parameters provided by semiquantitative evaluation of the kidney biopsy by different techniques have been established to be not only of prognostic significance but also of particular clinical importance in decision making about the most appropriate therapeutic approach in SLE patients.

The now widely accepted original WHO classification of lupus glomerulonephritis (GN) basically separates normal glomerular histology class I (14–5.2%), mild mesangiopathy class II (40–15.0%) and mostly fairly indolent membranous GN class V (31–11.6%) from severe forms of renal disease, strictly requiring immunosuppressive therapy, focal segmental class III (65–24.3%) and particularly diffuse proliferative class IV (117–43.8%) lupus GN. Up to 50% of WHO class transformations have been demonstrated by our biopsy follow-up study of 155 SLE patients treated according to agreed standards. By considering additionally the histomorphologic pattern of glomerular inflammatory reaction in our 370 biopsy cases, mixed membranous and proliferative type of GN was confirmed to be particularly characteristic for SLE (141–38.1%). Furthermore, our studies provided evidence for a heterogeneity of GN types related at least to some extent to differences in pathogenesis in WHO classes III and IV.

A mesangial-transmembranous immune deposit distribution pattern has been found characteristic for SLE (55.9%) especially when the deposits contain »fingerprints« (17.3%). Our studies confirmed that prominent subendothelial immune deposits are among the most objective evidence of the activity of lupus GN. Furthermore, we share the opinion that kidney biopsy monitoring of the activity index and chronicity index, introduced in the early eighties into clinical trials by a group from NIH, can usefully contribute to planning the most appropriate therapy and biopsy follow-up evaluation.

Various immune mechanisms, including those related to extraglomerular deposits, as well as nonimmune mechanisms, play a role in the development and progression of tubulo-interstitial lesions, which have been confirmed to correlate best with the clinical parameters of renal insufficiency.

Extraglomerular vascular changes of various histopathological characteristics and pathogenesis have been far less extensively studied than glomerular despite the fact that they may also significantly influence the course and prognosis of lupus GN. Three main forms of vascular lesions were confirmed in our study of kidney tissue samples in 261 SLE patients 1. immune deposit (153–56.4%) accompanied by lupus microangiopathy, uncomplicated and hyalinizing, and vasculitis 2. premature arteriosclerosis (101–38.0%) and 3. thrombosis and thrombotic microangiopathy frequently related to positive anti-cardiolipin antibodies in the sera (11–4.1%).

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SP0101 CURRENT STANDARD TREATMENT FOR LUPUS NEPHRITIS

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Glomerulonephritis is a major cause for morbidity in systemic lupus erythematosus (SLE). In this disease, immune complex formation/deposition in the kidney results in intraglomerular inflammation with recruitment of leukocytes, and activation and proliferation of resident renal cells. Intense injury may destroy resident renal cells by necrosis or apoptosis resulting in fibrinoid necrosis. When injury is less intense, endocapillary cells respond by proliferating and production of extracellular matrix (proliferative lesions).

Determination of disease severity: Renal biopsy, examination of the urine sediment and measurement of C3 levels (and to a lesser degree of anti-DNA titers) are essential for the management of lupus nephritis. Treatment depends on the severity of the disease. Accordingly disease severity is determined by the presence or absence of high-risk factors. These include demographic (male gender, black race), clinical (failure to achieve response or marked delay in response, multiple relapses, pregnancy), laboratory (impaired renal function, severe anaemia with hematocrit less than 26%) and histologic features (mixed membranous and proliferative or proliferative nephritis; cellular crescents and/or fibrinoid necrosis; and moderate to high degrees of interstitial fibrosis and/or tubular atrophy).

Treatment: Patients with mild proliferative disease without risk factors are usually treated with corticosteroids alone or in combination with azathioprine. If the disease does not remit within 3–4 months, cytotoxic drugs such as cyclophosphamide or newer agents such as mycophenolate may be tried. For patients with moderate to severe proliferative nephritis, controlled trials have shown that pulse cyclophosphamide is the treatment of choice. Long-term follow-up of patients participating in these controlled trials suggest that combining pulse cyclophosphamide with pulse methylprednisolone increases efficacy but not toxicity. In general cytotoxic therapy continues 1 year beyond remission as shorter courses of cyclophosphamide have an increased risk for flares. Induction of response with cyclophosphamide followed by maintenance with agents such as azathioprine or cyclosporine is under investigation. For lupus membranous nephritis steroids, pulse cyclophosphamide therapy or cyclosporine may be used. Relapse rates are high when cyclosporine is discontinued. In addition to immunosuppressive therapy, aggressive management of co-morbid conditions (hypertension, dyslipidemia, osteoporosis) is of paramount importance.

Response rates and flares: Rates of clinical response and flares vary in different studies according to type of nephritis, treatment regimen, duration of therapy, and definition of clinical response and flare used. Flares pose a significant problem because of the risk for renal function deterioration due to cumulative damage as well as cumulative toxicities due to additional immunosuppressive therapy. Patients with nephritic flares (defined as increase in plasma creatinine level and reappearance of active nephritic urinary sediment), are more likely to progress to end-stage renal disease in spite of additional immunosuppressive therapy.

Side effects: Pulse cyclophosphamide is associated with an increased risk for herpes zoster infections on the short-term and with sustained amenorrhea or azoospermia on the long-term. Gonadotropin-releasing hormone agonist (GnRH-a) may prevent accelerated recruitment and depletion of ovarian follicles (via suppression of the gonadotrophin production in the pituitary gland) and therefore protect against premature ovarian failure. In a small case series, testosterone was found to be effective in preserving fertility in patients with nephrotic syndrome treated with a short course of cyclophosphamide.

New approaches: A recent controlled study reported that mycophenolate mofetil is equally effective to a regimen of oral cyclophosphamide and azathioprine used sequentially in patients with proliferative lupus nephritis. However, in this study follow up was short, patients had relatively mild disease and patients with high-risk factors were not included. A controlled study comparing mycophenolate mofetil to pulse cyclophosphamide is in progress. Other investigations explore the therapeutic potential of high-dose, immunoablative cyclophosphamide therapy alone or in combination with autologous stem cell transplantation, low-dose cyclophosphamide in combination with nucleoside analogues, or biologic response modifiers. High-dose cyclophosphamide or combinations of low-doses with fludarabine may result in profound bone marrow and immune suppression. Combinations of cyclophosphamide with biologic response modifiers have shown encouraging results in preclinical animal studies and may provide a major breakthrough in the treatment of severe lupus, similar to the introduction of cytotoxic agents a few decades ago.

SP0103 CHRONIC RENAL FAILURE IN SYSTEMIC RHEUMATIC DISEASES

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Prevalence of end-stage chronic renal failure (ESRF) in patients with systemic lupus erythematosus (SLE) and lupus nephritis varies considerably, supposedly due to not completely comparable groups of patients and different modes of treatment, but it may be estimated that about 15–20% of patients with lupus nephritis ultimately reach ESRF. This proportion is probably similar in adults and children, but may be substantially higher in African Americans (43% in one study). Rapid progression to ESRF during the first year of follow-up is uncommon and may occur in some patients with active multisystem disease, more than half of patients with lupus nephritis ultimately reaching ESRF do so in more than 5 years. Chronic renal failure may be reversible in about 20% of patients with lupus nephritis starting dialysis treatment. Although the mechanisms of this very high reversibility of renal failure in lupus nephritis remain unclear, immunosuppressive treatment does not seem to be of utmost importance and other factors (e.g. hypertension, renal vasoconstriction, endothelial dysfunction, etc.) may play a role. The view that the activity of SLE remits when lupus nephritis progresses to ESRF (so called lupus burn-out) is probably no longer substantiated and according to the Dutch study 71% of patients with lupus nephritis progressing to ESRF had flares with multi-system involvement in the last 4 years before the initiation of dialysis treatment. Lupus nephritis may represent between 1–4% of all patients treated by renal replacement therapy, their mean age is about 30 and males are more represented than in unselected SLE population. Estimated 5-year survival during hemodialysis treatment is between 81–89% and is at least comparable to other dialysis patients. Rather surprisingly, 5- and 10-year survival of patients with lupus nephritis treated by renal replacement therapy is not different from the survival of patients not progressing to ESRF. Extrarenal activity of SLE seems to be lower in patients treated by hemodialysis, but some extrarenal activity may be present in about 2/3 of dialyzed patients. Vascular access thrombosis may be much more frequent in dialyzed patients with lupus nephritis compared to other causes of ESRF,

the role of antiphospholipid antibodies is suspected, but not firmly substantiated. Experience with peritoneal dialysis in patients with lupus nephritis is limited and the potential risk of infectious complications is of major concern. Renal transplantation results in relatively high risk of not surviving in the first year after transplantation (5–15% mainly due to infectious complications. 5-year cadaveric graft survival is about 60% and renal transplantation probably does not result in higher 5-year survival than hemodialysis. Recurrence of lupus nephritis in transplants is rare, milder and better controlled by the instituted therapy. Repeated requirement of longer dialysis treatment (usually 6–12 months) before transplantation to achieve disease quiescence does not seem to be fully substantiated.

Acute renal failure is a common presentation of ANCA-positive renal vasculitis with focal segmental necrotizing/crescentic glomerulonephritis. Dialysis dependent renal failure may occur in 24–63% of these patients (of mean age 50–60 years) according to the severity of disease and time of referral. Early immunosuppressive treatment is able to spare renal function, e.g. initial dialysis was required in 59% and long-term dialysis in only 36% of patients from Wessex. Need for dialysis clearly confers poorer 5-year survival (about 50% vs. 75%). Renal transplantation is probably performed in no more than 10% of (usually younger patients with 92% 1-year patient and 85% 1-year graft survival. Delay in diagnosis and treatment remains to limit the therapeutic potential of current immunosuppressive treatment to improve long-term outcome of these patients.

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SP0106 CURRENT CONCEPTS IN ARTIFICIAL REPLACEMENT OF THE RHEUMATOID WRIST AND FINGER JOINTS

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Prosthetic replacement of wrist and finger joints is a key stone in the surgical treatment in rheumatoid arthritis. Severely destroyed joints are a source of pain and create deformities, which will severely affect the functionality of the hand. The wrist joint consists of a radiocarpal joint which provides flexion/extension and a radio-ulnar joint which allows pro-/supination.

A mobile radiocarpal joint helps to compensate for impaired elbow and finger joint. There is a variety of wrist prosthesis on the market. Overall the results with these prosthetic devices are mixed. There is generally a high failure rate with sometimes difficult revisions situations due to missing bone stock. The Swanson silastic implant, with reasonable longtime results, might be an alternative to preserve some motion. Nevertheless arthrodesis is still the gold standard on which the current wrist implants have to be measured. On the level of the radio-ulnar joint ulnar