

## CARE OF THE PATIENT IN RENAL DISEASE

By

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The problem concerning the long-term care of nephropathic patients has not yet been settled. During the last five years we have followed up the history of about 400 such discharged patients most of whom were suffering from some form of glomerulonephritis or from pyelonephritis. In the present paper these two types of renal disease will be dealt with, it being understood that neither the number of our cases nor the time of observation justify definitive conclusions.

The most important renal diseases requiring continued medical supervision are as follows. (1) Chronic glomerulonephritis; (2) nephrosis; (3) chronic pyelonephritis; (4) renal ptosis; (5) congenital anomalies of the urogenital apparatus, polycystic kidney in particular; (6) nephrolithiasis; (7) renal tuberculosis; (8) renal tumours.

Continued medical care is especially difficult in cases of double or multiple syndromes, and it has unfortunately been found that the best one can hope for is to delay the fatal termination. A few examples of combinations observed in our material are presented in the following. Interstitial nephritis + nephrotic nephritis, hypersensitive angitis (Zeek) + salt-losing nephritis, systemic lupus erythematosus + scleroderma involving the kidney, pyelocystic kidney + pyelonephritis, pyelonephritis + renal amyloidosis, renal amyloidosis + renal vein thrombosis, of the Kimmelstiel-Wilson's syndrome + polyneuropathy, pyelonephritis + essential hypertension + Goldblatt mechanism (caused by atheromatous plaques obstructing the right renal artery) + generalized arteriosclerosis (with reduced elasticity of the aortic wall).

Recovery from acute glomerulonephritis may be delayed (up to two years), and such patients have to be kept under medical supervision. Particularly worrying is the problem of 14-year old children with acute nephritis, who are discharged from the

children's hospital on account of their age before complete cure, and do not solicit medical aid at a competent institute.

It is rather difficult to determine whether and when recovery is complete. Ideally, medical care should cease only after full *restitutio ad integrum* which has to satisfy the following requirements. (1) Absence of clinical symptoms; (2) immunological norm-activity; (3) normal structure of biopsic renal specimen as seen under the electron microscope; (4) satisfactory results of all function tests (including clearance test).

The expressions "residual albuminuria", "residual haematuria", "defective healing", or "symptomless bacteriuria", though giving confidence to the patient, may blunt the physician's vigilance. We had better avoid the use of the term "residual albuminuria" unless all kidney-function tests (including filtration fraction) have given consistently normal values. A diagnosis of residual haematuria is justified only if the erythrocyte count determined by the method of ADDIS [2] does not exceed 8 to 10 millions. The behaviour of the filtration fraction deserves especial attention because it is a sensitive index of function. When, following glomerular lesion, G. F. R. has returned to normal values, the filtration fraction may be still considerably reduced indicating that glomerular restoration is still incomplete. French clinicians hold that three symptoms, though each insignificant in itself, should be taken seriously if they occur simultaneously. Accordingly, residual albuminuria combined with residual haematuria and a residual decrease of the filtration fraction indicates the existence of latent chronic nephritis.

It is not easy to determine the onset of chronic nephritis. It begins, according to HETÉNYI [30], if hypertension associated with acute nephritis does not subside in three weeks. We cannot accept this view, since patients with acute nephritis are often

hyperreactors, and essential hypertension in such cases may be misleadingly suggestive of chronic nephritis [26]. There is no doubt if the capacity of concentration is impaired no matter whether one is dealing with glomerulonephritis or pyelonephritis.

Bacteriuria, symptomless or accompanied by an episodic mild pyelonephritis, may have a background of grave chronic pyelonephritis [52]. As regards the question as to when a diagnosis of "true" bacteriuria is justified, it is emphasized by WHALLEY *et al.* [56] that bacteriuria has no significance unless the same microorganism grows from the urine in large numbers on two successive occasions. The critical count is generally agreed to be  $10^5$  per ml of urine, in our experience it is  $10^3$  per ml of clear voided urine in males, and of catheter specimens in females [23, 24]. In our experience the growth of different microorganisms from urine specimens taken at close intervals is no evidence against true bacteriuria, provided the bacterial count is high enough. If the urogenital tract is susceptible to infections, it may be affected by different pathogens in succession, or at the same time. Pyelonephritis may be maintained by two different microorganisms.

#### DEVELOPMENT OF CHRONIC STAGE

Certain renal diseases appear *a limine* in a chronic form, e.g. chronic renal tuberculosis. Again, other renal diseases, for instance congenital anomalies, persist throughout the patient's life, but it is difficult to understand how acute glomerulonephritis or pyelonephritis becomes chronic.

Glomerulonephritis is an allergic disease, and there exist various theories regarding its immunological mechanism.

(1) It is streptococcal allergy according to the classic concept [46, 49]. Streptococcal proteins are supposed to sensitize the organism, the first phase of this process being attachment of the antibodies to the tissues. The first manifestation of the disease is believed to occur when the antigen, making repeated invasions into the blood stream, reacts with the sessile antibodies.

(2) Reverse active anaphylaxis. The theory presumes, as the first phase of the process, binding of the antigen to the tissues [34, 48]. Manifestation of the disease is connected with the reaction of the

antibodies, produced during the latency stage, with the kidney-bound antigens.

(3) The disease arises owing to auto-immunization [11, 50, 53].

(4) The soluble antigen-antibody complexes act as pathogenic agent [14, 40]. Recent investigations have made it probable that antigen-antibody reaction takes place in the intravascular compartment during the latency of the serum disease. It is in the blood stream that toxic complexes arise which -- partly during circulation and partly after being deposited on the vessel walls -- stimulate the development of proliferative glomerulonephritis.

It is probable that all these factors are involved in the pathogenesis or at least in certain manifestations of the disease (slow progress of chronic nephritis or its sudden exacerbation), but it is not clear whether they act simultaneously or in succession. The latter is more probable, as shown by the diphasic concept regarding the pathogenesis of the Masugi-nephritis, a concept convincingly substantiated by KAY's [32, 33] experiments with the combination of rabbit kidney and duck serum. This theory was furthermore confirmed by those model experiments [28] which exemplified the successive action of different allergic mechanisms. Non-lethal anaphylactic shock was produced in rabbits sensitized with minimal doses of nephrotoxic duck serum; upon the shock effect the hitherto latent process became manifest, whether normal or nephrotoxic duck serum had been used for reinjection. Auto-immunization is presumably the last factor of the process and is also responsible for the slow progress of chronic nephritis. This theory, set out by us in detail in an earlier communication [21] is in harmony with that of PFEIFFER and BRUCH [45] who ascribed acute glomerulonephritis to an infectious allergy which subsides in the majority of the cases, but, occasionally, may give rise to an auto-immune mechanism: acute nephritis passes in such cases into the therapeutically no longer manageable chronic phase which ultimately leads to secondary renal atrophy.

Acute exacerbations of chronic nephritis which are due to repeated streptococcal infections and are liable to cause sudden relapses in the patient's condition, have a different origin. It has been observed [15], and we are in a position to confirm it, that the latency period of acute exacerbation is

shortened. In our view, the classic theory of streptococcal sensitization offers the best explanation for the short period of latency.

It is stressed by PETRÁNYI [44] that hypertension coexistent with acute glomerulonephritis may generate a vicious circle which is responsible for the chronic course of the process and leads to hypertensive transformation of the kidneys. In more than 50 per cent of cases with chronic nephritis alterations characteristic of malignant hypertension may be found without any sign of oedema or inflammation. Changes of this kind obviously precipitate the failure of renal functions.

Aetiology and pathogenesis of glomerulonephritis chronic from its very outset are still obscure. It may belong to the category of collagen diseases [44].

How does chronic pyelonephritis arise? Our knowledge of organ immunity is rather scanty, and it is only in very general terms that we are able to explain why bacterial infections of the kidney fail to heal. Either the pathogen must be very virulent or the defence mechanism of the affected organ too weak. The principal predisposing factors are calculi, congenital anomalies and pregnancy. Obstructive forms require surgery, and non-obstructive (non-surgical) forms, eradication of the responsible foci for their cure.

The results of experiments carried out by BABICS and RÉNYI-VAMOS [3-5] justify the conclusion that, in cases of the obstructive type, urine is absorbed by the adipose tissue adjacent to the pelvis of the kidney and then by the interstitial space, a process involving in the sinus of the kidney a massive release of histamine. Adipose tissue undergoes cicatrization. Occlusion of the lymphatics makes lymph circulation inadequate which interferes with the renal transport of proteins. This is the decisive factor responsible for renal degeneration, according to the said authors.

#### DIAGNOSTIC PROBLEMS IN CONNEXION WITH THE ACTIVITY OF CHRONIC RENAL DISEASES

It is generally accepted that a chronic disease may be regarded as active if any of its cardinal features is or becomes predominant. Obviously the various signs have not the same significance. It is, for instance, true that increase of proteinuria is no favourable sign and that a high degree

thereof points to nephrosis. On the other hand, a decrease of proteinuria need not be a sign of improvement. Since proteinuria is of glomerular origin, the urinary output of proteins, obviously, decreases with advancing glomerular deterioration. Appreciation of the role of hypertension is made difficult by clinical types involving a dual mechanism, i.e. where in the origin of renal hypertension the renin-angiotensin mechanism combines with neurogenic factors [26]. We have found the ADDIS-count of microscopic haematuria [2] to be the most reliable indicator [22, 24, 25, 27].

It can be seen from Fig. 1 that prednisolone has a favourable effect on acute nephritis of a protracted course. Sudden interruption of prednisolone therapy after the onset of improvement gives rise to exacerbation: there follows a considerable increase of microscopic haematuria, and the complement titre of serum suffers transient reduction (interruption syndrome). In assessing the activity of glomerulonephritis BROD [8] takes the following factors into account: proteinuria, haematuria, excretion of leucocytes, cylindruria, and erythrocyte sedimentation rate.

Reduction of complement in the serum is an evidence of immunological activity [22, 24, 25, 27, 37, 38]. There is still little information about the correlations between the titre of the auto-antibodies and the clinical course of the disease; it is, however, a fact that, as a rule, significant titres

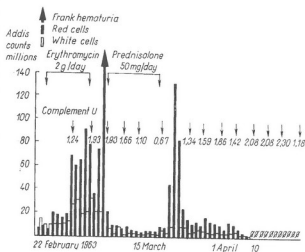


FIG. 1. A 58-year old male patient. Consequence of sudden interruption of prednisolone therapy. Diagnosis: acute glomerulonephritis of a protracted course. Note upward jump of ADDIS figures and the transient fall of the complement titre to 0.67 U. (The lowermost limit is 1.0 U. according to LANGS)

of auto-antibodies are consistently found in the very case of chronic nephritis [12, 36, 45, 54]. Persistence of antirenal auto-antibodies demonstrable by serial tests is claimed by KRAMER *et al.* [35] to carry a poor prognosis in chronic nephritis.

In our experience, significant micro-haematuria and reduction of complement are not invariably associated in a protracted acute or in a chronic nephritis. Quantitative analysis of urinary sediment is generally a more sensitive method than the titration of complement. It may occur that the titre of complement remains low although the acute nephritis is clinically healed. Prognosis in such cases is uncertain, but there can be no doubt that such patients require continued medical care.

The behaviour of complement titre is a valuable indicator of the activity of lipid nephrosis. LANGR *et al.* [38, 39] as also WEDGWOOD and JANEWAY [55] found a very close correlation between the clinical course of nephrosis and the fluctuations of the complement titre. We have failed to observe a close correlation between the two phenomena, but are ready to admit that a decrease in the titre of the complement is a fairly reliable sign of progression. Complement titres as diagnostic aid have two limitations: (1) the complement titre may remain unchanged in cases of fatal nephrotic nephritis; (2) low complement values promptly return to normal if acute glomerulonephritis is associated with some inflammation or thyrotoxicosis. This phenomenon has been described by FISCHER and GAJDUSEK [17], and we are in a position to confirm it on the evidence of two of our cases in both of which intercurrent inflammation was due to abscess following intramuscular injection.

Pyelonephritis is active if there is "true" bacteriuria combined with pyuria, no matter whether the patient has fever or not. Changes in the bacterial and in the white cell counts give a true reflection of the course of the process. An ADDIS-count of leucocytes [2] requires a catheter specimen in women but, for obvious reasons, catheterization is no daily routine procedure.

Accumulation of blood urea N in cases of nephropathy indicates the terminal stage of the process rather than its activity.

#### HOW TO PREVENT THE EXACERBATION OF CHRONIC PROCESSES

Exacerbations of chronic glomerulonephritis or pyelonephritis are caused by reinfection and can be

prevented by the early antibiotic treatment of bacterial (especially coccal) infections. Patients with chronic glomerulonephritis should not visit crowded places at a time when the seasonal incidence of respiratory infections is high, so as to avoid exposure to nephritogenic streptococcal strains. They should not have occupations where exposure to infections is high; they should not be employed for instance as nurses, conductors, waiters or ushers. Long-term penicillin therapy (on the analogy of rheumatic fever) is not always necessary since only a few types of streptococci are nephritogenic.

Patients with chronic pyelonephritis should strictly observe the rules of hygiene. Daily ablutions of the external genitalia with dilute potassium permanganate should never be omitted by female patients.

Catheterization, as required for the inulin and PAH clearance tests, involves the hazard of urinary infections. Preventive injection of 250 mg of neomycin into the bladder after the test has been adopted, therefore, as a routine procedure. It is advisable to employ broad-spectrum antibiotics in connection with urological examinations. COLBY [13] discards ureteral catheters once they have been used in patients infected with *Proteus* or *Pseudomonas pyocyanea*.

#### HOW TO DELAY THE PROGRESS OF CHRONIC PROCESSES

Chronic glomerulonephritis or pyelonephritis predict the terminal stage of the process. The ideal way of averting this outcome would be, obviously, prevention, in other words, to bring the process under control at its acute stage. Once, however, nephropathy has reached the chronic phase, all we can do is to eliminate all factors that might precipitate its fatal course. The most important harmful factors are reinfection, physical strain, mental stress and inadequate regimen. It is likewise important to gain control over the activity of the process as far as possible. Therefore, long-term steroid therapy should be employed in chronic glomerulonephritis [8, 9, 22, 24], in nephrotic-syndrome [1, 19, 22, 24, 47], long-term chemotherapy and antibiotic treatment in chronic pyelonephritis [6, 7, 10, 23, 24, 31, 43, 51].

Long-term steroid therapy has its risks. We find it unwarranted in nephrotic-syndrome origi-

nating from amyloidosis, having had the impression that it had precipitated the fatal course in one of our cases. MAXWELL *et al.* [41] share our view in this respect.

We propose to outline in the following the routine procedure followed by us. Patients with radiographically verified gastric or duodenal ulcer are a *limine* excluded. If the barium-meal-finding is negative in this respect, treatment is started with the daily peroral administration of 50 to 60 mg prednisolone; this therapy is continued (even for a few months) until the activity of the process ceases or, else, until the appearance of side effects. The administration of medium doses has usually to be modified when the patients become excited, begin to complain of strong pyrosis, intestinal spasms, insomnia or palpitation; some patients simply refuse to take the drug any longer. We reduce the daily doses in such cases according to the tolerance of the patient. A daily 10 to 15 mg dose of prednisolone has generally no ill-effects even if continued for a number of months. Medium doses of prednisolone cause hypopotaemia but normal values can usually be maintained by 3.0 g of potassium chloride per day. Sodium hydrocarbonate should be given according to necessity. Patients should be warned of the dangers of dietetic indiscretions. Coarse, heavy food may promote the perforation of possible ulcers or the development of pancreatitis.

Energetic prednisolone therapy requires continuous clinical supervision. Barium-meals should be repeated at three-weekly intervals so as to detect possible steroid ulcers in due time. Evidence of this latter calls for the arrest of prednisolone therapy and for intramuscular administration of cortisone (20 mg/day) in order to avert adrenocortical failure, called also "interruption syndrome". If no sudden interruption is necessary, the prednisolone therapy should be abandoned gradually, over a period of about two weeks. ACTH is not necessary. Small doses may be taken at home as well.

Fig. 2 illustrates a case in which repeated sudden interruption of

prednisolone therapy was followed by frank haematuria in a patient with acute nephritis of a protracted course. Renewed administration of prednisolone arrested the reactive haematuria, and it was possible to prevent rebound phenomenon by a gradual decrease of the dosage.

It is generally accepted that the prognosis of pyelonephritis depends on whether bacteriuria can be stopped. Most authors employ specific antibiotics. BROD [6, 7] emphasizes that a single negative bacteriological test does not justify the arrest of therapy and that treatment must be continued even after repeated negative urine samples. He advocates small doses of urine-soluble sulphonamides for long-term antibacterial therapy. We prefer the use of broad-spectrum antibiotics (usually  $\frac{1}{2}$  to one tablet of Tetran B per day) for the purposes of long-term maintenance treatment. Also intermittent long-term antibiotic and sulphonamide therapy has been tried, but it was successful only if the treatment had begun early, *i.e.* at a time when the creatinine clearance was still normal or almost normal [10].

A well soluble sulphonamide preparation should be prescribed if the pathogen of pyelonephritis turns out to be a polyresistant strain, for sulphonamides ineffective *in vitro* may still prove efficacious *in vivo*. To prescribe nothing may also be justified in such cases. We prescribe some dye preparation — more in the nature of placebo than

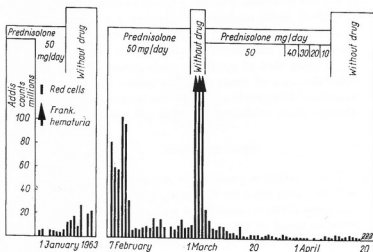


Fig. 2. A 20-year old female patient. Consequences of repeated interruptions of prednisolone therapy and the effect of prednisolone on reactive haematuria. Diagnosis: acute glomerulonephritis of a protracted course. Prednisolone stops the reactive gross haematuria, and by gradual reduction of the dosage rebound phenomenon is prevented

in the hope of actual pharmacological success.

Congenital anomalies of the urogenital apparatus should be regarded as potential sources of pyelonephritis. After surgery for renal malignancy we should endeavour to detect possible recidives as early as possible.

Full psychic harmony between patient and physician is an important factor of success.

#### NEPHROPATHIES AND PREGNANCY

By the use of antibiotics it has become possible to gain some control over the condition of the kidneys during pregnancy; moreover, in view of the progress achieved in the matter of ensuring the survival of viable prematures, it is no longer necessary for nephropathic gravidæ to carry the foetus until full term.

Chronic nephritis (especially in the pre-uraemic phase) makes artificial abortion imperative. It is, of course, rather difficult to make a decision if a woman presents with nephrotic nephritis in the fifth to seventh month of pregnancy. If clinical observation shows the patient's condition to go downhill, the foetus has to be sacrificed.

#### NEPHROPATHIES and MILITARY SERVICE

Chronic nephritis makes the patient obviously unfit for military service. The problem arises only if one has to decide whether a man who has recovered from acute nephritis, for instance a year ago and has been free of any sign or symptom ever since, should be allowed to do military service. We suggest that at least two years should elapse after the cure of acute nephritis before the permission of doing military service can be considered since we have no absolute proof of full restitution.

#### REHABILITATION

It is of extreme practical importance to find a suitable occupation for the nephropathic patient. The rehabilitation committees go by standardized schemes based on the nature and the stage of the process. Standards of this kind have certainly their use. Let us refer in this respect to FÖLDI's study on the rehabilitation of nephropathic individuals [18]. Of course, no predetermined scheme can meet each individual contingency. BROD [8] looks upon endogenous creatinine clearance as a

suitable guide in the assessment of working capacity. He suggests that sedentary work of daily eight hours is permissible as long as the average G. F. R. is more than 50 ml/min., while only a half-time (*i.e.* four hours) occupation should be allowed if the G. F. R. of filtrate falls below this level or if the patient develops hypertension. This can, according to BROD, go on until the appearance of signs pointing to uraemia. We are not in favour of setting up general rules of this kind. No two nephropathies are quite similar: let us bear in mind the wide variety of nephritides, extending as it does from minute affections to foudroyant cases which end fatally in 24 hours. Attempts at rehabilitation yield sometimes surprising results. According to his request, we allowed a patient with polycystic kidney, on the verge of uraemia, to resume his administrative duties: the case was a full success. In another case, a joiner with ureteral compression and microscopic haematuria is doing his job without any harmful consequence. On the other hand, we have had fatal episodes as well. A young miner, who had almost completely recovered from acute glomerulonephritis, resumed his job against our advice. The ambulance brought him back to the clinic 18 months later, and he died of uraemia shortly thereafter. A young man — in the latent phase of chronic nephritis — matriculated at the high school of forestry. Exertions connected with his studies and possible acute exacerbation induced, within a few months, fatal uraemia.

Since work of any kind has to be regarded as tolerance test, nephropathic patients should at first be kept under careful supervision, an important task for the factory medical consultant whose close co-operation with the medical institute is indispensable in this respect. It is up to the institute (clinic) and the factory doctor to select a job for the patient which can be done by him without impairing his actual condition. The problems arising in this respect are not so easy in practice and certainly not easier than in any other disabling condition.

Strictly speaking, no person with renal disease should resume his work until complete recovery. Since, however, present therapeutic methods cannot always prevent the development of chronic cases, certain compromises are unavoidable. Patients are allowed to work if their chronic condition is stationary or nearly so.

No person with renal disease must work if (1) the renal process is markedly active; (2) he has to be regarded as renally disabled (*e.g.*, if he is in a preuraemic condition or if the degree of renal hypertension is high).

Nephropathic patients can be trusted to be able to do mental work and not too heavy physical work. They must not stand on their legs too much, nor must they lift heavy weights. Their place of work must not be too hot, and they must in no case work in places where nephrotoxic substances (*e.g.* mercury) are used.

We agree with GÖMÖRI [20] that patients with residual albuminuria should receive the same attention as persons in the early phase of chronic nephritis and forbidden to do heavy physical work.

It is advisable that patients of school-age with protracted acute nephritis should rather lose a year than risk the chances of a complete cure.

#### PROBLEMS OF ORGANIZATION

The care of nephropathic individuals pursues the same object as does the care of other patients, so that the network of welfare organization plays essentially the same role (though on a higher level) as did the family doctor of yore. The patients' condition is steadily followed, and adequate treatment is instituted if signs of deterioration are noted. Welfare organization serves the purposes of rehabilitation by being able to watch the condition of the patient after return to work. It has the task to prevent relapses if possible and to provide for suitable occupations. The main issues of these tasks are: (1) follow-up examinations; (2) possible stabilization of the actual condition; (3) detection of relapses in due time; (4) supervision of long-term steroid therapy and prolonged antibiotic or chemotherapeutic treatment; (5) rehabilitation.

We do not think that special institutes are necessary for the care of nephropathic persons. The tasks, listed above, can be satisfactorily performed by outpatients' consultations with adequate laboratory facilities which are indispensable as they alone provide the necessary basic information. The co-operation of the panel doctor has to be secured since he is most familiar with the condition of the patients of his panel. He is in a position to observe slight manifestations that point to a change in the patient's condition,

whereas the overcrowding of our clinics makes repeated hospitalizations for the sole purpose of follow-up examinations impossible.

The ambulatory supervision of nephropaths by the outpatients' departments of existing hospitals and clinics requires no significant financial efforts and can be organized to meet all necessary requirements. The patients would have to report on certain days and at certain hours, and be possibly seen always by the same doctor who could thus familiarize himself with the individual circumstances of each case, and might, at the same time, accumulate valuable material concerning the dynamics of chronic renal diseases. The establishment of a special institute for kidney diseases would, of course, be highly desirable from a scientific point of view, but requirements in this respect can be met by the existing hospitals and clinics, especially if suitably equipped nephrological units could be set up in their framework.

The most expedient organizatory measure for the present would be to oblige panel or factory doctors to refer their nephropathic patients to the competent nephrological outpatients' department at certain intervals, and, in addition, to see to it that these patients should have a complete check-up at a clinic at least once a year. Panel doctors will be able to give full satisfaction in nephrological matters if their postgraduate training is adequately organized.

How long should the care of nephropathic patient last? Well, we think throughout his life.

#### THE FUTURE

Until recently, in the terminal phase kidney disease has not been accessible to successful care. There are now possibilities of replacing destroyed kidneys: transplantation and artificial kidney. Routine transplantation is still limited by the phenomenon of immunological incompatibility, a problem it is hoped will be solved in due time.

The application of teflon-silastic shunts has practically settled the matter of maintenance haemodialysis. Patients visit the artificial-kidney unit twice per week where they are connected to the dialysing apparatus by means of the teflon-silastic arteriovenous cannulae [16, 29, 42]. Quite a number of people live nowadays without kidney.

## SUMMARY

400 patients with renal disease have been followed up by the author over the last five years.

(1) Medical supervision is required, outside chronic renal disease, by the type of acute nephritis with a protracted course. To gain certainty of complete recovery from acute nephritis may take two years. Double or multiple syndromes usually end fatally despite careful medical attention.

(2) Diagnoses like residual albuminuria, residual haematuria, symptomless bacteriuria or incomplete recovery may allay the fears of the patient but tend to lull the necessary nephrological vigilance. No recovery is complete without a normal value of filtration fraction.

(3) The slow progress of chronic glomerulonephritis is presumably due to auto-immunization, while the brevity of latency in cases of acute exacerbation is best explained by the classic theory of streptococcal sensitization ("sessile" antibodies). The most important factors predisposing to chronic pyelonephritis are renal calculi, congenital anomalies of the urogenital tract, and pregnancy.

(4) Activity of chronic nephritis manifests itself through microscopic haematuria (determined according to ADDIS) and/or through a low level of the complement. The dynamics of chronic pyelonephritis can best be followed on the evidence of germ count + leucocyte count (determined likewise according to ADDIS).

(5) Acute exacerbation of chronic processes should be prevented by prompt antibiotic treatment of bacterial infections, by keeping clear of occupations where the patient is unduly exposed to contagion, and by a strict observance of hygienic rules. Characterization should be followed by intravesical application of neomycin.

(6) The progress of chronic processes may be slowed down by (a) the elimination of damaging factors; (b) suppression of activity in cases of glomerulonephritis and the related diseases by means of long-term steroid therapy, in cases of pyelonephritis by long-term antibiotic and chemotherapeutic treatment. The patients' mode of life should be adapted to his condition. Treatment of possible foci and surgical repair of abnormalities of the uropoietic tract are indispensable. Steroid therapy is contraindicated in renal amyloidosis.

(7) No patient with chronic renal disease is fit

for any kind of work if the illness is active. Rehabilitation under careful medical supervision may be attempted in the latent phase.

(8) Nephrological outpatients' consultations provided with laboratory facilities should be the kernel of organized medical care, but periodical clinical examinations are indispensable. It is up to the attending physician to detect sudden changes for the worse. Nephropathic patients should remain under medical supervision throughout life.

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Minor tranquilizer  
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N-(3,4,5-Trimethoxybenzoyl)-tetrahydro-1,4-oxazine

Fear, tension or emotional stress  
Anxiety, neurotic headache  
Premenstrual tension, menstrual stress  
Behaviour disorders in children  
Stage-fever                      Occupational stress

### TABLETS

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