MEDICAL GRAND ROUNDS

PARKLAND MEMORIAL HOSPITAL

March 12, 1964

NEPHROSIS AND STEROID THERAPY

1. Patient [redacted]

The first admission of this 45 year old [redacted] man was on [redacted] 1958. He had noted swelling of legs and abdomen for the 2 weeks prior to admission. He may have had some leg swelling several months before this admission. He had been an epileptic since childhood and was mentally deficient. He had been on no medication for several years, and had had no seizures during at least the past year. There were no genitourinary tract symptoms.

Physical Examination: BP 140/90; there was a generalized anasarca with ascites; fundi normal; heart not enlarged; liver not felt; body weight 177 lbs.

Laboratory Data: Urinalysis 4+ protein; few granular casts; BUN 26 mg%; creatinine 0.9 mg%; PSP 45% in 30 minutes; 75% in 2 hours.

	1 May 1958	12 June 1958
Albumin	1.9 gm%	3.4 gm%
Globulin	3.1 gm%	3.3 gm%
Cholesterol	640 mg%	834 mg%

24 hour urine protein:

3 May	11 May	19 May	26 May	12 June
1.7 gm	5.6 gm	2.8 gm	1.0 gm	Neg.

Therapy: On [redacted] he was started on 100 mg Prednisone daily. Urines became negative for protein.

Discharged [redacted] 1958 on no therapy.

Readmitted [redacted] 1958 because of return of anasarca. Again responded quickly to 100 mg dose of Prednisone. Was discharged on no treatment.

Two other admissions in 1959 were necessary because of return of massive edema. Each time there was a rapid return to a negative urine protein during the course of steroid therapy. Finally, in [redacted] 1960 intermittent therapy was started.

Renal Clinic: [redacted] 1960 - urine negative protein; albumin 4.2 gm%; globulin 2.9 gm%. [redacted] 1960 - urine 2+ protein; albumin 4.6 gm%; globulin 2.6 gm%; cholesterol 350 mg%. Intermittent therapy continued.

Admitted Woodlawn Hospital [redacted] 1961 for a suppurative pneumonia. Steroids were continued. Urines throughout this admission were negative for proteins and only very rarely showed a hyaline cast. BUN varied from 15 to 20 mg%. He was discharged [redacted] 1961.

Renal Clinic: [redacted] 1961 - had by mistake been instructed to take only 25 mg Prednisone daily X 3 weekly. Urine; trace protein; changed to 75 mg dose. Missed several clinic appointments, but for the most part remained on steroids. [redacted] 1963- urine 1+ protein; sediment

contained many WBC and RBC with a few hyaline and granular casts.

He was last seen on [redacted] 1964 when he had been off steroids several months. BP 120/80. Urinalysis: negative albumin; few hyaline casts; one RBC cast; many small fat drops; occasional clumps of RBC; specific gravity 1.020.

Albumin	4.8 gm%	Globulin	3.0 gm%
Cholesterol	295 mg%	BUN	15 mg%
Creatinine	1.0 mg%		

2. Patient [redacted]

This 15 year old [redacted] girl was admitted to the medical service [redacted] 1963 complaining of painless swelling of her legs of three days duration. There was no history of recent illness. She denied previous swelling and specifically denied hematuria but gave a long history of recurrent dysuria.

In [redacted] 1962, she had delivered a normal child at [redacted]. Previous to delivery she had asymptomatic bacilluria. Several urinalyses during pregnancy and at the time of delivery contained no protein. One urinalysis post partum contained a trace of protein. She had 1+ ankle edema at delivery, and both the edema and bacilluria cleared up after delivery.

Physical Examination: BP 108/88; there was swelling of the hands and face and pitting edema of the lower extremities. The remainder of the physical examination was recorded as normal. Body weight was 147 lbs.

Laboratory Data: Urinalysis 4+ protein; many lipoid bodies and granular casts; no RBC.

Albumin	1.9 gm%	Globulin	1.1 gm%
Cholesterol	348 mg%	BUN	7 mg%
Creatinine	0.9 mg%	ASO -	125 and 166 T.U.
LE preps	Negative	Urine culture sterile	

24 hour urine protein:

[redacted].	[redacted].	[redacted].	[redacted].	[redacted].	[redacted].
3.2 gm	3.6 gm	4.7 gm	3.2 gm	4.7 gm	5.2 gm

Prednisone, 80 mg/day was started [redacted] 1963 and continued for 15 days. In [redacted] 1963 intermittent steroids were started, 60 mg daily X 3 days weekly. Renal Biopsy was done on [redacted] 1963.

She was discharged [redacted] 1963. There had been a 7 lb. weight loss, but no significant change in protein excretion or serum albumin concentration.

Renal Clinic: Steroids have been continued without effect. In [redacted] 1964, it was discovered that she was again pregnant (5 months). She remained edematous, normotensive, with 4+ protein reaction in urines.

3. Patient [redacted]

The patient, a 52 year old woman, was admitted [redacted] 1962 with a 3 month history of asymptomatic swelling. About 2 or 3 weeks prior to admission she began to notice abdominal swelling which was progressive. This swelling was accompanied by shortness of breath and because of this she sought medical aid.

She had been in good health all of her life. Five months prior to this admission she was told that she had high blood pressure. There was no history of genitourinary tract infection.

Physical Examination: BP 170/100; fundi were not remarkable. The heart was not enlarged. There was a generalized anasarca with ascites. The remainder of the examination was not remarkable.

Laboratory Data: Urinalysis 4+ protein; many lipoid bodies with some granular casts.

	[redacted]. 1962	[redacted]. 1962
Albumin	1.7 gm%	4.8 gm%
Globulin	3.5 gm%	2.7 gm%
Cholesterol	500 mg%	299 mg%
BUN	28 mg%	
Creatinine	1.7 mg%	

24 hour urine protein: 5.0 gms/24 hours falling to 1.4 gm at discharge.

Renal Biopsy was done on [redacted] 1962.

Therapy: 100 mg Prednisone for 14 days; discharged on 75 mg Prednisone daily X 3 weekly.

Renal Clinic: From [redacted] 1962 to [redacted] 1963 urines showed only trace protein reaction. BUN and creatinine were normal; she was free of edema. On the [redacted] 1963 she had been off steroids for 6 weeks; urine 3+ protein; sediment disclosed many RBC and one RBC cast seen. She was restarted on intermittent steroid therapy.

[redacted] 1963 - urine trace protein. [redacted] 1963 - steroids discontinued. Negative urine protein since June.

[redacted] 1963 - trace protein in urine; albumin 4.6 gm%; globulin 2.7 gm%; cholesterol 187 mg%.

[redacted] 1964 urine 1+ protein; intermittent steroid therapy restarted.

[redacted] 1964 urine slight trace protein; continued on steroid therapy.

4. Patient [redacted]

This is a 57 year old white woman whose 6th [redacted] admission occurred on [redacted] 1963. She was first seen here in 1961 and gave a history of long standing rheumatic valvular heart disease. Since [redacted] 1961 she had been bothered by varying amounts of generalized edema. Before the present admission she had been digitalized for CHF, had a mitral commissurotomy [redacted] 1961) and been on various diuretic regimens.

From her previous record, it was noted that proteinuria and low serum albumin concentration had been noted on many occasions. Further, during an admission in [redacted] 1961 for post-commissurotomy syndrome she received 20 mg Prednisone daily for several days. This was associated with urines negative for protein, and her highest serum albumin concentration was 3.1 gm%.

The sixth admission was a result of increased edema, nausea, vomiting, and episodes of documented auricular flutter.

Physical Examination: Important findings were a BP of 140/90; negative fundi; and marked generalized edema. There was also cardiomegalia with appropriate murmurs.

Laboratory Data: Urinalysis 4+ protein; lipoid bodies and granular casts.

BUN	28 mg%	Creatinine	1.2 mg%
Albumin	1.4 gm%	Globulin	2.8 gm%
Cholesterol	684 mg%	PSP	29% in 30 minutes
VP	10 cm H_2O	CT	18 seconds

Two 24 hour urine proteins 3.5 and 4.0 gm respectively.

Renal Biopsy on [redacted] 1963.

Therapy: 75 mg Prednisone per day began [redacted] 1963 and continued through 23 October 1963. The urine showed only a trace reaction for protein.

Renal Clinic: 75 mg Prednisone/day X 3 days weekly.

6 [redacted] 1963: urine trace albumin; weight loss from time of 6th admission had been 8 lbs; BP 120/80; some edema.

BUN	31 mg%	Albumin	4.2 gm%
Globulin	2.0 gm%	Urine sediment	Negative
Cholesterol	338 mg%		

[redacted] 1964: Urine continues with trace protein reaction; some edema still present; cholesterol has fallen to 240 mg%. She is normotensive. BUN remains in the low 20's.

5.. Patient [redacted]

The first admission of this 31 year old [redacted] male was [redacted] 1958. He had noted marked swelling of his feet for 6 weeks prior to admission. He denied any recent illness, hematuria of dysuria. His past history and family history were not significant. He considered his health to be excellent.

Physical Examination: BP 110/60; except for periorbital edema, 3+ pedal and pre-tibial edema, the examination was not remarkable.

Laboratory Data: Urinalysis 4+ protein; many hyaline and granular casts; lipoid bodies present.

BUN	18 mg%	Creatinine	0.9 mg%
Albumin	1.6 gm%	Globulin	2.4 gm%
Cholesterol	590 mg%	LE prep	Negative X 3
ASO =	50 T.U.	PSP	91% in 2 hours

24 hour urine contained 4.0 gm protein.

Therapy: 100 mg Prednisone for 15 days; urine became protein free; then started on 75 mg/day X 3 weekly. Discharged [redacted] 1958.

Renal Clinic: Took steroids and had negative urine until [redacted] 1958, then patient stopped steroids.

[redacted] 1959: edema had returned; albumin 2.1 gm%; BUN 49 mg%.

[redacted] 1959: second admission; retreated with 100 mg Prednisone for 10 days; urine again became protein free.

Returned to clinic only occasionally; was re-admitted [redacted] 1961 for retreatment; again responded.

Renal Biopsy on [redacted], 1961.

Renal Clinic: returns sporadically; while on steroids, urines are negative. Last seen [redacted] 1963, had been off steroids for at least 6 months. Had 4+ protein reaction in urine; refused admission. At that time BP was 110/74; BUN 17 mg%; albumin 3.1 gm% and globulin 2.6 gm%.

6. Patient [redacted]

This 15 year old [redacted] boy was admitted [redacted] 1960 with a weeks history of swelling which began in his feet, but after a day or two included his hands and face. There was a vague history obtained by one observer of a mild sore throat with subjective fever which occurred about 3 weeks prior to admission. About 3 days prior to admission, the patient had a mild asthmatic attack, a not unusual occurrence for this patient. There had been no recent history of fever, malaise, weakness, joint pains or genitourinary tract symptoms. Since early childhood, he had had asthma and hay fever. In the past, he had had several severe sore throats with difficulty swallowing.

Physical Examination: BP 140/80; fundi not remarkable; heart not enlarged; marked generalized edema; body weight 164 lbs.

Laboratory Data: Urinalysis 4+ protein; lipoid bodies; few granular casts; BUN 68 mg%; creatinine 1.5 mg%.

	[redacted]	[redacted]
Albumin	1.9 gm%	3.0 gm%
Globulin	2.3 gm%	1.7 gm%
Cholesterol	420 mg%	320 mg%

24 hour urine protein: [redacted] 8.6 gm/24 hours.

Course: He was started on 100 mg/day Prednisone on [redacted] and continued through [redacted] At the time of discharge his BUN was 16 mg%, creatinine 0.7 mg%. His 24 hour urine contained only a trace of albumin and he lost 43 lbs. during the period of admission. He was discharged on intermittent steroid therapy 60 mg/day X 3 weekly.

Renal Clinic: In [redacted] the steroid dose was raised to 75 mg because of the finding of a 2+ proteinuria.

[redacted] 1960; urine 1+ protein; weight 147 lbs.

Albumin	4.3 gm%	Globulin	1.9 gm%
Cholesterol	135 mg%	BUN	9 mg%
Creatinine	0.7 mg%	No edema	

[redacted] 1960; urine negative protein.

Patient failed to keep clinic appointments.

[redacted] 1961: Urine 2+ protein; no edema; probably without steroids for one month.

[redacted] Urine 4+ protein; edema; weight 177 lbs; had again discontinued steroids. Albumin 1.8 gm%; globulin 2.4 gm%. Started on 100 mg Prednisone daily. One week later had only a trace of urine protein and no edema.

Through remainder of clinic course, patient from time to time disregarded steroid therapy. This apparently resulted in proteinuria which always responded by restarting steroids.

[redacted] 1962 a Renal Biopsy was done.

From [redacted] 1962 through [redacted] 1963 no urine was positive for protein. Steroids were discontinued. Unfortunately, he has not returned to Clinic since then; final BP 100/60.

Final Laboratory Data:

Albumin	5.0 gm%	Globulin	1.9 gm%
Cholesterol	143 mg%	BUN	9 mg%
Creatinine	0.9 mg%	Urine sediment negative	

7. Patient [redacted]

This 17 year old [redacted] male was first admitted on [redacted] 1960 with complaints of progressive weakness, nausea and vomiting and mild edema. He had noted a progressive decrease in urine volume for the two weeks prior to admission. He had been in good health until four weeks before admission when he injured his left pretibial region while playing baseball. The skin was broken and failed to heal. He sought medical aid on [redacted] because of this injury and on that day and on [redacted] an injection of combiotic was given. Because of his generalized complaints and fever (102°) his private physician examined his urine which was negative for protein and had an unremarkable sediment. His hemoglobin, however, was reported to be 60% of normal. Because of his continual complaints, he presented to PMH and was admitted.

There was no history of any genitourinary symptoms, although sometime after admission it was learned that for the past year he occasionally passed "dark thick urine."

Past History: His health was unquestionably good until at least the year prior to admission.

Family History: Unfortunately, the patient knew nothing of his parents (or siblings, if any). Several "Aunts" turned out to be no blood relation.

Physical Examination: BP 120/80; temperature 98.6°; fundi were normal; conjunctival and mucous membranes were pale; heart was not enlarged; no CVA tenderness. There was no edema. There was what appeared to be an infected but probably healing abrasion over the left tibia.

Laboratory Data: The urinalysis was strikingly abnormal with 4+ protein reaction, 30-40 RBC and ± 100 WBC/HPF with rare broad waxy and granular casts. Specific gravity 1.019; hemoglobin was 4.7 gm%; WBC 7100; ESR 152 mm/hour.

BUN	240 mg%	Creatinine	30 mg%
CO_2	15 mEq/L	ASO =	all less than 333 T.U.
Albumin	3.3 gm%	Globulin	2.1 gm%

Liver function test was normal and the 24 hour urine protein was 1.75 gm.

Culture from leg wound - Coag Neg. Staph. Culture from throat - B strep not group A or D.

Course: It was originally thought that he had acute nephritis as a result of his leg infection, however, no evidence of a streptococcal infection was ever found. He was oliguric, his urine volume remaining at less than 500 cc/day for the next 27 days. During this time he underwent both peritoneal and hemodialysis on several occasions.

Renal Biopsy #1 on [redacted] 1960.

By early September, urine volume increased and by mid September urine volume was over 2 liters per day. He continued to do well, BUN eventually fell to normal; he remained normotensive, but persisted with small amounts of protein and few RBC in urine sediment. He was discharged on [redacted] 1960.

Renal Clinic: He was followed closely in Renal Clinic until [redacted] 1961. His BUN, creatinine and BP remained normal. On [redacted], 1961 an urine concentration test disclosed a maximum concentration of 925mOM/L. However, during this period of time he consistently had a mild proteinuria with an abnormal sediment.

He was not seen again until his second admission on [redacted] 1962. At this time he was again azotemic (BUN 177 mg%) and his BP 170/90. He was oliguric and required dialysis. ASO titres were below 125 T.U.

Renal Biopsy # 2 on [redacted] 1962. Again he responded with an increase in urine volume and was discharged on [redacted] 1962 with a BUN 32 mg% and a creatinine of 2.0 mg%. His blood pressure remained modestly elevated.

On [redacted] 1962 he was seen in Renal Clinic with full blown nephrotic syndrome and was again admitted. Except for anasarca, findings were similar to those at the time of discharge.

24 hour urine proteins:

[redacted]	[redacted]	[redacted]	[redacted]
11.4 gm	5.6 gm	4.8 gm	6.0 gm
15 July	17 July	27 July	1 August
3.4 gm	2.8 gm	3.9 gm	1.6 gm

Prednisone, 100 mg daily was started on [redacted] and continued through [redacted] 1962. Although edema was lost and proteinuria decreased, it never disappeared.

He was discharged on intermittent steroid therapy and remained clinically much the same for many months although his BUN slowly rose as did his BP. On [redacted] 1963 his BUN was 65 mg%; creatinine 9.8 mg% and BP 220/140.

Albumin	4.6 gm%	Globulin	2.4 gm%
Cholesterol	280 mg%	PSP	7.6% in 2 hours
Urine	3+ protein		

On [redacted] 1963 he was admitted with signs of profound uremia and expired.

8. Patient [redacted]

This 47 year old [redacted] woman was admitted on [redacted] 1962, because of painless swelling of the legs for 3-4 months duration.

She had had similar swelling from time to time since at least 1956. She had an old medical record dating back to 1935 with numerous urinalyses. Among these were several with a trace protein reaction. In 1956 she underwent surgery in another hospital to "raise her kidneys", but this had little effect on her complaint of swollen legs. In 1951 she was first noted to have a mild diastolic hypertension. Aside from her edema, she considered herself to be in good health.

Physical Examination: Fundi some arteriolar narrowing; BP 180/100; heart not enlarged; 3+ pretibial edema. The remainder of the examination was not remarkable.

Laboratory Data: Urines had from 4+ to trace protein. BUN 11 mg%; creatinine 0.8 mg%.

Albumin	2.2 gm%	Globulin	2.9 gm%
Cholesterol	503 mg%		

24 hour urine protein: all 1.0 gm or less.

At bed rest and low salt diet, edema was delivered. Albumin at discharge was 2.7 gm%. No steroids were given.

Renal Biopsy on [redacted] 1962.

Renal Clinic: To December 1963, the patient has had recurrent edema, serum albumin concentrations of from 2.5 to 3.0 gms%; urine proteins 4+ to 2+; BUN and creatinine have remained normal.

At attempt at intermittent steroid therapy was made in December 1963, but the clinic visits have been too erratic to evaluate therapy. BP has remained mildly elevated. Her heart is now thought to be slightly enlarged.

9. Patient [redacted].

The patient, a 35 year old [redacted] woman complained of swollen legs of 7 weeks duration at the time of her first medicine admission, [redacted] 1963. This swelling was first only intermittent but became constant about 3-4 weeks before admission, at which time she first noted swelling of the hands and face. Except for frequent nocturia for several weeks before admission, she denied all genitourinary complaints.

From her old record, one normal urinalysis was available from July 1959. On a single clinic visit in July 1960, a BP of 160/100 was recorded. She considered herself to be in good health until the onset of the present illness.

Physical Examination: BP 150/98; fundi not remarkable; heart not enlarged; 3+ pitting edema of legs; 1+ pre-sacral edema; swollen face and hands.

Laboratory Data: Urinalysis 4+ protein; BUN 25 mg% and creatinine 1.6 mg%.

Albumin	2.1 gm%	Globulin	2.7 gm%
Cholesterol	612 mg%	Liver function studies normal	

24 hour urine protein:

[redacted] 1963	[redacted] 1963
4.6 gm	5.8 gm

Renal Biopsy on [redacted] 1963.

She was not started on steroids and did not return to clinic.

The next admission was [redacted] 1963; patient was uremic and required dialysis. She has remained oliguric. Urine protein 1 to 2+.

Albumin	3.6 gm%	Globulin	2.8 gm%
Cholesterol	260 mg%	ASO =	50 T.U.

24 hour urine protein: 1.0 gm.

10. Patient [redacted].

On [redacted] 1959, this 19 year old girl was admitted to the medical service with a 2 month history of generalized swelling. There was no previous history of renal disease (had a negative urine protein in September 1959) nor of symptoms relating to the genitourinary system. Past history and family history were not remarkable. She delivered her first child (normal) in

September 1959.

Physical Examination: BP 120/80; aside from generalized anasarca, the examination was not remarkable.

Laboratory Data: Urine 4+ protein; many lipoid bodies; no azotemia; LE prep neg; albumin 1.4 gm% and globulin 2.5 gm%.

24 hour urine protein: 4.7 gm.

Started on Prednisone 80 mg daily and continued for 14 days without response. Increased to 100 mg per day for 10 days; this was accompanied by loss of edema and a rather generalized furunculosis. Urine protein decreased but was still 1 - 2+ reaction; she was discharged on intermittent therapy 29 February 1960.

Renal Clinic: She did not keep appointments; finally returned [redacted] 1960; had anasarca; BP 120/80; 4+ urine protein; hypoalbuminemic, but refused admission.

[redacted] 1960 started intermittent Prednisone, 100 mg daily X 3 days weekly; urine protein slowly fell and was trace reaction by October 1961. She became pregnant in November 1961. Urines negative for protein from November 1961; steroids continued through pregnancy. Occasional urines showed trace protein until June 1962. Since then all urine negative; delivery normal with normal child [redacted] 1962.

Renal Biopsy on [redacted] 1962.

Steroids discontinued [redacted] 1963. BP normal; urine sediment negative; BUN 12 mg%.

II. Patient [redacted].

On [redacted] 1962 this 19 year old [redacted] boy was admitted for the first time to [redacted]. He complained of swelling of his face, abdomen, and legs that began nine days prior to admission. He denied dysuria, flank pain, fever, sore throat, shortness of breath and headache. Three weeks before this admission he was treated by a LMD for a penile "drip" with 2 injections of penicillin. There had been no other illness of any type within the past 18 months.

In August 1960, he was seen in EOR complaining of CVA pain. Examination was negative. An urinalysis revealed a specific gravity of 1.025, a negative protein and a negative sediment. He was afebrile. Nevertheless, diagnosis of acute pyelonephritis was made and he was sent to Urology Clinic where on [redacted] an IVP and bilateral retrogrades were done. Neither disclosed abnormality. There was no history of renal disease in his family.

Physical Examination: BP 130/80; fundi negative; heart not enlarged; 2+ pretibial and sacral edema. There was abdominal shifting dullness.

Laboratory Data: Urinalysis 4+ proteins; many hyaline, granular and waxy casts; many lipoid bodies and WBC; few RBC; a random urine with a 1+ protein had specific gravity of 1.020. BUN 35 mg%; creatinine 2.2 mg%; LE preg neg.; ASO = 166 T.U.

	[redacted]	[redacted]	[redacted]	[redacted]
Albumin (gms%)	1.6	1.8	1.7	1.4
Globulin (gms%)	3.1	1.9	3.9	2.1
Cholesterol (mg%)	540		640	

Renal Biopsy on [redacted] 1962.

24 hour urine protein(gms/24 hours)

[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
10.2	13.5	16.5	12.8	9.1
[redacted]	[redacted]	[redacted]	[redacted]	
9.5	11.0	6.4	8.4	

Prednisone, 100 mg per day started [redacted] and continued through [redacted]. Earlier he complained of post-prandial epigastric pain, and for the first time told of having this type of pain for over a year. His stools became positive for occult blood; the pain was controlled with a modified ulcer regimen while on steroids.

During the administration of steroids, he lost his edema (223 to 187 lbs.). No significant change in urine protein. Because of his peptic ulcer symptoms, intermittent steroid therapy was not given.

The patient was admitted [redacted] 1962 for a second 15 day steroid treatment. Again, there was no response in urine protein excretion.

From July to October 1962 diastolic blood pressures of from 90 to 100 mm were noted in the clinic. He was not taking steroids and was edematous.

On [redacted] 1963 he was admitted in profound renal failure and expired the second day.

12. Patient [redacted].

The patient, a 13 year old [redacted] boy was admitted [redacted] 1963 with the complaint of facial swelling of about 10 days duration. The history, as obtained from the patient and the patient's mother, is probably not reliable. Nevertheless, for 3 weeks prior to admission, the mother noted that the patient was less inclined to play than usual, although there were no specific complaints until the week before admission when he developed a non-productive cough. This cough was not associated with fever or sore throat. Likewise there was no history of sore throat, fever or other infections within the recent past. All genitourinary tract symptoms were denied.

Past History: He had repeated sore throats since early childhood, the last in August 1961 at which time he was treated with penicillin.

Family History: Maternal uncle died at age 5 years of an illness that began with facial swelling

Physical Examination: Temperature 98.8°; fundi were normal; BP 135/95; chest clear; heart not enlarged; no CVA tenderness. There was moderate generalized edema, with periorbital edema.

Laboratory Data: Urinalysis 4+ protein; many lipoid bodies; many RBC, many granular hyaline and waxy casts. Specific gravity 1.010-1.015 on random urines. BUN 10 mg%; creatinine 0.8 mg% on admission.

	[redacted]		[redacted]	
Albumin	2.3	gm%	1.8	gm% PSP 45% 30 min.
Globulin	2.4	gm%	0.5	gm%
Cholesterol	347	mg%	413	mg%

	[redacted]	[redacted]	[redacted]	
ASO =	166	250	625	Sustained

[redacted]

BUN 32 mg%

Creatinine 1.1 mg%

24 hour urine protein(gms/24 hours)

[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
5.4	3.9	3.9	3.4	3.7

Renal Biopsy done [redacted] 1963.

He was treated with Prednisone 50 mg daily from [redacted] through [redacted] 1963 with no apparent response. He was re-treated with 80 mg from [redacted] through [redacted] 1963, again with no response. During steroid therapy, his diastolic BP ranged from 100 to 115 mm Hg. He returned to normotensive levels when daily administration stopped. Intermittent therapy, 80 mg daily X 3 days weekly, was begun on [redacted] 1963. His BUN was 23 mg% at the time of discharge on [redacted].

He failed to return to clinic and probably did not take the intermittent steroid therapy. He returned for admission [redacted] 1964 with much the same findings as noted above.

13. Patient [redacted]

Third admission to [redacted] for this 24 year old [redacted] man began on [redacted] 1963. He complained of facial and leg edema of only 3 days duration. There were no other symptoms. When he was 8 years old he had the nephrotic syndrome which, over several months,cleared spontaneously (old chart available from T.C.). He and his mother maintained that he had had no edema since his nephrotic episode in childhood. He had had no medical follow-up after that illness, however.

In November 1962 he had his first and second admissions to [redacted] for what ultimately was treatment (by clipping) of a berry aneurysm. During these admissions BP's ranged from 134/70 to 130/110. Several urines all gave positive tests for protein (4+ to trace). Several BUN's were between 10 and 16 mg%. No mention of edema was made in the charts.

Physical Examination: BP 156/100; fundi negative; heart not enlarged. There was moderate generalized edema.

Laboratory Data: Urinalysis 4+ protein, many lipoid bodies with casts with lipid inclusions; no RBC.

BUN	11 mg%	Creatinine 1.0 mg%
Albumin	1.6 gm%	ASO = 100 T.U.
Globulin	2.5 gm%	PSP 84% in 2 hours
Cholesterol	640 mg%	

Renal Biopsy was done on [redacted] 1963.

Only one 24 hour urine protein of 3.5 gms was obtained.

The patient left the hospital [redacted] after receiving only 6 days of 100 mg daily Prednisone. This treatment appeared to have no effect.

He returned to the Renal Clinic on [redacted] 1963 and at that time was started on intermittent steroid therapy (75 mg daily X 3 days weekly).

On [redacted] 1963, he was readmitted with pneumococcal pneumonia and without apparent change in his nephrotic state. He became edema free in about 10 days as intermittent therapy was continued but he showed no change in protein excretion (about 4.0 gms per 24 hours). He left [redacted] on [redacted] 1963.

He returned for admission on [redacted] 1963. He may have taken some steroids between his previous [redacted] discharge and [redacted], but the amount is open to question. He returned because of productive cough and shortness of breath that began about a week prior to admission. At least one consultant suspected multiple pulmonary emboli. His pulmonary findings subsided during the first week. He was started 100 mg daily Prednisone [redacted] 1963. This was continued until [redacted] 1963. Intermittent steroids were begun [redacted] 1963. On [redacted] he had spontaneous thrombosis of his left sub-clavian vein. Heparin was begun and acute symptoms subsided in several days. During this hospitalization, his BUN ranged from 15 to 20 mg% and creatinine from 1.0 to 1.6 mg%. Massive proteinuria occurred (13.6 to 8.5 gms/24 hours), and he remained mildly hypertensive. Despite little change in serum albumin concentration, (1.6 - 2.0 gm%) he became free of edema. He left [redacted], [redacted] 1963.

TABLE I

1. Classification of histologic lesions.

	Light M	EM
a)	Minimal	Foot Process fusion
b)	Proliferation PAS can show apparent BMT	a) + Proliferation of endothelial and/or mesangial cells
c)	Basement membrane thickening - Particularly of peripheral capillaries	a) + Basement membrane thickened or apparently thickened by new pathologic material
d)	Lobulation with proliferation and Basement membrane thickening. Extra-capillary proliferation (Crescents).	a) + More pronounced representations of b) and c)
e)	Sclerosing hyalinization usually include glomerucli as in d) also	d) + May show advanced axial or mesangial proliferation - may see collagen within the glomerulus.

Response to Steroid Therapy

Type:

1. Complete remission - no proteinuria; normal urinary sediment.

2. Significant reduction in proteinuria to less than 3.5 gms per day.

3. Reduction in proteinuria with increase in serum albumin and/or loss of edema and/or reduction in BUN.

4. No response.

Definitions of Terms Used in this Report:

1. Continuous steroid therapy - Initial, high dose therapy given in divided doses daily.

2. Intermittent steroid therapy - usually long term therapy - large dose given for three consecutive days per week. No therapy other four days.

3. Chronic continuous - Modest doses given for long periods every day.

Survival Rates - Best Data are in Children Under 10 Years of Age :

1. Varies from 10 to 50 +%. Data are difficult to interpret. Need statements as to specific 5 and 10 year survival.

2. Perhaps regardless of age, at least 20% dead in 10 years.

3. Riley's study (Reference 54) discloses at least a 15% increase in survival in children as a result of steroid therapy.

Clinical Findings Pointing to a Less Favorable Prognosis:

1. Age of patient - favorable prognosis decreases with age (according to most authors)

2. Presence of hypertension or azotemia.

3. Presence of hematuria - minor hematuria appears insignificant. RBC casts point towards a poor prognosis.

4. The longer the period between onset of nephrosis and the start of therapy, the more guarded the prognosis.

   a) A previous episode of nephrosis with spontaneous or therapeutic remission probably should be considered as ominous with respect to prognosis.

Pat.	Sex Age	Duration Prior to Admission	Microscopic Lesion		Complications	Steroid Therapy	Response
			Light	Electron			
1. [redacted]	M 45	2 weeks	Minimal change Slight Prolif.	----------	BP 140/90 BUN 26	Adequate	Type I - Since has many casts and RBC in sed.
2. [redacted]	F 15	3 days	Mesangial Prolif. BMT	BMT † Mesangial Proliferation	None	Adequate and continues	Type 4 -
3. [redacted]	F 52	3 months	Proliferative Focal BMT	----------	BP 170/100 BUN 28 RBC+	Adequate and continues	Type I - relapsed off steroids
4. [redacted]	F 57	2 years	Mild exudate Mesangial Prolif.	----------	BP 140/90 BUN 28	Adequate and continues	May be Type I - Has trace proteinuria now
5. [redacted]	M 31	6 weeks	Prolif. Rare glomerular adhesion	----------	None	Adequate	Type I - relapsed off steroids
6. [redacted]	M 15	1 week	Mild Prolif. BMT	BMT	BUN 68	Adequate	Type I
7. [redacted]	M 17	3 weeks	Prolif., BMT Crescents, Occ. Sclerosed Glom. Exudated	----------	BUN 32 RBC+ BP 170/90	Adequate	Type 3 - died in dry uremia
8. [redacted]	F 47	4 months	Proliferative	Mild Prolif.	BP 180/100	Not treated	Type 4 - As of 15 months
9. [redacted]	F 35	7 weeks	BMT Early Lob. Sclerosis	----------	BP 150/98 BUN 25	Not treated	Type 3- Oliguric uremia requiring dialysis within 10 months.
10. [redacted]	F 19	2 months	Mild BMT (During complete remission)	BMT (or deposits) Still has foot process fusion	None	Adequate	Type I - Required over 12 months for urine to become protein free
11. [redacted]	M 19	9 days	Proliferative c̄ crescents	Mesangial Prolif.	BUN 35 RBC +	No intermit. therapy	Type 4 - died in wet uremia at 10 months
12. [redacted]	M 13	10 days	Sclerosing Lob. c crescents	----------	BP 135/95 RBC+	Adequate thus far	Type 4 - at 6 months
13. [redacted]	M 24	3 days	Mesangial Prolif. Focal Sclerosis	Marked mesangial Proliferation	BP 156/100	? Adequate	Type 3 - at 10 months

* Refers to hypertension, azotemia, hematuria present at start of therapy

† BMT = Basement Membrane Thickening

TABLE III

Complications of Steroid Therapy

PMH Series II Patients

1. Infection - 3
   a) Skin - 1
   b) Pulmonary (not TBC) - 2
2. Hypertension - 1
3. Moon-faces - 2
4. GI bleeding - 1
5. Thrombosis - ? 1
6. Mental changes - 0

TABLE IV

Spontaneous Remissions in Adult Nephrotics - Type I Response

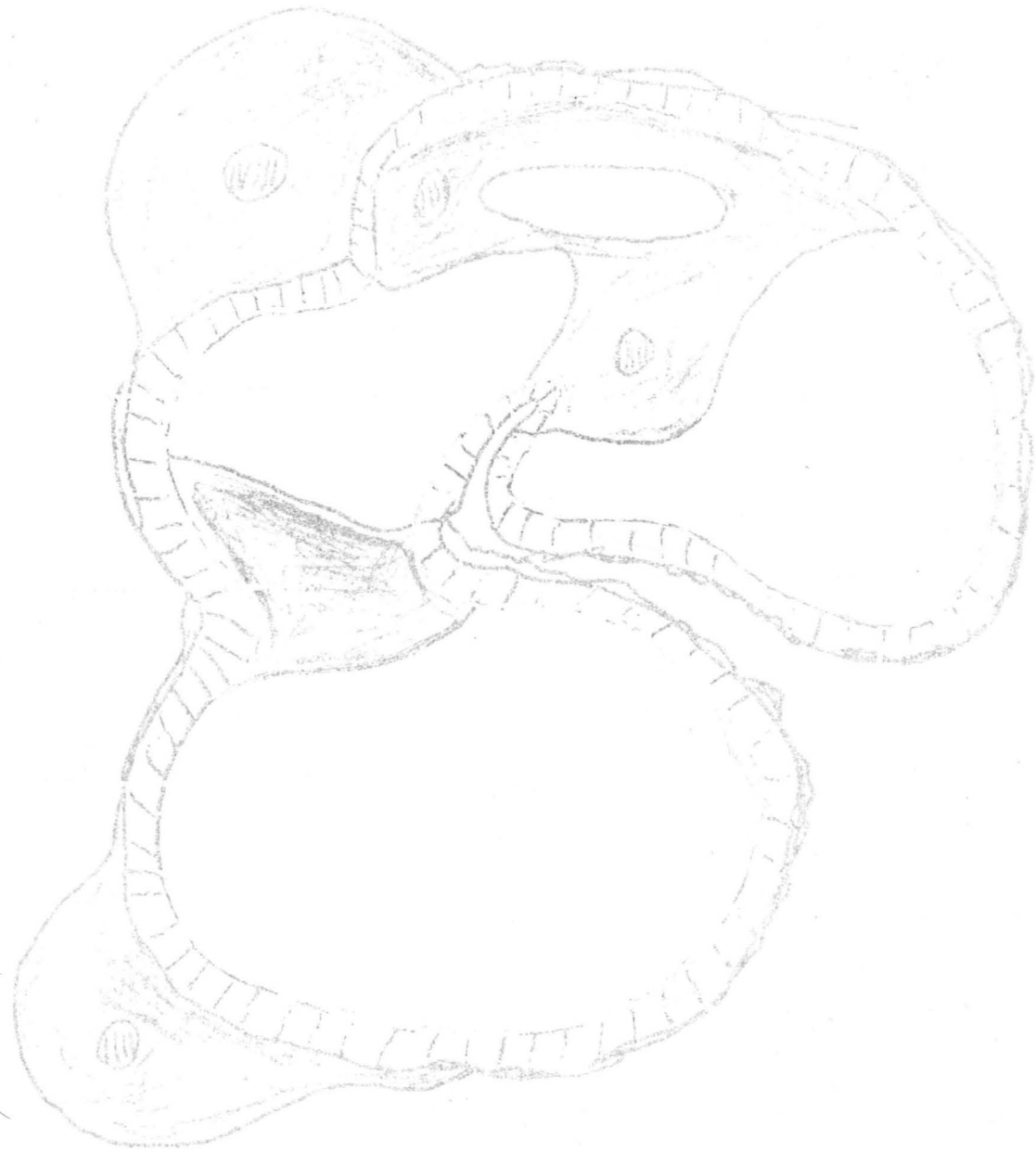
Reference No.	Responses/Total Patients
62	0/14
63	5/40
64	3/12
65	1/26
75	6/42
Total	15/134
% Responses	11%
PMH Series	0/2

TABLE V

Results of Steroid Therapy in Adults

Type I Responses

Reference No.	Responses/Total Patients
65	7/54
66	3/9
68	4/25
69	2/8
70	3/21
71	4/13
72	11/32
73	7/33
75	7/42
Total	48/237
% Response	20%
PMH Series	5/13
% Response	37%



1. Epithelial Cell
2. Endothelial Cell
3. Capillary Lumen
4. Epithelial Foot Processes
5. Basement Membrane

REFERENCES

1. Mueller, C.B.: Structure of the renal glomerulus. Am. Heart J. 55:304, 1958.

2. Rhodin, J.: Electron microscopy of the kidney. Am. J. Med. 24:661, 1958.

Two reviews of the microanatomy of the glomerulus.

3. Caulfield, James B.: Application of the electron microscope to renal diseases. New E.J.M. 270:186, 1964

A good review article dealing with electron microscopy of the kidney.

4. Kurtz, S.M.: Fine structure of lamina densa. Lab. Invest. 10:1189, 1961.

A review of the anatomy and pathology of the basement membrane of the glomerular capillary.

In animals with experimental nephrosis, has been build-up of basement membrane on the epithelial side and therefore concludes that basement membrane is produced by these cells.

However, most authors believe basement membrane is a product of the endothelial and perhaps mesangial cells.

5. McGregor, L.: The cytological changes occurring in the glomerulus of clinical glomerulonephritis. Am. J. Path. 5:559, 1929.

Historically of interest because this author noted glomerular changes in autopsy material from nephrotics which today seem quite modern.

1. Endothelial proliferation an important part of the pathologic lesion.

2. Crescents derive from epithelial proliferation.

3. Noted hyaline fibers between the capillaries thought to be forerunners of glomerular hyalinization (mesangial or axial stalk proliferation?).

6. Bell, E.T.: Lipoid Nephrosis. Am. J. Path. 5:587, 1929.

An early paper defending lipoid nephrosis as a definite entity.

7. Bell, E.T.: A clinical and pathological study of subacute and chronic glomerulonephritis including lipoid nephrosis. Am. J. Path. 14:691, 1938.

8. Bell, E.T.: Renal Diseases. Philadelphia, Lea and Febiger Co., 1950. pp 206-228.

By 1938 the author characterized the morphology of lipoid nephrosis as follows:

A. Chronic proliferative

B. Mostly membranous but to some extent proliferative

C. Normal glomerulus (seen in children under 12 years of age) or pure membranous.

Thus the term membranous nephritis was born.

Note: Most authors that use the term believe that lipoid nephrosis does not have a light

microscopic lesion. Furthermore, most authors today restrict the term "membranous" to those cases that have basement membrane thickening.

There is however, considerable confusion in the use of both of these terms.

9. McCallum, W.G.: Glomerular changes in nephritis. Bull. Johns Hopkins Hosp. 55:416, 1934.

By a special method of distending the glomerular capillary loops (Kerosene injected into the renal artery) and by using thin, specially stained sections and of course light microscopy, the author was able to satisfy himself that a mesangial tissue did indeed exist. It appeared most marked in the centro-lobular region of the glomerulus. It was found to proliferate in a variety of disease states.

10. Ellis, A.: Natural history of Bright's disease. Lancet 1:1, 34, 72, 1942.

Only 5 of 145 patients with Type II disease (nephrosis)recovered.

Admitting that histologic study early in the course of nephrosis is lacking (no biopsies), Ellis describes a progressive lesion in his Type II patients. It begins as a slight proliferation with a tendency for lobulation. With time, the proliferation and lobulation become more pronounced and ultimately there is a hyalinization of glomeruli.

11. Jones, D.B.: Glomerulonephritis. Am. J. Path. 29:33, 1953.

Using light microscopy, special stains, and thin (2μ) sections, this author believes the basic lesion in "lipoid nephrosis" is an increase in the number of mesangial cells.

12. Allen, A.C.: The clinicopathologic meaning of the nephrotic syndrome. Am. J. Med. 18:277, 1955.

13. Allen, A.C.: The Kidney. Medical and Surgical Diseases. 2nd Edition, New York, 1962, Grune and Stratton. pp. 246-285.

This author believes that all cases of nephrosis have a membranous glomerular lesion that can be seen by ordinary sections with light microscopy without special stains (including cases with so called lipoid nephrosis). He also described advanced forms of the disease as morphologically representing lobular glomerulonephritis and finally a hyalinization of glomeruli.

14. Ehrich, W.E.: Glomerular nephritis and lipid nephrosis; Identities and mechanisms. J. Chronic Dis. 5:14, 1957.

An article that reaches back to the early 1900's classifying "Lipoid Nephrosis" as a "tubular storage" nephrosis that is not a progressive illness.

15. Jones, D.B.: Nephrotic glomerulonephritis. Am. J. Path. 33:313, 1957.

Light microscopic study using thin sections (1-3μ). Of most interest, finds that the minimal lesion in children consists of a proliferation of mesangial cells. Moderate lesions are an extension of this proliferation together with some scarring with basement membrane thickening.

16. Grishman, E. and Churg, J.: Acute glomerulonephritis: A histopathological study by means of thin sections. Am. J. Path. 33:993, 1957.

By means of 0.5μ sections of glomeruli, the proliferation within a mesangial space was noted in acute glomerulonephritis by light microscopy.

17. Pak Poy, R.K.F.: Electron microscopy of the mammalian renal glomerulus. The problems of intercapillary tissue and the capillary loop basement membrane. Am. J. Path. 34: 885, 1958.

Electron microscopy study of rat and human glomeruli convinced the author of the presence of a third cell type (mesangial cell). He surmized that this cell may have fibrioblastic properties.

18. Robertson, D.M. and More, R.H.: Structure of glomerular axial region is normal and nephritic rabbits. Arch. Path. 72:331, 1961.

From studies in rabbits with experimental serum sickness nephritis, these authors claim that the cytoplasm of endothelial cells is PAS negative, whereas, that of axial cells (mesangial cells) is PAS positive.

19. Latta, H., Maunsbach, A.B., and Madden, S.C.: The centrolobular region of the renal glomerulus studied by electron microscopy. J. Ultra Struct. Res. 4:455, 1960.

Study by EM of rat glomeruli revealed what the authors interpreted as a centrolobular region with intercapillary cells or mesangial cells.

20. Farquhar, M.G., Vernier, R.L. and Good, R.A.: An electron microscopic study of the glomerulus in nephrosis glomerulonephritis and lupus erythematosus. J. Exp. Med. 106:649, 1957.

1. All cases of nephrosis had foot process fusion.
2. Endothelial cells were frequently swollen.
3. With one and two above, light microscopy appeared essentially normal.
4. As light microscopy lesions became apparent, basement membrane thickening and endothelial proliferation were seen with EM.

21. Farquhar, M.G.: Ultrastructure of the nephron disclosed by electron microscopy. A review of normal and pathologic glomerular ultrastructure. Proc. 10th Ann. Conf. on Nephrotic Syndrome. Ed. J. Metcoff, 1958, p. 2.

At this time denied the presence of the mesangial cell, however has since "discovered" the third cell. Adult basement membrane thickness 2700 to 3000 Å.

Four important points:

1. Fusion of the foot processes present in all forms of nephrosis.
2. In children with nephrosis there is a nodular thickening of basement membrane.
3. In nephrotic adults there is generalized basement membrane thickening by the addition of an irregular layer of dense heterogeneous material on the epithelial side of membrane.
4. As shown by re-biopsy in remission, the foot process lesion is completely reversible (see our Case 10).

22. Kark, R.M., Pirani, C.L., Pollak, V.E., Muehirche, R.C. and Blainey, J.D.: The nephrotic syndrome in adults: A common disorder with many causes. Ann. Int. Med. 49:751, 1958.

A histologic (light microscopy) classification of nephrosis.

Under glomerulonephritis:

1. Membranous
2. Mixed
3. Proliferative
4. Lipoid (essentially normal glomeruli)

23. Parrish, A.E., Watt, M.E. and Howe, J.S.: Membranous glomerulonephritis. Arch. Int. Med. 100; 620, 1957.

A light microscopic study of biopsies from nine adult nephrotics.

1. Two patients progressed from membranous to lobular lesions.
2. One patient progressed from a lesion of acute glomerulonephritis to one of membranous nephritis but despite this recovered with steroid therapy.

24. Galán, E. and Masó, C.: Needle biopsy in children with nephrosis. At study of glomerular damage and effect of adrenal steroids. Pediatrics 20:610, 1957.

A light microscopic study in 20 nephrotic children with 36 biopsies. Thickening of the basement membrane was the most common lesion found. Six patients were re-biopsied; 5 showed histologic improvement after therapy.

25. Churg, J., Mautner, W., Grishman, E., and Eisner, G.M.: Structure of glomerular capillaries in proteinuria. Arch. Int. Med. 109:97, 1962.

A study including both light and electron microscopy.

Two basic lesions:

1. Fusion of foot processes reversible.
2. Membranous changes, especially thickening (occurring more often in adults) may not be reversible.

26. Joekes, A.M. Heptinstall, R.H. and Porter, K.A.: The nephrotic syndrome. Quart. J. Med. N.S. 27:495, 1958.

Of 20 adult nephrotic patients, 8 were said to have Ellis type 2 nephritis. In these the most constant pathology was basement membrane thickening. There were no type I responses in these 8 patients.

Presumably as a personal preference of Heptinstall, three biopsies were classed as "focal", probably would be lobular nephritis in most other series.

27. Adams, D.A.: Pathophysiology of nephrotic syndrome. Arch. Int. Med. 106:117, 1960.

A good review paper with an excellent bibliography.

Membranous glomerulonephritis is the commonest pathology in the adult nephrotic.

28. Spiro, D.: The structural basis of proteinuria in man. Am. J. Path. 35:47, 1959.

According to this author the basement membrane is normally only 1000 Å thick.

In nephrosis claims to have seen on EM actual breaks in the basement membrane of from several 100 to 1000 Å in extent. At these points, the epithelial and endothelial cells appear to be touching.

This point of view is not generally accepted. Some regard the so-called breaks as areas of antigen-antibody aggregation within the basement membrane.

29. Movat, H.Z.: In Proceedings of 11th Annual Conference on Nephrotic Syndrome. Ed. J. Metcoff, Natl. Kid. Dis. Found. New York, 1959, p. 244.

This author specifically takes issue with Spiro. Believes that so-called holes are really deposits of protein between the basement membrane and the epithelial cells.

30. Movat, H.Z. and McGregor, D.D.: The fine structure of the glomerulus in membranous glomerulonephritis (lipoid nephrosis) in adults. Am. J. Clin. Path. 32:109, 1959.

Stress that both light and electron microscopic studies of renal biopsies in nephrosis are needed for adequate evaluation. This is a report of observations in two adult nephrotics.

They conclude that EM changes of the basement membrane are a result of increased permeability of the membrane (a true lesion of the membrane can not necessarily be seen by EM) and that the deposits on the epithelial side of the basement membrane are protein material that has transgressed the basement membrane.

31. Movat, H.Z., McGregor, D.D. and Steiner, J.W.; Studies of nephrotoxic nephritis. II. The fine structure of the glomerulus in acute nephrotic nephritis of dogs. Am.J. Clin. Path. 36:306, 1961.

An interesting morphological study in dogs after the administration of nephrotoxic serum. Proteinuria begins within hours.

Results suggest first change is endothelial swelling followed by proliferation of these cells together with fusion of foot processes. Eventually there is focal thickening of basement membrane. Finally there is a proteinaceous deposit between the membrane and epithelial cells.

32. Movat, H.Z., Stenier, J.W., and Slater, R.J.: The fine structure of the glomerulus in Bright's disease: A clinicopathologic study. Ciba Foundation Symposium on Renal Biopsy. Wolstenholme, G.E.W. and Cameron, M.P. eds. London, 1961, J. and A. Churchill, p. 103.

Refers to the earliest lesion of nephrosis as Quellung, i.e., swelling with imbibition and irregular rarefaction. A guess the presence and alteration of axial cells (mesangial cells). Believes that lipoid nephrosis and membranous nephritis are two different diseases. The latter may not be reversible.

33. Vernier, R.L., Worthen, H.G., and Good, R.A.: Pathology of nephrotic syndrome. J. Pediat. 58:620, 1961.

This paper encompasses 73 biopsies from 54 nephrotic children.

Differences between biopsies obtained early (less than 6 months) and later (6 months or longer) in the course of the disease suggest that the glomerular lesions seen in nephrosis are progressive. This is true even in those patients who eventually recover.

These authors believe that steroid therapy may, in addition to stopping proteinuria, prevent progression of the glomerular lesion.

The severity of the foot process lesion is related to the degree of proteinuria, and the lesion disappears in both children and adults with successful treatment. (See our case #10).

34. Vernier, R.L.: Ultrastructure of the glomerulus and changes in fine structure associated with increased permeability of the glomerulus to protein. Ciba Foundation Symposium on Renal Biopsy, ed. Wolstenholme, G.E.W. and Cameron, M.P., London, 1961. J.and A. Churchill. p. 4.

An excellent review of the electron microscopy of the glomerulus in Nephrosis.

35. Friaschi, E., Andres, G., Gracomelli, F., and Naccarto, R.: Renal histopathology in para-nephritic nephrotic syndrome: Optical and electron microscopic studies of kidney biopsies. Sc. Med. Ital. 7:639, 1959.

This is one of the outstanding papers on the histopathology of primary nephrosis. Photomicrographs are excellent; many are in color. Both light and electron microscopy.

Histopathologic Classification:

1. Proliferative
   - (a) 1. Epithelial
     2. Mesangial
     3. Endothelial
   - (b) Crescent formation
2. Membranous - often effects only a portion of the capillaries.
3. Lobular - sharper delineation of a single glomerular lobule with simplification of it. Capillary structure. Frequently a PAS positive stalk contains proliferating mesangial cells.
4. Glomerular atrophy - Diminution in number of all cell types.

These authors believe that so-called lipoid nephrosis probably always has a light microscopic lesion, and that it always has an electron microscopic lesion.

Lesions of nephrosis are progressive with time. The most common lesion in their series of 9 children and 31 adults was a mixed proliferative-membranous change.

36. Habib, R., Michielsen, P., De Montera, E., Hinglais, N., Galle, P., and Hamburger, J.: Clinical, microscopic and electron microscopic data in the nephrotic syndrome of unknown origin. Ciba Foundation Symposium on Renal Biopsy. ed. Wolstenholme, G.E.W., and Cameron, M.P., London 1961. J. and A. Churchill. p. 70.

Perhaps the best review of the histopathology of nephrosis in children and adults available at this time.

37. Becher, E.L.: The nephrotic syndrome in adults. Bull. New York Acad. Med. 38:3, 1962.

A good review of clinical and pathological considerations. Points out that there is considerable overlap if the Ellis Type I and II Classification is adhered to in the strictest sense.

38. Heymann, W.; Pathogenesis of the nephrotic syndrome: Considerations based on Clinical and Experimental Studies. Pediatrics 58:609, 1961.

These authors favor the "Unitarian Concept" of the nephrotic syndrome; e.g., not lipoid and nephritic, but rather both are the same disease although perhaps quantitatively different.

They stress that a single stimulus may morphologically effect the glomerulus sequentially in several different ways. There appears to be only a limited number of morphological responses of the glomerulus to a variety of stimuli, however.

39. Pollak, V.E., Folli, G., Pirani, C.L., Reid, R.T.W. and Muehrche, R.C.: On the electron-microscopic recognition and clinical care of lipoid nephrosis in adults. J. Clin. Invest. 37:922, 1958. (abstract)

Lipoid nephrosis is a distinct clinical entity. Successful steroid therapy results in disappearance of the foot process lesion (see our case 10).

40. Lawrence, J.R., Pollak, V.E., Pirani, C.L., and Kark, R.M.: Histologic and clinical evidence of post-streptococcal glomerulonephritis in patients with the nephrotic syndrome. Medicine 42:1, 1963.

On what are most certainly very doubtful grounds, these authors believe they can morphologically identify those cases of nephrosis resulting from a hyperimmune post-streptococcal state. Most interesting is the observation that using these criteria only 10-11% of patients with primary or idiopathic nephrosis would fit into this category. 90% then are truly idiopathic.

41. Baldwin, D.S. and McCluskey, R.T.: Natural history of the nephrotic syndrome in glomerulonephritis . Postgrad. Med. 26:603, 1959.

Here one of the proponents of streptococcal nephritic producing chronic disease concludes on the basis of clinical and biopsy data that nephrosis is not a sequela of classic acute glomerulonephritis.

42. Berman, L.B. and Schreiner, G.E.: Clinical and histologic spectrum of the nephrotic syndrome. Am. J. Med. 24:249, 1958.

A good review paper that is superseded by reference 43.

43. Schreiner, G.E.: The nephrotic syndrome, in Diseases of the Kidney. Ed. Strauss, M.B., and Welt, L.G. Little, Brown and Co. Boston, 1963. pp 335-444.

Despite the fact that this author believes, on the basis of faith primarily, that most nephrosis is post-streptococcal in origin, this is a good review article.

Of 18 patients with mixed proliferative membranous changes, 3 had a type I response (17%).

Recommended treatment: 60 mg Prednisone daily for 16 days followed by intermittent therapy for 2 months.

Only one patient failed to respond to 60 mg who later responded to a higher dose. Has patients who failed to respond to steroids that did respond to nitrogen mustard.

Albumin injection test for glomerular permeability. Patients excreting only 10-20% of the injected dose in 24 hours generally have a good response to steroid therapy.

44. Lange, K., Slobody, L., and Strang, R.: Treatment of nephrotic syndrome with interrupted ACTH or oral cortisone therapy. Proc. Soc. Exp. Biol. and Med. 82:315, 1953.

This was the start of intermittent therapy which has made the effective prolonged treatment of nephrosis possible. Surprisingly, this concept has not been fully exploited in other disease states treated with steroids (such as S.L.E. and asthma).

45. Lange, K., Strang, R., Slobody, L.B., Wenk, M.A.: The treatment of the nephrotic syndrome with steroids in children and adults. Arch. Int. Med. 99:760, 1957.

46. Lange, K., Wasserman, E. and Slobody, L.B.: Prolonged intermittent steroid therapy for nephrosis in children and adults. J.A.M.A. 168:377, 1958.

Lange still advocates initial therapy with ACTH for 12 to 21 days (used + 30 days occasionally). At this time advocated intermittent cortisone therapy (3 or 400 mg/day for three consecutive days/week) to continue for one year.

In this series of 46 patients 12.8 deaths were expected without treatment. Only one death occurred.

47. Armstrong, S.H. and Kirshner, D.S.: Current status of steroid therapy in chronic glomerulonephritis in adult. Unnatural history of Bright's disease. Am. J. Med. 29:377, 1960.

Apparently, this editorial resulted in many clinicians giving up steroid therapy in adult nephrotics. Armstrong stressed the high incidence of induced Cushing's syndrome, but was using a continuous dosage plan.

Most interesting, noted that 40% of Negro patients dead in one year; 90% in 4 years.

48. Goodman, H.C. and Baxter, J.H.: Adrenocorticotropin and corticoid treatment of the nephrotic syndrome. Metabolism, 7:40, 1958.

An excellent review of ACTH and steroid therapy in primary (idiopathic) nephrosis.

49. Luetocher, J.A., Demins, Q.B. and Piel, C.F.: Advances in the management of the nephrotic state. J.A.M.A. 153:1236, 1953.

In this rather early report on the use of ACTH and steroids, the authors conclude that both are probably effective, especially in children. Correctly concluded that studies to prove their usefulness would be hard to obtain.

50. Squire, J.R., Blainey, J.D. and Hardwicke, J.: The nephrotic syndrome. Brit. Med. Bull. 13:43, 1957.

Prognosis must be guarded when hematuria, decreased creatinine clearance, and/or hypertension are present or develop during steroid therapy.

51. Derow, H.A.: The nephrotic syndrome. N.E.J.M. 258:77 and 124, 1958.

A short review of nephrosis. Stresses the importance of the early use of steroids as well as adequate dosage.

52. Heymann, W., and Hunter, J.L.P.: Importance of early treatment of the nephrotic syndrome. J.A.M.A. 175:563, 1961.

This study in 63 nephrotic children strongly suggest that remission with steroid therapy

is linked with the period of disease before therapy begins. The shorter the period, the better the prognosis.

Treated within first 3 months - 86% remission. Treated after first 3 months - 52% remission.

(This suggests that even the childhood lesion is progressive).

53. Dodge, W.F., Daeschner, C.W. Jr., Rosenberg, H.S., Brennan, M.B., Travis, L.B. and Hoppe, H.C.: Percutaneous renal biopsy in children. III Nephrotic syndrome. Pediat. 30:459, 1962.

Deals with nephrotic syndrome in children.

The most important factor with regard to response to therapy is the duration of the disease prior to onset of steroid therapy. Although most patients that respond do so in the first three weeks of therapy; considerable numbers of patients will respond after one to three months of therapy.

54. Riley, C.M. and Scaglione, P.R.: Current management of nephrosis: statistical evaluation and proposed approach to therapy. Pediatrics 23:561, 1959.

A retrospective statistical study of over 750 childhood nephrotics collected from 18 Northeastern Clinics.

1946-1950 - Pre-Steroid, anti-microbial period - 4 years follow-up 60% alive.

1952-1957 - Steroid period - 75% alive at 4 years.

"Though not conclusive, the evidence strongly suggests that the improved survival of children with nephrosis is due.... to the increased, and more intensive use of adrenal-active hormones."

These authors suggest 40-60 mg Prednisone daily for 3-4 weeks followed by intermittent therapy. Believe that using intermittent therapy at outset might be satisfactory.

55. Arneil, G.C.; 164 Children with nephrosis. Lancet 2:1103, 1961.

Concerning 164 cases of nephrosis in children during the period 1929 to 1957. Of 164 patients, 102 were alive at time of writing. Total of 62 deaths (38%); of these 21.4% were a result infection. 18% of the deaths resulted from renal failure.

	1929-36-Pre-Sulfa Drugs	1937-45 Sulfa Drugs	1946-50 Antibiotics	1951-57 Steroids
Alive	64%	66%	62%	84%
Asymptomatic*	28%	32%	48%	48%
Dead	36%	34%	38%	16%
No. of Pts.	11	41	37	75

Abstract of Table 10
*Not clear that these all represent Type I Response
Concluded that steroids have made a most significant change in death rate.

56. Worthen, H.G., Michael, A.F., Veinier, R.L. and Good, R.A.: Late recurrence of the nephrotic syndrome. Am. J. of Dis. of Children. 103:794, 1962.

An interesting report of recurrence of the nephrotic syndrome in 5 children from 12 to to 45 months after an initial response to steroids. In all cases, these children with minimal glomerular lesions (3 biopsies) again responded to steroid therapy.

57. Folli, G., Pollak, V.E., Reid, R.T., Pirani, C.L., and Kark, R.M.: Electronmicroscopic studies of reversible glomerular lesions in adult nephrotic syndrome. Ann. Int. Med. 49:775, 1958.

A single case report where three biopsies were done, before during, and after steroid therapy. There was a Type I response.

Biopsy No.	Light	EM
1	Slight Proliferation	Fusion of Foot Processes
2	Normal	Same as 1
3	Normal	Normal

58. Powell, R.D., Spargo, B., and Arnold J.D.: Clinical and electron microscopic studies in patients with the nephrotic syndrome. J.A.M.A. 177:94, 1961

An interesting single case report of primary nephrosis in an adult with serial renal biopsies. The patient had normal BUN, normal BP, occasional RBC in urine sediment, negative LE preps. Responded twice to steroids; left with trace proteinuria.

Biopsy	Light	Electron
1. At start of therapy	Slight hyper-cellularity $\frac{-}{c}$ BMT.	(Not done)
2. During relapse	As above $\frac{-}{c}$ one crescent and periglomerular fibrosis	Endo. prolif. slight. Deposits on Ep. side of BM. Foot processe focally fused.
3. During remission	BMT only	No deposits. BM now thickened.

59. Silberman, I.A., and Adams, D.A.: The nephrotic syndrome and pregnancy. N.E.J.M. 267: 1286, 1962.

An interesting case report of nephrosis and pregnancy. There was no significant ill effects to mother or 2 offspring resulting from continuous "intermittent" steroid therapy for 58 months.

60. Barnett, H.L. and Eder, H.A.: The nephrotic syndrome. J. Chronic Dis. 5:108, 1957.

A mortality of over 50% is given for nephrotics below the age of 30 years (no significant difference between children and adults.) Over the age of 30 years the mortality is greater than 80%.

Concluded that childhood nephrosis is the same disease as adult nephrosis.

61. Bainess, L.A., Moll, G.H. and Janeway, C.A.: Nephrotic syndrome. I Natural history of the disease. Pediatrics 5:486, 1950.

A review of childhood nephrosis from 1926 to 1948.

Few if any patients recovered from nephritic nephrosis. About 50% of those with "lipoid nephrosis" recovered, but 10% of these were left with either some proteinuria and/or hypertension. Antibiotics significantly reduced mortality.

62. Rennie, J.B.: The edematous syndrome of nephritis with special reference to prognosis. Quart. J. Med. 16:21, 1947.

Concerning spontaneous remission rate in adult nephrotics: No adult remissions in 14 patients.

63. Roscoe, M.H.: The nephrotic syndrome. Quart. J. Med. 25:353, 1956.

Concerning complete remission in adults without steroids: 5 adults out of 40 had remissions (Type I).

64. Rosenheim, M.L. and Spencer, A.G.: Treatment of nephrotic syndrome with cation-exchange resins and high-protein low-sodium diet. Lancet 2: 313, 1956.

In adults, 3 out of 12 patients had a Type I remission without steroid therapy.

65. Johnson, J.R. and Reader, R.: Prognosis in the nephrotic syndrome: A review with particular reference to the adult and older child. Australasian Annals Med. 8:200, 1959.

26 adult patients with bed rest and diet therapy only yield one Type I response.

7 of 54 patients treated with steroids yielded a Type I response.

66. Goodman, H.C. and Baxter: Nephrotic syndrome: Clinical observations on therapy with prednisone and other steroids. J.A.M.A. 165:1798, 1957.

Nine adult nephrotics - 3 had a Type I response with steroids.

There appears to be no response difference between hydrocortisone and prednisone therapy (Luetscher at one time thought hydrocortisone superior.)

Microscopic hematuria and moderate renal insufficiency do not preclude a good response to steroid therapy.

67. Charlton, D., Latner, A.L., Platt, J.W., Smart, G.A., Thompson, R.B. and Walker, W.: Nephrotic syndrome. Observations of the effects of ACTH in 40 patients. Acta. Med. Scand. 161:1958.

Results of ACTH therapy. 40 patients - mostly children. Eight had Type I response.

68. Danowski, T.S., Mateer, F.M., and Puntereri, A.J.; ACTH or adrenacortical steroid therapy of proteinuria in adolescents and in adults. Am. J. Med. Sci. 237:545, 1959.

Although very difficult to tell from the data presented, it appears that 4 out of 25 adults had a Type I response to steroids.

69. Sharpe, A.R. Jr., and Unger, A.M.: The nephrotic syndrome. Renal biopsy findings in adults responding to prednisone. Arch. Int. Med. 104:684, 1959.

Study of 8 adult nephrotics. Two of 8 had Type I response to steroids.

Concluded that steroid response can occur without necessarily altering histopathology of glomerulus.

70. Blainey, J.D., Brewer, D.B., Hardwicke, J., and Soothill, J.F.: The nephrotic syndrome. Quart. J. Med. N.S. 29:235, 1960.

Concerning diagnosis, prognosis, and steroid therapy in adult nephrotics. (21 idiopathic).

Histologic Criteria

1. Membranous - all glomeruli effected. Only moderate increase in cellularity.

2. Proliferative - both epthelial and endothelial proliferation. Polys may be present as well as capillary thrombi together with adhesions to Bowmans capsule and crescent formation.

   (This in total is old "sub-acute" of Vohard and Fohr - Most authors today recognized a simple proliferative lesion ± adhesions or crescents - do not use term sub-acute).

3. Chronic - Fibrosis and hyalinization of many glomeruli with tubular atrophy and dilatation.

4. Minimal changes - glomeruli normal.

Response to Therapy (Doses of steroid as cortisone)

Concluded that steroids reduce mortality.

1. Membranous - 6 patients - 2 dead - 4 not improved. Age range 25 to 58 years. Dose 50 to 250 mg/day.

2. Proliferative - 6 patients - 2 rapid improvement - 2 slow improvement - 2 dead. Age range 23 to 58 years. Dose 150 to 300 mg/day. One patient on rebiopsy showed disappearance of crescents.

3. Chronic - 3 patients - 1 rapid improvement - 2 dead. Age range 14 to 15 years. Dose 20 to 100 mg/day.

4. Minimal changes - 6 patients - 4 rapid improvement - 2 slow. Ages 25 to 45 years. Dose 100 to 200 mg/day. One patient on rebiopsy had developed membranous changes.

   (Slow improvement means 3 to 8 months)

Note: Only 3 of 21 patients had Type I response

71. Port, R.S., Eckel, R.E.: Hormone therapy of the adult nephrotic syndrome of unknown etiology. J. Chron. Dis. 12:211, 1960.

A good report. Thirteen adult patients were treated with ACTH for 14 days followed by intermittent therapy for as long as one year.

Noted that as intermittent therapy is stopped, nephrosis usually returns, but is easily controlled by restarting therapy.

Four of 13 patients attained a Type I response.

72. Adams, D.A., Maxwell, M.H., and Bernstein, D.: Corticosteroid therapy of glomerulonephritis and the nephrotic syndrome: A review. J. Chron. Dis. 15:29, 1962.

An excellent review article. In the authors' series, 11 of 32 (34%) adults had a Type I response to steroids. Suggest that starting directly with intermittent therapy may be adequate.

73. Burch, R.R., Pearl, M.A., Sternberg, W.H.; A clinicopathological study of nephrotic syndrome. Ann. Int. Med. 56:54, 1962.

The study includes 33 adult nephrotics studied from 6 months to 5 years. Concluded that the response to steroids varied with the histologic picture of the renal biopsy. (No electron microscopy).

Histologic Classification:

Group		
1.	Membranous	10 patients
2.	Proliferative	5 patients
3.	Mixed	6 patients
4.	Sclerosing	6 patients
5.	Indeterminate (most glomeruli normal)	6 patients

Renal function usually normal except in Group 4. Best response to steroids (40 mg Prednisone daily X 4 weeks) was in Groups 2 and 5, but there were responses in all groups.

Group	Type I Response	
1.	1/6	
2.	3/4	Total Type I = 7/33 = 21%
3.	0	
4.	0	
5.	3/4	

These authors attributed 2 deaths in their series to steroid therapy, and therefore suggest treating only those nephrotics in histologic groups 2 and 5.

74. Pearl, M.A., Burch, R.R., Carvajal, E., McCracken, B.H., Woody, H.B. and Sternberg, W.H.: Nephrotic syndrome; a clinical and pathological study. Arch. Int. Med. 112:130, 1963.

Study includes 56 patients with primary nephrosis.

12 (9 children) of 40 treated patients had a Type I response (30%). There were 15 deaths in 56 patients (27%). Seven out of 8 patients with a sclerosing lesion died.

75. Nesson, H.R., Sproul, L.E.,Relman, A.S. and Schwartz, W.B.: Adrenal steroids in the treatment of idiopathic nephrotic syndrome in adults. Ann. Int. Med. 58:268, 1963.

A report of 42 adults with primary nephrosis (youngest 13 years)studied during 1953 through 1961. There were biopsies in 22 patients and autopsies in 2 other patients.

1. Urine became protein free while on steroids - 17%
2. Urine became protein free 3 or more months after steroids were stopped. These were called spontaneous cures. - 14%.

3. Type 2 or 3 response - 17%.
4. Type 4 response - 52%.

Conclusions:

1. 20% of adult nephrotics can be expected to have a Type 4 response to steroids.

2. From the literature, they conclude a spontaneous remission rate of 19% (from the same literature, I cannot conclude this).

3. Since 31% had either a steroid "cure" or spontaneous remission, a rate that appears higher than for spontaneous remission alone (19%), then steroids are indeed effective.

4. Around 8% deaths in 5 years are to be expected in adult nephrosis.

5. Slight hypercellularity of the glomeruli is compatible with the best steroid and spontaneous remissions rate.

76. Goodman, H.C.: Current studies on the effect of antimetabolites in nephrosis, other non-neoplastic diseases, and experimental animals. Moderator, Goodman, Ann. Int. Med. 59:388, 1963.

A recent report that suggests that antimetabolites may have little therapeutic effect on non-steroid responding nephrotics.