A Case Report of Primary Aldosteronism Caused by Bilateral Adrenal Aldosteronomas
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A 31-year-old female with typical primary aldosteronism caused by bilateral adrenal adenomas presented with benign hypertension and hypokalemia. Plasma renin activity was suppressed, even after sodium deprivation, and making her maintain an upright posture after furosemide administration. Plasma aldosterone and the excretion rate of urinary aldosterone were elevated. Plasma cortisol and urinary excretion of 17-OHCS and 17-KS were persistently normal. The presence of bilateral aldosteronomas was demonstrated by retroperitoneal pneumography, adrenal phlebogram, measurement of the aldosterone concentration in adrenal venous plasma and calculation of the ratio of aldosterone to cortisol in adrenal venous plasma, respectively. Following bilateral adrenalectomy, histologic examination revealed bilateral adenomas without hyperplasia.

Inappropriate Lactation Syndrome (ILS) and Serum Prolactin in Chronic Renal Failure
Naoki Yoshiyama (Tokyo)
Abnormal lactation was observed in 5 uremic female patients on regular dialysis treatment (RDT) and endocrinological studies were performed in them, and in 120 uremic patients without abnormal lactation and in 27 normal controls. Lactation appeared 5-18 years after delivery with progression of renal failure. Amenorrhea was observed in most ILS patients during the lactation period. Lactation showed progressive decrease in the course of RDT. High basal serum LH level in uremics (60.6 ± 13.9 mIU, n = 15) was observed. LH response to LH-RH infusion was remarkably disturbed in ILS patients and this response recovered in accordance with diminution of lactation and reappearance of regular menstruation cycle on RDT.
Basal FSH levels were almost within normal range, while FSH response to LH-RH infusion was suppressed. Estradiol in amenor-rheal and lactating patients was 28.5 ± 7.9 pg/ml and was significantly lower compared to uremic patients with normal cycle (143.3 ± 32.3 pg/ml, luteal phase). From these data, it can be suggested that there is a primary dysfunction of ovary in uremics, especially with ILS.
Basal TSH levels were within normal range. TSH response to TRH infusion was remarkably disturbed in the lactating period. Hypo-thalamo-pituitary dysfunction was also suspected. Serum prolactin levels (male: 36.0 ± 3.2, female: 62.8 ± 6.5 ng/ml) of uremics were significantly higher than normal controls. Amenor-rheal and ILS patients showed both significantly higher values than normal cycle uremic females. Long-term RDT and single hemodialysis showed no effects in serum prolactin levels.
In conclusion, hyperprolactinemia, and ovarian and hypothalamo-pituitary dysfunction can be regarded as common disorders in end-stage renal failure, and as one of its manifestations, ILS appeared in uremic females.
Effects of the Administration of Eight Essential Amino Acids and Histidine on Patients with Chronic Renal Failure

Kazuhiro Nakata (Osaka)

In patients with a moderate chronic renal failure (Cr 5-15 ml/min), the preparation of essential amino acids (defined by Rose) and histidine was administered intravenously or orally with a low protein (0.5-0.6 g/kg/day) high calorie (2,000 cal) diet.

1. In 20 patients, the supplement of essential amino acids and histidine resulted in improvement of nitrogen balance, decrease of blood urea nitrogen and elevation of serum albumin level. (2) By administration of essential amino acids and histidine, productions of methylguanidine and guanidinosuccinic acid significantly decreased in 12 patients.

Thus, a low protein diet with eight essential amino acids and histidine supply for patients with chronic renal failure accelerates protein synthesis, probably by facilitating a utilization of endogenous nitrogen, and corrects abnormal nitrogen metabolism, which are suggested by the decreases of blood urea nitrogen and production of methylguanidine and guanidinosuccinic acid. This therapy could markedly prolong the duration of a conservative management.

Morphological Studies on Renal Changes with Age I. Glomerular, Tubular and Interstitial Changes

Hiwshi Kakuta (Niigata)

70 cases which had no evidence of renal disease or no effect on the kidney were selected out of 6,224 autopsy cases, ranging from birth to 90 years of age, and were examined histologically to clarify renal changes with age. Glomerular size increased rapidly until the 2nd decade and was largest in the 3rd decade. Glomerular size in each zone of the renal cortex was largest in the inner zone and smallest in the outer. A few hyalinized glomeruli, Bowman’s capsular thickening and collapsed glomeruli appeared already at the beginning of the 2nd decade in the inner zone. Those glomerular changes were rarely found in the middle and outer zones, but occasionally from the 3rd decade. After the age of 45 years, two groups were seen, in one those changes increased gradually, in the other they increased rapidly. Crescent formation and tuft adhesion to Bowman’s capsule were very rarely observed. Localized tubular atrophy with interstitial increase in cortex and diffuse interstitial increase in medulla were parallel to the glomerular changes. Granules of lipofuscin-like pigment in distal tubules were found in young people, but were more extensive in adults.

It is suggested that the glomerular, tubular and interstitial changes may be concerned with sclerotic changes of renal arteries according to age.

Clinical Significance of Urinary Fibrin Fibrinogen Degradation Products in Renal Disease I. Urinary Fibrin Fibrinogen Degradation Products in Primary Glomerulonephritis

Shoji Miyamura (Niigata)

The urinary excretion of fibrin/fibrinogen degradation products (FDP) were examined by the method of the tanned red cell hemagglutination inhibition immunoassay (TRCHII) in 140 patients with primary glomerulonephritis without nephrotic syndrome. The results obtained are as follows: (1) More than 4 µg/ml of urinary FDP was regarded as positive. 5 of 10 patients with acute glomerulonephritis, 7 of 75 patients with smoldering
form of chronic glomerulonephritis and 13 of 33 patients with progressive form of chronic
glomerulonephritis showed positive results. (2) In acute glomerulonephritis and smoldering
form IV type the excretion of urinary FDP did not always correlate with the activity of
glomerulonephritis, judged by the histological findings, hematuria with pro-teinuria in excess
of 1 g/24 h, or serum complement levels. (3) The urinary FDP excretion did not correlate
with fibrin on immuno-fluorescent and electron microscopy. (4) In comparison to the urinary
FDP-negative cases of the progressive form, the positive cases showed more decreased renal
function. (5) The values of serum FDP measured by TRCHII in 102 patients were all within
normal limits and did not correlate with the amount of urinary FDP.

Studies on Hemodynamics and Cardiovascular Disease in Long-Term Hemodialysis Patients

I. Hemodynamic Studies

Tsukasa Ohmori (Niigata)

This report gives the following clinical evaluation on a hemodynamic study in regular
dialysis treatment.

(1) Cardiac output was increased in chronic dialysis patients due to anemia, there was
increased venous return from subcutaneous A-V fistula and excess of body fluids. This was
normalized by im-
proving anemia, occlusion of A-V fistula and removal of fluid by hemodialysis (HD).
There was no significant difference in cardiac output between the normotensive patients and
the hyper- and hypotensive patients. Peripheral vascular resistance (PVR) was more increased
in hypertensive than in normotensive patients, and was more decreased in hypotensive than in
normotensive patients. This suggested that the increase in PVR produced high blood pressure
and the decrease did the reverse.
The cardiac reserve in pulmonary congestion could be impaired, due to hypertensive cardiac
changes (hypertrophy and/or dilatation) and myocardial injury. Cardiac output in patients
without pulmonary congestion was reduced significantly after HD, while in patients with
pulmonary congestion cardiac output was usually increased after the correction of fluid
excess by HD, showing no significant differences between them. Mean blood pressure of
patients with pulmonary congestion in both pre- and post-dialytic readings was above that of
patients without pulmonary congestion in pre-dialytic reading. Although the cardiothoracic
ratio (CTR) was decreased significantly in the two groups, CTR of patients with pulmonary
congestion remained above 50% even after HD, which was greater than the pre-dialytic value
of patients without pulmonary congestion. This suggested the cardiac impairment including
hypertrophy and dilatation might be the cause in patients with congestion.
Cardiac function was studied analyzing the left ventricular conduction time, which disclosed
the prolongation of Q-IIai and ICT in the two groups (with and without pulmonary
congestion) compared with the control group. These abnormalities were not significant
between the two groups, suggestive of impaired myocardial function. Normalization of
prolonged Q-IIai, shortening of ETi and increased PEP/ET ratio were noted after HD,
suggesting that the myocardial function was suppressed in regular dialysis treatment.

Experimental and Clinical Studies of Hollow Fiber Artificial Kidney

Hiroshi Furukawa (Tokyo)

The effective method and techniques of dialysis using hollow fiber artificial kidney (HFAK)
was investigated. Clearances of various electrolytes (Na, K, P) and non-electrolytes (urea,
creatinine, uric acid, amino acids) were higher than those with another available dialyser.
Unbiased distribution of blood inside the dialyser was confirmed by both total clearance of HFAK and single fiber clearance, suggesting that total surface area worked effectively. Ultrafiltration rate was correlated to transmembrane pressure with the correlation of 0.97 (CDAK 0.9). Fiber bundle obstruction (%) of HFAK was calculated by measuring both the blood flow and the pressure drop during dialysis. Discontinuation of dialysis was decided, if ever, by fiber bundle obstruction (%) calculated from the blood flow and the pressure drop. Solute clearance was negatively and linearly correlated to the molecular weight. The respective solute clearance was decreased as the dialysate flow was lowered. Percent decrease in solute clearance was negatively correlated to molecular weight of the respective solute. The sieving coefficients obtained from the so-called ultrafiltration method were approximately 100% in the various solutes such as amino acids, urea and creatinine; 13% with inulin (MW 5,200). Permeability ratio of CA membrane to CU membrane (CA/CU) was Varia

correlated to the molecular weight. Provided that middle molecular substances worked as the uremic toxins, the dialysis with CA membrane might be more effective than CU membrane to restore the condition of uremia.

A case of Nephrotic Syndrome Associated with Renovascular Hypertension
Kenji Mizuno, Michiaki Sakaue, Manabu Ogata, Soitsu Fukuchi, Katsuo Sato and Kunio Saito (Fukushima/Koriyama)

A 38-year-old man complained of headache when he visited a physician in June, 1973. Hypertension, 160/90 mm Hg, was pointed out, and no findings were revealed in urinalysis at that time. The blood pressure was decreased to 130/80 mm Hg after 3 months administration of hydrochlorothiazide (50 mg/day). In February, 1976, proteinuria was first mentioned, and the blood pressure was 180/120 mm Hg. 11 months later he had severe headache and edema of the lower extremities. Hypertension ranged from 240/150 to 160/120 mm Hg. Laboratory findings showed urine protein 10-50 g/day, plasma albumin 2.4 g/100 ml, plasma cholesterol 356 mg/100 ml, plasma potassium 3.1 mEq/l, plasma renin activity 14.0 ng/ml/h and plasma aldosterone concentration 58 ng/100 ml. Intravenous pyelogram, renogram and renoscintigram showed that the right kidney was working poorly, and retrograde transfemoral aortogram revealed stenosis of the right main renal artery. Hypertension was drug resistant and a right nephrectomy was performed. About 3 weeks postoperatively, the blood pressure fell to 146/90 mm Hg and proteinuria decreased to 1.0-2.5 g/day. Plasma renin activity and plasma aldosterone concentration fell to 1.2 ng/ml/h and 6.0 ng/100 ml, respectively. Hypercholesteremia, hypoalbuminemia and hypokalemia were improved.

Microscopic examination of the right kidney revealed that most glomeruli were completely hyalinized, arterioles showed a great increase in medial width and neither infiltration of small round cells nor necrosis was found around the arterioles. The pathologic diagnosis was renal atrophy followed by artery stenosis due to arteriosclerosis. It is suspected that the nephrotic syndrome was induced by hypertension and high renin-angiotensin-aldosterone levels.

Bartter’s Syndrome
Studies on a Patient with Evidence for Excessive Prostaglandin Synthesis
Hakuo Takahashi, Manabu Yoshimura and Hamao Ijichi (Kyoto)
A 51-year-old male with features typical of Bartter’s syndrome is described. Several theories have been proposed to explain the pathogenesis of this disorder. We therefore investigated the response of this patient to β-adrenergic blockade with propranolol, and indomethacin, potent inhibitors of prostaglandin biosynthesis. Prostaglandin E1 (PGE1), plasma renin activity (PRA) and plasma aldosterone concentration (PAC) were measured by radioimmunoassay. Measured PGE1 ranged from 10.1 to 25.4 ng/ml and clearly exceeded the normal range for adults of 1.56 ± 0.98 ng/ml.

Treatment with indomethacin, which decreased plasma PGE1 level by 73.5%, did not significantly affect blood pressure. PRA decreased from 10.1 to 1.8 ng/ml/h and PAC from 44.0 to 10.2 ng/dl.

Serum potassium level and angiotensin sensitivity recovered to normal level with treatment of indomethacin. Angiotensin II analogue which acted antagonistically before treatment, acted agonistically after treatment as in normal adults. Propranolol suppressed the elevation of PRA and PGE1, but they remained above the normal range, and serum potassium level stayed within normal range.

These results suggest that the renal salt wasting caused by excessive prostaglandin in this disorder, stimulates the RAA axis and results in secondary hyperaldosteronism. Suppressed prostaglandin synthesis by indomethacin may have an important role in dramatic improvement of clinical features of Bartter’s syndrome.

Influence of Renal Function on the Kinetics of Pancreatic Hormones in Chronic Renal disorders

Rihei Kann (Fukushima)

Blood sugar, serum immunoreactive insulin (IRI), serum C-peptide immunoreactivity (CPR) and plasma pancreatic glucagon (IRG) were determined on intravenous glucose tolerance test and arginine test (infusion of 0.5 g/kg, for 30 min) in 58 patients with chronic renal disorders, whose creatinine clearance rates (Ccr) ranged from 6.0 to 118.5 ml/min. Fasting blood sugar levels were 66-102 mg/100 ml, K values were 0.87-5.30%/min, and those were correlated to Ccr (r = –0.355, p < 0.01; r = 0.467, p < 0.001), respectively.

Fasting levels of serum IRI, serum CPR and plasma IRG were, respectively, 3-31 µU/ml, 1.8-9.4 ng/ml and 75-333 pg/ml. CPR and IRG showed remarkably high levels in patients with Ccr below 50 ml/min. CPR and IRG were correlated to Ccr (r = -0.606, p < 0.001; r = -0.631, p < 0.001), though IRI was not correlated to Ccr (r = -0.139).

As Ccr decreased, serum IRI showed high response, serum CPR showed delayed and high response, and plasma IRG showed high levels, to the intravenous administration of glucose. ΣΔIRI (60 min) was correlated to Ccr (r = -0.378, p < 0.01).

As Ccr decreased, plasma IRG showed high response to the infusion of arginine. ΣΔIRG (120 min) was correlated to Ccr (r = -0.570, p < 0.001).

These data suggest that the kidney plays a major role in the metabolism of C-peptide and pancreatic glucagon. And it is concluded that function of pancreatic α- and β-cells is not diminished in the patients with severe chronic renal dysfunction, whereas glucose tolerance becomes impaired with the fall of renal function. Furthermore, hyperglucagonemia has an influence on the impaired glucose tolerance in chronic renal dysfunction.

Production of Enterobacterial Common Antibody and Immunofluorescent Localization of Common Antigen in Renal Tissue in Rats with Experimental Retrograde Pyelonephritis

Yukio Ariga (Fukushima)
Antibody titers to OA rapidly increased (mean 1:80) within the first 3 weeks after the bacterial injection, followed by decrease to mean level of 1:20 in the 4th week, 1:8 in the 6th week and 1:6 in the 14th week. On the other hand, antibody titers to CA almost never rose within the first 5 weeks (mean 1:4), and increased to mean level of 1:7 in the 6th week, 1:11 in the 10th week and 1:13 in the 12th week. In the increasing stage of OA titers, acute pyelonephritis with infiltration of neutrophils and phagocytes in the interstitium and with a large amount of immunofluorescent whole bacterial CA in the renal tissues were found in most of the animals. In a stage when CA titers had not increased yet after the peak of OA titers, active chronic pyelonephritis with plasmocytic and lymphocytic infiltration and with whole bacterial or amorphous CA in the interstitial phagocytes were displayed in most involved kidneys. In the stage of a decrease of OA titers and an increase of CA titers, chronic pyelonephritis was found with PAS-positive epithelioid-like cells, surrounded by plasmocytic and lymphocytic infiltration and containing a large amount of the amorphous antigens. In the stage of reduction of the titers to both OA and CA, chronic pyelonephritis with weak PAS-reactivity and a small amount of amorphous CA was noted. In rats without increase of CA titers, minimal lesions such as pyelitis with little or no CA were found in the kidneys. It is concluded that the determination of common antibody titer is significant to the diagnosis of chronic pyelonephritis.
meters are intermediate between those of low and high renin groups. (7) The characteristics of the high renin group was as follows; both the amounts and concentrations of removed sodium by the preceding dialysis were high, R was high. Intake of sodium was low, there was young age, short duration of dialysis, advanced organ damage, and hyponatremia. It seems likely that the resting levels of PRA in chronic dialysis patients reflect the state of sodium balance in the body, and renin contributes to the hypertension, especially to the high diastolic blood pressure in the high renin group.

Experimental Study of Calcium Metabolism in Renal Failure I. Production of Renal Failure in Rats as Experimental Model
Kazuyuki Daijoh, Juichi Kawamura and Osamu Yoshida (Kyoto)
To induce chronic renal lesions with secondary hyperparathyroidism, sodium sulfatylthiazole (SAT; 0.15 g/kg body weight) was administered intraperitoneally to male Wistar rats, twice a week for 4 weeks. Renal lesions consisted of interstitial nephritis, dilated tubular lumens with atrophied epitheliums and tubular obstructions by sulfocrystals. The SAT-administered rats showed increased levels of BUN and serum phosphate, decreased level of serum calcium and a mild anemic state. Average values of inulin clearance (± SD) was 0.37 ± 0.35 ml/min which was comparable to one fifth of that of control rats. Fractional excretion of phosphate was increased and parathyroid glands showed hyperplasia of chief cells. Calcium content was increased in the lung, heart, stomach and kidneys. The data suggest that the SAT-induced uremic rats provide an appropriate model of investigating disturbances of calcium and phosphate in chronic renal disease.

Microinjection Study on Potassium Transport of Rat Kidney
Makoto Miyamoto (Tokyo)
A renal microinjection experiment was performed to clarify the mechanism of various segments of rat nephron with respect to regulation of urinary potassium excretion. Wistar rats were divided into the following four groups. (A) Control group, (B) high-potassium diet group, (C) low-potassium diet group, (D) nephron population reduction (NPR) group. Micro-injection of the artificial solutions containing both 86Rb and 3H-inulin was performed into the proximal and distal convoluted tubules as well as cortical peritubular capillaries in rats undergoing mannitol diuresis. Excretory patterns of these substances were analyzed in successive urine samples. 3H-inulin is entirely recovered in the urine of the experimental kidney following the injection into the proximal and distal tubules. 86Rb is an adequate tracer for potassium and is absorbed into the potassium pool from either proximal tubular injections or peritubular capillaries. 86Rb excreted with a time course similar to that of 3H-inulin is termed ‘direct recovery’ and that excreted more slowly ‘delayed recovery’. The 86Rb recoveries which were obtained after proximal injections were independent of the injection site and averaged 9%. Secretion of 86Rb into the urine was stimulated during enhanced K secretion and decreased during reduced K secretion along the distal nephron. Distal tubular injections gave 100% direct recovery in control, high K diet, and NPR rats. It was apparent that the 86Rb recovery was significantly reduced, although not delayed, in animals deprived of dietary potassium for several weeks. At the collecting duct, the extensive net
potassium reabsorption is observed in potassium-depleted rats, whereas K absorption might be reduced or even secretion is seemingly taking place in potassium-loading rats.

In conclusion, distal convolution and collecting duct play the major role in the regulation of urinary potassium excretion.

Serum Levels and Urinary Excretion of 25-Hydroxyvitamin-D in Renal Failure
Kenichi Ohhara (Tokyo)

Serum 25-hydroxyvitamin-D (25-\(\text{OH-D}\)) was determined in 24 normal subjects and in 60 patients with chronic renal failure (CRF). Mean concentration of 25-\(\text{OH-D}\) was low (25.4 ± 11.2 ng/ml) in sera from the patients as compared with that (33.9 ± 10.6 ng/ml) of normal controls, although the values in an earlier stage of renal failure were considered to be within normal ranges. In more progressive stage, however, the value decreased extremely (11.8 ± 5.5 ng/ml). In contrast, the patients receiving regular hemodialysis 3 times a week showed an almost identical serum 25-\(\text{OH-D}\) level (26.4 ± 11.2 ng/ml) to those of other normal controls, the level of which had been measured in winter. The reduction of serum 25-\(\text{OH-D}\) levels in patients with CRF could be attributed to the limitation of vitamin D intake resulting from low protein diets.

25-\(\text{OH-D}\) excretion in the urine was performed in 5 normal subjects and in 24 patients with renal diseases showing proteinuria. Mean urinary excretion of 25-\(\text{OH-D}\) in 5 controls was 4.8 ± 4.7 ng/day; in patients with urinary protein < 3.5 g/24 h and urinary protein ≥ 3.5 g/24 h it was 24.3 ± 19.9 and 75.5 ± 43.9 ng/day, respectively. Concomitant 25-\(\text{OH-D}\) binding activity appeared in the urine, suggesting renal loss of low molecular weight protein (transcalciferin?) was the cause of low circulating serum 25-\(\text{OH-D}\) levels in heavy proteinuric patients.

The present data suggest that low levels of serum 25-\(\text{OH-D}\) in patients with CRF might be due to the leakage of 25-\(\text{OH-D}\) in the urine as well as to the diet therapy with low protein intake.

Studies on Uremic Toxins Biochemical Analysis of Uremic Serum
Fumitake Gejyo (Niigata)

Many investigators have suggested the presence of some unknown toxic substances, which accumulated in uremic sera but not in normal sera. However, these substances have not been identified chemically, and their biological roles and serum levels in uremic patients have not been clarified.

The present study was undertaken to elucidate and identify unknown toxic substances in uremic sera by the methods of gel filtration, ion exchange chromatography, high voltage paper electrophoresis and amino acid analysis.

The results obtained were summarized as follows: (1) The chromatographic pattern on Sephadex G-75 of uremic sera consistently showed three peaks (I, II and III) higher than those of normal sera. (2) Ion-exchange chromatography of peak I and the structure analysis of the major component of the peak revealed the accumulation of \(\beta\)-microglobulin in uremic serum. (3) Analysis of peak II of uremic serum by high voltage paper electrophoresis demonstrated the presence of five unidentified ninhydrin-positive substances. These substances were identified as \(\beta\)-aminoisobutyric acid, \(\beta\)-aspartyl-glycine, N-monoacetylcyystine, homocysteic acid and cysteic acid by comparison with authentic samples, respectively. (4) The quantitative determination of \(\beta\)-aspartylglycine, N-monoacetylcysteine and \(\beta\)-aminoisobutyric acid in plasma revealed that the plasma concentrations of these substances in uremic patients was considerably increased.
Studies on Acute Renal Failure

I. Factors Influencing Prognosis in Acute Renal Failure
Eiichi Magara (Niigata)
A survey has been made of 210 cases of acute renal failure. The overall mortality was 37.1%. Of the patients, 128 were male and 82 female, ranging in age from 5 to 79 years. The clinical, biochemical and other data were compared statistically, and factors affecting the prognosis in these patients were evaluated prospectively. Some major factors have been identified as having an adverse influence on prognosis, namely age, sex, etiology of acute renal failure, maximal blood urea nitrogen, and complications. Mortality rate rose with age, being especially high in those patients over the age of 60, and was twice as high for males as for females, probably due to the preponderance of females in the etiologic group with the lower mortality rate and maybe due to unknown factors. Mortality was high in the post-traumatic group and the postsurgical group, especially gastrointestinal and brain surgery. Mortality rose with the daily rise of BUN, but was not statistically significant. Maximal level of BUN was high in the poor prognosis group. Complications: infections, especially septicemia and pneumonia, gastrointestinal hemorrhage, congestive heart failure, coma had an adverse influence on prognosis.

Experimental Membranous Glomerulonephritis Induced in Rats by the Injection of Pronase-Digested Homologous Renal Tubular Epithelial Antigen

II. Sequential Ultrastructural Observation of the Glomerular Lesion by Electron Microscopy
S. Umegae, T. Fukasawa and T. Naruse (Maebashi/Tokyo)
A laboratory model of membranous glomerulonephritis was induced in rats by the injection of pronase-digested homologous renal tubular epithelial antigen, and the renal lesions in the experimentally induced nephritis were studied sequentially by electron microscope. Proteinuria developed about 6 weeks after the antigen injection. In the renal specimens taken 3 weeks after the antigen injection, a few electron-dense deposits were first detected along the subepithelial surface of the GBM. Epithelial foot processes often fused to each other at the place of deposition. After the appearance of proteinuria, the amount of deposits increased in number and size, and the fusion of foot processes became widespread. Small deposits were also found near the epithelial slit membrane. In the more advanced cases, about 3 months after the appearance of proteinuria, the GBM was thickened irregularly, containing many deposits. In rats surviving longer, the deposits were rough granules. There were some areas of low electron density or electron-lucent areas. These ultrastructural changes observed in experimental nephritis were similar to those observed in human membranous glomerulo-nephritis. In some rats, however, which weakened gradually and died within 6 months after the development of proteinuria, marked thickening of the GBM with numerous dense deposits were found. No electron-lucent areas in the GBM were observed in these rats.

Serum Transferrin Levels in Chronic Renal Failure II. The Relationship between Anemia and Nutrition in Regular Hemodialysis Patients
Yoshiaki Miura (Niigata)
In 51 regular hemodialysis patients, the relationship between the degree of anemia and the nutritional status was investigated. In patients without iron deficiency (serum iron > 110 µg/dl), the serum transferrin levels correlated well with the caloric and protein intake, and also with the degree of obesity. Thus the serum transferrin levels are regarded as an indicator of nutritional status. In these patients, the serum transferrin levels correlated significantly with the RBC and hemoglobin levels. The correlation between dietary intake and hemoglobin levels was also significant. These findings suggest that if protein and calorie intake is inadequate in dialysis patients, anemia becomes more severe, probably due to decreased globin synthesis. In patients with low serum iron levels (serum iron ≤ 110 µg/dl), there were no significant correlations between the degree of anemia and each of serum transferrin levels and dietary intake. This seems attributable to changes in serum transferrin levels, decreased red cell production or reduced globin synthesis probably caused by the presence of iron deficiency, insidious chronic inflammation, or RE block.

From the viewpoint of nutrition and anemia, it is conceivable that caloric intake of 35-40 cal/kg and protein intake of about 1.2 g/kg is adequate in patients on thrice weekly hemodialysis.

Dipyridamole Therapy in the Nephrotic Syndrome
Shizuo Tojo, Mitsuharu Narita, Haruo Suzuki, Motoaki Sano, Akio Koyama, Takanori Tsuchiya, Shunichi Yamamoto, Hiroki Tsuchida, Hideo Shishido and Kotaro Watanabe (Tsukuba/Chiba)

Dipyridamole was used in 30 cases of nephrotic syndrome, mostly of intractable type. The results indicate that the drug therapy proved to be effective in decreasing urinary protein and controlling nephrotic condition in 40% each of cases after an initial period of treatment. Long-term results of the drug on urinary protein and on nephrotic condition were rated as good in 36.4 and 53.3%, respectively.

The exact mechanism of action of dipyridamole in the nephrotic syndrome is still obscure in many respects. However, the fact that the drug shares its antiplatelet action with the nonsteroid anti-inflammatory drugs, e.g. aspirin and indomethacin, and the rapidity with which it produces its urinary protein-decreasing effect strongly suggest that it acts to inhibit the release of vasoactive amines and other chemical mediators from blood platelet. Adverse side-effects of dipyridamole were few or minimal, even when the drug was used in large doses over a prolonged period of time.

From these results it is considered that dipyridamole provides a new remedy which is worth trying in nephrotic syndrome as a means of reducing the requirement of steroids and immunosuppressive drugs.

Study of Focal Glomerulosclerosis
On the Findings of Kidney Biopsies Obtained at Intervals
from 13 Patients with Idiopathic Nephrotic Syndrome
Takao Saito, Takashi Furuyama, Yoshio Kyogoku, Yasuhiko Sasaki, Hiroshi Saito, Takashi Arikawa and Hisakazu Jin (Sendai)

We report 13 patients with idiopathic nephrotic syndrome examined by kidney biopsies at 5-month to 12-year intervals. All initial biopsy specimens showed ‘minimal change’. At the second biopsy, however, 5 cases were diagnosed as focal glomerulosclerosis (FGS), because we observed sclerosing lesions with eosinophilic deposits, hyaline thrombi, foam cells and
vacuoles in three or more glomeruli. In these specimens interstitium was also more increased than in initial biopsy specimens.

Retrospectively, 4 initial biopsy specimens from FGS patients showed segmental mesangial thickness and capsular adhesions to capillary loops in one or two glomeruli. Clinically, these 4 cases had been steroid-resistant from the early stage and more than 1 g/day of urine protein remained throughout the follow-up periods. 1 of the 4 FGS patients never showed any improvement in the nephrotic syndrome and took a downhill course to uremia necessitating hemodialysis 7 years after the onset of the disease. In another patient with FGS, steroid therapy was at first effective, but he died of renal failure 16 years after the onset. In the other 8 patients second biopsy specimens showed no abnormality but a few proliferative or hyalinized glomeruli. These cases were steroid-responsive and renal function did not deteriorate throughout the follow-up period, although they often needed steroid therapy because of relapses of nephrosis. 4 biopsy specimens from patients with FGS (3 at the second biopsy and 1 at the third biopsy) and 3 second biopsy specimens from patients with ‘minimal change’ were studied by immunofluorescent technique. Significant depositions of IgM and β2G were demonstrated in all FGS cases but there was no deposition in ‘minimal change’. These findings lead us to assume that FGS is caused by different factors from that of ‘minimal change’ type nephrotic syndrome.