96/70, (2nd admission). 7-28-32 - B.P. 108/88.

Autopsy

Edema

Body is that of well-developed, well-nourished, white, female child, 9 years of age, measuring 134 cm. in length and weighing (given weight) 41.6 kg. Generalized edema, grade III, most marked in lower part of body. Edema in lower extremities is about grave IV. Edema of lower part of abdomen is marked and rapidly diminishes over chest. Marked edema of face and eyelids. Body is extremely pale and waxy. Skin tense due to edema. Hemorrhagic discolored, circular area over dorsum of right foot, 5 cm. in diameter. Subcutaneous fat abundant. Varies over trunk, depending upon extent of edema. In region of umbilicus, measures 18 mm.

Ascites (turbid)

Peritoneal Cavity - filled with fluid. Fluid is turbid (milky appearance) due to white flakes and white

flakes and white stringy material within it. About 1500 c.c. of fluid in abdomen.

Hydropericardium

Increase of pericardial fluid. Heart - 180 grams. No hypertrophy or dilation. Musculature and valves appear normal. Root of Aorta and coronaries show no changes.

Right Lung 170 grams, Left 150. Puckered scar in right apex. Some congestion of bases.

Septic

Spleen - 140 grams. Normal capsule. Feels somewhat more firm than usual. Moderate amount of pulp can be scraped away. Appears to be mildly septic.

Fatty

Liver - 1450 grams. Edges are rounded. Surface is yellowish. Entire liver is soft. On cut surface, diffuse, yellowish infiltration throughout liver substance which reaches maximum in large diffuse area in center.

Gall-bladder normal; no cholesterol deposits.

Edema

Gastro-Intestinal Tract. Serous surfaces have lost luster. Bowel is pale. No marked redness as expected by presence of streptococcic infection of cavity. Thickness of stomach and upper part of small bowel is approximately normal. Mucous membrane shows no change. In lower part of ileum, bowel appears to be slightly thicker than normal. Mucous surface appears finely granular. Entire colon markedly thickened. Thickening principally in mucous and submucous layers and seems to be due mostly to edema rather than fibrous deposits. Mucous membrane hangs into lumina in large redundant folds almost like polypi. Mucous membrane is very pale and appears water-logged. Process reaches maximim in sigmoid and lower colon.

Normal

Pancreas shows no changes .
Adrenals appear normal.

Large, Pale

Right kidney 210 grams, Left 245 grams. Capsules strip quite easily. Surfaces smooth. Pelves and ureters no change. Kidneys are extremely pale. On cut surface, pallor again noted. Demarcation between cortex and pyramids indefinite. Fine, reddish streaks in cortex. Cortex seems thicker than normal. Bladder - no changes.

Small (?)

Genital Organs. Ovaries and tubes appear well-developed. Uterus markedly hypoplastic (?). Cervix is normal but fundus is small as infant.

Atheromata.

Aorta. Thoracic and upper abdominal aorta no changes. In lumbar part, immediately above bifurcation, are 5 or 6 indefinite, yellowish plaques which appear to shine through intima as though they are deep seated. Largest plaque measures about 1-3/4 cm. in length and .5 cm. in width, and has a diffuse outline.

Normal

Thyroid appears normal.

Lymph nodes appear normal throughout body. Small accessory spleen, measuring 1 cm. in diameter, found near splenic flexure of colon imbedded in mesentery of colon.

Permission for examination of Head was not granted.

Diagnoses:

1. Lipoid nephrosis.
2. Streptococcic peritonitis.
3. Generalized edema.
4. Ascites, slight hydropericardium.
5. Right apical scar, probably tuberculous.
6. Fatty liver.
7. Splenitis.
8. Edema of lower small bowel and colon.
9. Hypoplasia of uterus?
10. Accessory spleen.
11. Fatty deposits in aorta.

Comment:

Special studies of microscopic sections of kidneys reveal "typical" findings of nephrosis, i.e., Azo-carmine stains show involvement of glomeruli as described by Bell. All examinations by Dr. Bell.

	1st Adm. '30					OPD '30		2nd Adm. '31				OPD '31 '32			3rd Adm. '32.		
	Aug.	Sept.	Oct.	Nov.	Dec.	Apr.	May	July	Aug.	Sept.	Oct.	Dec.	Apr.	May	June	July	Aug.
Hgb.	90-98	92-104	-	-	-	-	-	75-113	79	78	-	-	-	95	-	68 to 56	-
Wbc	14,000	-	-	-	-	-	-	11,000	-	-	-	-	-	1,740	-	-	-
24 Hr Amt	40 to 650	70 to 860	150 to 1300	30-700	55 to 845	-	-	60 to 800	34 to 625	-	50- * 200	-	-	110 to 730	130-400	68-420	125-240
Sp. Gr.	8/1-15/30 1.029 8/15 - 9/1/30 1.006-1.035	1.002 1.032	1.012 1.032	(con. dil. 1.004 to 1.032	1.022 1.031	S.S. 1.028	S.S. 1.029	1.011 1.040	1.012 1.032	- -	1.015* 1.032"	-	-	-	-	-	-
Alb.	3-4+	1-4+	3+	3+	0-2+	cld.	3+	2-4+	0-4+	-	2-3+*	2+	4+	4+	4+	4+	4+
Q Alb/L	2.5-3.5	2.5-4	1-5.5	.5-3	.2-6	-	-	.6-2.5	1.5-5	-	2.5-3.7"	-	-	7-250	7.5-19	5-14	3-8
Rbc	2x Occ.	6x Occ	-	-	-	-	few	-	8x 0 cc.	-	-	-	-	3x	+++	Gross	blood
Casts	+	++	-	-	-	-	-	+	+	-	+	-	-	++	++++	++++	++++
NPN	48	34-44	21-34	-	27	-	-	31-38	35	37	24* 19.8"	-	-	23	50-80	35-100	44.5
PSP	-	-	-	-	-	-	-	47.5	45	-	-	-	-	80	-	-	-
Chol.	420	1025	402-583	-	-	-	-	945	554	650	221	-	-	754	816-1750	767	-
Cl.	420	375	-	-	-	-	-	-	342	-	-	-	-	-	-	-	-

T. Prot.	4.53	5.78-4.95	4.5-6	-	6.17	-	-	4.78	5.2	4.8	4.9* 6.1"	-	-	3.77	3.2-3.6	4.52-5.9	-	
Alb.	-	-	4.65	-	4.4	-	-	-	-	1.7	1.26* 3.16"	-	-	.606	-	.87	-	
Glob.	-	-	1.4	-	1.77	-	-	-	-	3.0	3.67* 2.95"	-	-	3.164	-	3.6	-	
B.P.	-	-	-	88/30	-	-	-	110/60	96/70	-	-	-	-	-	-	108/88	-	
Wt.	76	74½	71.8	68.5	65.5	65¾	66¾	68	71	75-86	53	69¾ 73¾	76¾	87¼	85	86	89	

Comment First cycle — Contracted severe cold — Euphylin Salyrgon Thyroid 8-22-31 — Return to normal — Another cold — another cold (severe) — Peritonitis

*1st 2 wks. (water intake irregular)
"2nd 2 wks.

Note:

1. Presence of anemia, increased albuminuria, hematuria, casts, non-protein nitrogen reversal of A - G ratio, no change in blood pressure with development of "nephritis".
2. Definite relation of "colds" to cycles of edema.
3. Relation of exacerbations of edema to drop of serum protein and increase in cholesterol.
4. Relation of edema to total serum protein is not as definite as relation of edema to serum albumen.
5. Diuretics given after edema was clearing (2 days) probably not related, i.e. No cause and effect inferred.

IV. CASE REPORT:

EDEMA OF UNKNOWN ORIGIN.
TERMINAL OTITIS-MEDIA:
MASTOIDITIS.

Path. Pearson.

The case is that of a white, female infant, 2 years of age, admitted to University Hospitals 10-5-31 and expired 4-23-32 (201 days).

Prenatal history:
Mother attended clinic in St. Paul for prenatal care during second month of pregnancy. Recommendation made for bed rest, particularly after 5th month in order that child could be carried to term. Mother was said to have "tumor" of uterus. Bed rest carried out.

Birth
Delivered in St. Paul after 56 hours of labor. Dry birth. Weight 9 lbs. Face swollen at birth (difficult labor?)

Urination: infancy
Noted that infant did not pass urine during night, i.e. from 10 P.M. to 7 or 8 A.M. As she grew older, would occasionally not pass urine throughout course of day but would perspire profusely.

Development
At 1 month, breast feeding was supplemented by formula. Cod liver oil given. Vegetables were added at 5th month but patient never had much appetite. Always constipated. Never could be induced to drink much water. Never showed any animation or energy. Did not walk until 15 months of age or talk until 2 years.

Mother's Health:
not very good since delivery. Complained of severe menstrual pain and headaches. (In hospital recently with hypotension and weakness suggested early Addison's Disease).

Colds
Age 1: During first winter of patient's life, had very frequent colds.
1- -31 - Suffered severe cold with marked cough, associated with fever.

Edema, Pertusis
3- -31 - Eyelids began to swell.
4- -31 - Whole face seemed swollen. Soon, legs and arms became slightly swollen.

Better, worse, hematuria?
5- -31 - Developed whooping cough which persisted throughout subsequent summer. During this time swelling of face and extremities subsided somewhat.
7- -31 - Swelling recurred and increased in amount. On one occasion during this month, blood noted in urine. (Mother) During remainder of summer, some edema persisted.
9- -31 - Edema increased in amount. Abdomen became larger, most marked at night. Seemed to be sore and uncomfortable.

Admitted
10-5-31 - Physical examination - Throat - hypertrophied and injected tonsils; reddened pharynx. Neck - no adenopathy; papulo-pustular rash present. Abdomen - protrudes, liver palpable below costal martin, shifting dullness present. Edema, of eyelids, pitting edema (slight) of extremities. Skin - feels edematous and has rather pasty color.

Consultations
Skin lesions probably due to profuse sweating. Eye grounds - negative. X-ray - Sinuses - show bilateral maxillary sinusitis. K-U-B - negative. Wrist, lower tibia - negative bones.

Progress
In addition to changes in chemistry, corresponding with variations of treatment and intensity of edema, following is noted:
10-29-31 - Result of treatment satisfactory. Edema and ascites disappeared. Apparently more comfortable. Immediately on stopping treatment, sharp increase of water output and decrease of edema noted.
11-4-31 - Weight very slowly increasing.
11-7-31 - No change other than slight increase in weight.
11-23-31 - General condition unchanged. Weight fluctuates somewhat.

Pneumonia
2-19-32 - Past 2 days, temperature somewhat elevated, cough, dullness and rales in midportion of right chest.

3-20-32 - Area seems increased in size. X-ray shows definite haziness in right hilus region. Temperature up to 103.4. Cough quite marked.

2-24-32 - Pneumonia increasing. Appears to have some findings at left hilus. X-ray shows very extensive pneumonia, involving right lower lobe and part of right upper lobe, with some increased density at left base. Conclusions: Bronchopneumonia, right lower and upper. Beginning bronchopneumonia, in left lower.

2-29-32 - Pneumonia resolving. Temperature normal. Considerable diuresis since pneumonia subsided (due to treatment?).

Edema goes

3-1-32 - Diuresis continues. Patient lost 1.5 kilograms in past 26 hours. Face and legs appear free from edema. Ascites much less marked.

3-12-32 - Edema all gone. Had been irritable previously but following latest improvement has changed entirely and appears quite happy.

Otitis Media - Mastoiditis

4-2-32 - Slight fever again present.

4-10-32 - Edema increased. 2 kilogram rise.

4-12-32 - Left otitis media since last night. Definite findings in left ear drum. Paracentesis done, large amount of thin, yellow pus obtained.

4-13-32 - Ear drum reopened. Gram+ cocci in chains in smear.

4-15-32 - Temperature 102. Definite follicular tonsillitis. Left ear drum draining, right appears normal. 4:15 P.M. - few rales found in left angle of scapula.

4-18-32 - Temperature continues high, 103. Ear drum draining well. Does not appear to be any cause for fever. Possibility of mastoiditis considered. X-ray - shows area of destruction in left mastoid, characteristic of mastoid abscess. Conclusion: Acute mastoiditis with abscess.

Exitus

4-21-32 - Temperature 104.

4-22-32 - Patient cyanotic. Breathing rapidly. Pulse 160. Temperature 105. Numerous rales present in chest.

4-23-32 - Breathing more difficult and shallow. Cyanosis developing. 12:53 P.M. - expired.

Autopsy

Aside from edema and immediate infectious cause of death, no significant changes were found. Eminent glomerulus histopathologist E.T.Bell found nothing. Various theories advanced include innate failure to properly metabolize protein molecules as cause of edema. Apparent birth connection suggested by history. Common edema of newborn (practically all stillbirths) is called hydrops fetus universalis supposed to be linked on rather flimsy grounds to congenital leukemoid state. No opportunities apparently have existed to study this disease after birth. Well known to pathologists, hydrops of the fetus may at times assume amazing proportions. That this disease was not lipoid nephrosis or glomerulonephritis is perfectly obvious from all investigations.

CASE II.	10-6-31	10-22-31	10-27-31	10-31-32	11-6-31	12-8-31	1-1-32	1-20-32	2-12-32	2-18-32	2-24-32	3-4-32	4-4-32	4-20-32
Hgb.	81	-	-	-	-	-	85	-	-	-	68	-	-	58
Wbc	8300	-	-	-	-	-	7700	-	-	-	12,800	-	-	14,500
24-Hr. Amt.	-	1100	1600	-	-	-	-	-	600	1000	500	1300	850	-
Sp.Gr.	-	-	-	-	-	-	-	1.005-1.010	1.022-1.024	1.004-1.006	1.014	1.003	-	-
Alb.	o	o	o	o	o	o	o	o	o	o	o	o	o	trace
Rbc.	o	o	o	o	o	o	o	o	o	o	o	o	o	o
Casts	o	o	o	o	o	o	o	o	o	o	o	o	o	o
NPN	-	27.0	-	-	25.5	28.8	-	22.9	-	26.6	-	30.0	22.6	-
PSP	50%	-	-	-	-	-	-	-	-	-	-	-	-	-
Chol.	266	193.3	-	-	213.8	-	-	-	-	-	-	-	-	-
T. Prot.	-	2.54	-	3.64	3.67	4.35	-	4.34	-	3.47	-	5.86	4.39	-
Alb.	-	2.09	-	2.64	2.64	2.12	-	2.25	-	2.5	-	3.65	2.72	-
Glob.	-	0.45	-	1.00	2.23	-	-	2.09	-	.97	-	2.21	1.67	-
Phos.	-	5.65	-	3.7	-	-	-	-	-	-	-	-	-	-
Cal.	-	11.25	-	13.8	-	-	-	-	-	-	-	-	-	-
Wt. (Kilo)	-	15.2	-	13.8	14.2	15.0	-	-	15.2	14.0	-	13.4	13.8	-
Treatment			Parathormone		-	-	-	-	Pitressin	-	Transfusion	-	-	-
Remarks	Preparathormone	-	-	Parathormone effect	-	Parathormone effect lost	-	Stationary	-	Pitressin effect	-	Transfusion effect	lost	Mastoiditis

Water Intake Constant at 1200 cc.

Note:

1. **Complete absence of albuminuria, casts or rbc's in urine.**
2. **Immediate response to treatment indicated by drop in weight.**

V. Meeting:

Date: December 8, 1932.

Place: Internes' Lounge, 6th Floor, West Building.

Time: 12:15 to 1:45.

Program: The Child and the Tuberculosis Program.

Present: 91.

Discussion: Leo G. Rigler
C. A. Stewart
J. A. Myers
H. S. Diehl
Irvine McQuarrie

Theme:

Able, convincing demonstration through clinical history and lantern slide proof of statements advanced in regard to "The Child and the Tuberculosis Problem," Author J. A. Myers (name unintentionally omitted from abstract). All who heard wondered if any member of our organization or graduate of this school would ever go out into practice without a bottle of tuberculin in his hip pocket and a pad of x-ray request chest blanks on his desk. Drs. Stewart and Myers convincingly demonstrated that first infection with tubercle bacilli frequently (if not always) fails to give evidence of his presence in any other way than by tuberculin test and in many instances x-ray films of the chest. Healthy, normal-looking, children were shown by photographs with accompanying x-ray films. Contact infection through immediate sources probably explains all primary disease and does away with old theories of racial susceptibility in so-called non-resistant negroes, Indians and others. Such children in spite of apparent blank nature of disease should be watched to avoid breaking down or re-exposure as first infection does not immunize or protect in any way. Calcification is apparently limited to primary lesions (some discussion about this. Through tuberculin testing, every 6 months or year, children free of infection can be immediately determined; in the others, effort should be made to classify them as healed or hidden focus, active or inactive childhood or adult disease. It was pointed out that recent studies with correction for other cuases of death show tuberculosis is a constant early uniform menace in all age groups and not as we had once thought only in childhood and early adult life. Benign, primary tuberculous infection is only experienced once no matter what the age. Longitudinal (not cross-section) studies made of individuals with and without positive tuberculin reactions have changed many of our ideas in regard to this disease. Continued studies at Lymanhurst (Minneapolis School for under-privileged and tuberculin positive children) and the Health Service of the University of Minnesota will continue to yield valuable information. This meeting was by far one of the outstanding affairs of the year and we are deeply indebted to all who made it possible.

Gertrude Gunn
Librarian.

VI. SPECIAL NOTICE

Annual Lecture, Minnesota Pathological Society: Dr. Arnold R. Rich, Johns Hopkins Medical School.

Title: The General Aspects of Hypersensitiveness in its Relation to Immunity.

Institute of Anatomy, Tuesday, Dec. 20, 1932, at 8:00 P.M.