

NEPHROLOGY

Rounds®

An Update on Systemic Lupus Erythematosus-Related Kidney Disease

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Renal disease is a common complication of systemic lupus erythematosus (SLE). It can affect the kidney as glomerulonephritis, tubulointerstitial nephritis, and antiphospholipid antibody syndrome (APS), manifestations that may occur alone or together. Glomerulonephritis (usually synonymous with the term, "lupus nephritis") is the most common and best-studied form of kidney involvement. Traditionally, severe forms of lupus glomerulonephritis have been treated with glucocorticoids plus prolonged courses of cyclophosphamide. However, recent studies with newer, less toxic regimens have yielded encouraging results. This issue of *Nephrology Rounds* reviews the types of kidney disease that can affect SLE patients and how these conditions are treated.

General assessment of the patient with SLE and kidney disease

A comprehensive patient history should look for symptoms of active SLE, such as polyarthralgia, photosensitive rashes, or chest pains (due to pleurisy or pericarditis). The degree of prior immunosuppression should be quantified. Examination should include blood pressure (hypertension is common in severe lupus nephritis or APS), the skin (eg, SLE rashes such as the classic butterfly, or livedo reticularis, which may be associated with APS), the mouth (ulcers), the heart and lungs for rales (indicating serositis), the jugular venous pulse, and lower limbs (for signs of fluid overload). Some patients with SLE-related kidney disease, however, have minimal extrarenal symptoms and signs. Typical initial tests are shown in Table 1.

Kidney biopsy

A kidney biopsy is performed in most cases when significant lupus-related kidney disease is suspected. Sometimes, therapy (eg, high-dose steroids) is started before the histology is available, when the pre-test probability of significant disease is high.

SLE-associated glomerulonephritis

Pathogenesis

The pathogenesis of lupus nephritis has recently been reviewed.¹ Deposition of immune complexes in the glomeruli plays a central role. These immune complexes can deposit in the mesangial, subendothelial, or subepithelial spaces (sometimes in all 3 spaces, simultaneously). Since mesangial or subendothelial deposits are adjacent to blood, they can easily activate complement and attract neutrophil polymorphs and mononuclear phagocytes, thus inducing an inflammatory form of kidney disease. In contrast, subepithelial deposits are separated from blood by the glomerular basement membrane and, thus, tend to cause "isolated" podocyte damage (and proteinuria).

Histopathology

The clinical and histological severity of lupus nephritis varies greatly; not just between patients, but sometimes also within a given patient, over time. SLE-associated glomerulonephritis is categorized into 1 of 6 variants, based on histology (Table 2).² Note that class V can occur simultaneously with class II, III, or IV. This histological classification is clinically useful because it predicts prognosis in the absence of treatment, and allows stan-

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Table 1: Initial tests ordered in the assessment of a patient with presumed SLE-associated kidney disease

Routine	Comment
Creatinine	Elevation may reflect acute or chronic injury or both
CBC	Anemia is associated with poorer prognosis; thrombocytopenia suggests APS
LDH	Elevated in TMA, but not specific
Urine dipstick and microscopy	Hematuria and proteinuria and pyuria suggest lupus glomerulonephritis
Spot urine protein/creatinine or 24-hr urine protein	Proteinuria may reflect acute or chronic injury or both
Serum C3, C4 (or CH50)	Usually low in immune complex glomerulonephritis
Anti-dsDNA	Usually increased in severe forms of SLE-associated glomerulonephritis
As clinically indicated	
Haptoglobin	Reduced in TMA
Anti-cardiolipin IgG, IgM	In the proper clinicopathological setting, a positive test suggests APS
Lupus anticoagulant	In the proper clinicopathological setting, a positive test suggests APS

TMA = thrombotic microangiopathy;
APS = antiphospholipid antibody syndrome.

standardization between study groups in trials. A histological classification of activity and chronicity has also been described, but its utility remains a subject of debate.

Clinical features

The clinical presentation of lupus nephritis includes “isolated” proteinuria/microhematuria, nephritic syndrome, nephrotic syndrome, and the rapidly progressive glomerulonephritis syndrome. It is often difficult to accurately predict from the clinical features the pathological changes that may be found on biopsy. Hence, renal biopsy remains very important in the initial evaluation.

Risk factors for poor renal outcomes include: increased creatinine at presentation, nephrotic range proteinuria, anemia, black race, and severity of histological change (eg, the presence of crescents or superimposed APS).¹

Treatment

It is generally accepted that immunosuppression with glucocorticoids and a cytotoxic agent is required for the following forms of SLE-associated glomerulonephritis: severe forms of active class III, all forms of active class IV, and severe forms of class V (eg, when V is associated with prolonged nephrotic syndrome).

Mild forms of active class III nephritis are often treated with glucocorticoids alone (these are often required for extra-renal disease anyway). The treatment

Table 2: Revised World Health Organization (WHO) classification of SLE-associated glomerulonephritis (abbreviated)²

Tubulointerstitial and vessel disease should also be reported.		
Class	Characteristics	Prognosis, if untreated
I	Mesangial immune deposits, but normal light microscopy	Good
II	Mesangial hypercellularity	Good
III	<50% glomeruli with endocapillary or extracapillary hypercellularity	Poor in the more severe forms
IV	>50% glomeruli with endocapillary or extracapillary hypercellularity	Poor
V	Subepithelial deposits +/- any of II, III, IV above	Poor in severe cases
VI	>90% glomeruli are globally sclerosed	Poor (immunosuppression not indicated however)

of mild forms of V is not well defined. Options include glucocorticoids alone (especially if extra-renal disease is present) or watchful waiting with nonimmunological therapies (see below). Cyclosporine is sometimes used as an alternative to cytotoxic agents in severe forms of class V nephritis and, currently, is being compared with cyclophosphamide in this setting.¹

Treatment of severe glomerulonephritis can be loosely divided into an induction phase and a maintenance phase. The purpose of the induction phase is to quickly induce remission. There is no universally accepted definition of complete remission, but it typically includes all of the following: reduction or stabilization of plasma creatinine, resolution of hematuria and pyuria, and reduction in proteinuria. The purpose of the maintenance phase is to maintain remission, while minimizing the adverse effects of medications. In both phases, glucocorticoids and a cytotoxic agent are used. The addition of a cytotoxic agent is routine because trials with a prolonged follow-up have revealed inferior renal outcomes with steroid-alone protocols.^{3,4}

In severe disease, steroids are often initiated as intravenous methylprednisolone 500-1000 mg daily for 3-5 days; steroids are then continued as oral prednisone 1 mg/kg/day (or equivalent) with a slow taper. There is evidence supporting the use of additional monthly pulses of intravenous methylprednisolone.⁵ Although plasmapheresis might appear to be an attractive adjunctive therapy (by removing immune complexes and other humoral mediators of glomerulonephritis), it has not been shown to add benefit to standard therapy.⁶

Until recently, the standard-of-care in many US centers has been to use intravenous cyclophosphamide as the cytotoxic agent, at least initially. The gold standard “National Institutes of Health (NIH) regimen”

involves intravenous cyclophosphamide 500-1000 mg/m² once monthly for 6 doses, then every 3 months for 2 years. This *extended* regimen was shown to reduce the risk of late renal relapse – albeit with more adverse events — as compared to a regimen of only 6 months.⁷ Of note, at least 3 years of follow-up was required to demonstrate improved renal outcomes in the extended-therapy group. Unfortunately, standard cyclophosphamide regimens are associated with significant adverse effects, including amenorrhea, infertility (both major concerns, since lupus nephritis often affects young women), and serious infection. Furthermore, these cyclophosphamide + steroid regimens do not induce remission or prevent relapse in all patients. Therefore, there is major interest in developing alternatives to cyclophosphamide that have a higher therapeutic index.

Alternatives to the extended NIH regimen in the treatment of severe SLE-associated glomerulonephritis

Lower dose cyclophosphamide

One approach is to use the lower-dose cyclophosphamide regimen that was assessed by the Euro-Lupus Nephritis Trial.⁸ Ninety patients (majority white and with class IV lupus nephritis) were randomized to a “high-dose” regimen or a lower-dose regimen of 500 mg/m² every 2 weeks for 6 doses. Both groups then received azathioprine. After a median follow-up of 41 months, renal outcomes were similar, but there was a trend towards more infections in the high-dose group.⁸ A subsequent report showed similar renal outcomes with a median follow-up of 73 months.⁹ Arguably, the applicability of this trial to the US context (where many patients with severe lupus nephritis are black) is limited.¹⁰

Mycophenolate mofetil

Mycophenolate mofetil (MMF) is an inhibitor of inosine monophosphate dehydrogenase (IMPDH). Its main immunological effect is to inhibit lymphocyte proliferation, although other effects such as downregulating expression of adhesion molecules on lymphocytes may be important. Because lymphocytes are more dependent on IMPDH (and the associated *de novo* pathway) to synthesize purines, MMF should be more lymphocyte-selective than azathioprine. MMF is now widely used in renal transplantation as an alternative to azathioprine and, in most trials, significantly lowers rates of acute rejection. Interestingly, *post hoc* analysis of early trials suggested that black patients need higher doses of MMF than white patients to fully benefit from its anti-rejection effects.¹¹ The adverse effects of MMF include diarrhea, abdominal discomfort, marrow suppression, and teratogenicity. Importantly, MMF does not affect gonadal function or cause infertility. There has been great interest in assessing its efficacy and safety in SLE-associated

glomerulonephritis. Several randomized, controlled (but not blinded), trials have compared MMF to cyclophosphamide as an induction or maintenance agent. Overall, the results have been very promising.

Chan et al reported on 42 patients with lupus nephritis randomized to prednisone + 6 months of oral cyclophosphamide (azathioprine then replaced the cyclophosphamide) or prednisone + MMF.¹² After 12 months, the rates of remission were similar in both groups. Adverse effects were more common in the cyclophosphamide group. A later report in the same subjects – with a median follow-up of 63 months – revealed similar renal outcomes, but fewer adverse effects in the MMF group. Concerns regarding the generalizability of these results have included the lack of black patients (who have poorer outcomes) and that the cyclophosphamide regimen was not the “gold-standard,” as discussed above.

Ginzler et al recently reported the first randomized controlled trial of MMF as an induction agent in American patients.¹³ Importantly, the proportion of black subjects enrolled was high (56%). Seventy-one subjects were randomized to MMF and 69 to cyclophosphamide. Intravenous cyclophosphamide was administered according to the NIH protocol and MMF was given daily to a maximum of 3 g/day (note the high target dose). Complete remission was defined as return to within 10% of normal levels of plasma creatinine, urinary protein, and urine sediment at 24 weeks. Complete remission occurred in 22.5% of patients randomized to MMF, but only in 5.8% of those randomized to cyclophosphamide ($p=0.005$). Partial remission was defined as improvement in all renal measures by at least 50% at the same time-point. This occurred in 29.6% of the MMF group versus 24.6% in the cyclophosphamide group ($p=0.51$). Adverse events tended to be more common in the cyclophosphamide group. Limitations of the trial included exclusion of patients with the most severe renal disease (creatinine clearance <30 mL/min) and relatively high rates of patients who were “lost to follow-up” (21.7%) in the cyclophosphamide arm after only 24 weeks. Longer-term outcomes are not yet available.

With regard to MMF as a maintenance agent, Contreras et al, reported on 59 patients with lupus nephritis, who had already received induction therapy with glucocorticoids and intravenous cyclophosphamide.¹⁴ They were then randomized to intravenous cyclophosphamide every 3 months or daily MMF or daily azathioprine (all subjects continued to receive steroids). The composite outcome of death or chronic renal failure was significantly more common in the cyclophosphamide group compared with the other 2 groups. Adverse events and number of days hospitalized were also more common in the cyclophosphamide group; for example, note the striking difference in rates of amenorrhea (Table 3).

Table 3: Rates of certain adverse events during maintenance therapy for lupus nephritis¹⁴

Adverse event	Azathioprine	MMF	Cyclophosphamide
Amenorrhea (%)	8	6	32
Total Infections (%)	29	32	77
Major Infections (%)	2	2	25
Days of hospitalization per patient year	1	1	10

Combining the above studies, MMF appears to be a reasonable alternative to cyclophosphamide as an induction or maintenance agent in many patients with lupus nephritis, particularly where preservation of fertility or susceptibility to infection is a major concern. The efficacy of MMF (at least in short- and medium-term follow-up) is better or similar and the adverse effects are markedly less than with cyclophosphamide. One major concern is that long-term comparison data with cyclophosphamide are not yet available and, in previous studies, the beneficial effects of cyclophosphamide on renal function took years to be detected.^{4,7}

Many clinicians would still prefer the NIH cyclophosphamide regimen as first-line therapy in the following situations:

- when there is severe, acute glomerulonephritis associated with creatinine clearance <30 mL/min (such patients have not been included in the above trials)
- when there is co-presence of severe extrarenal disease, eg, cerebritis (where cyclophosphamide is standard-of-care)
- when there are major concerns regarding medication adherence with a daily PO regimen.

Azathioprine

Azathioprine is not commonly used as an induction agent, but it is sometimes used in the maintenance phase, (eg, after 6 doses of intravenous cyclophosphamide have been administered).^{8,14} In this setting, there is evidence that it has a better therapeutic index than continued cyclophosphamide¹⁴ and it does not affect gonadal function. Azathioprine also has the advantage of lower cost, fewer gastrointestinal adverse effects and, probably, less teratogenicity than MMF. In fact, there are no trials demonstrating that MMF is superior to azathioprine in the treatment of lupus nephritis.

Serological markers of disease activity in SLE-associated glomerulonephritis

In most patients with active glomerulonephritis, serum complement proteins C3 and C4 will decrease

and anti-double-stranded DNA antibody (anti-dsDNA) will increase. However, the reverse does not apply; decreased C3, C4, and a raised anti-dsDNA do not imply that *severe* glomerulonephritis will be found on biopsy. Serum C3 and C4 (and CH50) will usually increase and anti-dsDNA will usually decrease, if active glomerulonephritis is successfully controlled with immunosuppression. In some patients, changes in the concentrations of these markers “in the wrong direction” precede relapse; thus, serial monitoring of these markers can be useful. In practice, such changes usually prompt more frequent clinical monitoring for relapse rather than a change in immunosuppression *per se*.

Glomerulonephritis refractory to standard induction therapy

To avoid unnecessary immunosuppression, it is important to determine whether the glomerulonephritis is immunologically active. A persistently raised plasma creatinine or persistent proteinuria, for example, could represent stage VI disease (an irreversible condition where immunosuppression would likely cause more risk than benefit) or renal damage from APS (which is usually not treated with immunosuppression, see below). Ongoing activity is suggested by persistently raised creatinine, persistent proteinuria and hematuria and pyuria, as well as by the failure of C3, C4, and anti-dsDNA to normalize or at least improve. In some cases, a repeat kidney biopsy may be helpful to clarify the diagnosis.

The options for a lupus nephritis that remains active despite standard induction therapy include further pulses of high-dose intravenous methylprednisolone, switching from cyclophosphamide to MMF or *vice versa*, rituximab, intravenous IgG or, (in rare cases), high-dose cyclophosphamide with stem-cell transplantation.¹⁵

Rituximab

The monoclonal anti-CD20 agent, rituximab was developed for use in lymphomas, but there is great interest in studying this agent in connective tissue diseases. Adverse effects to date appear limited. Although preliminary results with rituximab in refractory lupus nephritis are encouraging, trials are awaited.¹⁶

Non-immunological therapies

The focus in lupus-related kidney disease has been mainly on the optimal immunosuppression protocol; nevertheless, standard “chronic kidney disease measures” should be employed. Hypertension is common and may be essential, due to glomerulonephritis, APS, steroids, or a combination of

these. Rigorous control of hypertension will slow the progression of renal disease.¹⁷ As per the Joint National Committee (JNC) VII, the blood pressure (BP) goal is <130/80 mm Hg.¹⁷ There is evidence that dual blockade of the renin-angiotensin-aldosterone system with an angiotensin-converting enzyme (ACE)-inhibitor plus an angiotensin receptor blocker (ARB) slows the progression of nondiabetic glomerular disease;¹⁸ as a result, this strategy should be strongly considered. It seems reasonable to apply other standard chronic kidney disease (CKD) treatment guidelines for management of anemia, hyperparathyroidism, etc. There is increasing appreciation that SLE is associated with premature atherosclerosis and that cardiovascular disease is a major cause of morbidity and mortality over the long-term.¹⁹ Aggressive control of hyperlipidemia in patients with SLE-associated kidney disease, therefore, seems appropriate.

Acute tubulointerstitial nephritis

This manifestation may be an isolated finding or, more commonly, may occur with glomerulonephritis. Isolated acute tubulointerstitial nephritis should be suspected where there is a raised plasma creatinine, but little proteinuria or hematuria (urine microscopy may show leukocytes). It is usually treated with glucocorticoids.

Antiphospholipid syndrome (APS)

It is increasingly recognized that APS can contribute to kidney disease in patients with and without SLE.²⁰ Renal vessels of any size may be affected, which can induce downstream acute, subacute, or chronic *non-inflammatory* injury (Table 4). Renal biopsy is required to demonstrate APS involving the smaller arteries, arterioles, and glomerular capillaries. Patients with SLE and kidney disease can have biopsy evidence of APS alone or of APS plus immune complex glomerulonephritis. This distinction is important, since renal APS alone is typically treated “only” with long-term anticoagulation, whereas the presence of both requires anticoagulation plus immunosuppression. Note that on electron microscopy, subendothelial deposits due to APS do not contain immunoglobulin, unlike the classic deposits (of immune complexes) with lupus nephritis.

Severe renal involvement may occur in catastrophic APS and is usually treated with high-dose steroids, plasma exchange, and anticoagulation.²⁰

Renal transplantation

Registry data indicate that recipient and allograft survival in SLE patients are equivalent to non-SLE controls.²¹ Thus, all patients with end-stage

Table 4: Types of renal involvement in APS

Vessel damaged or thrombosed	Clinico-pathological consequences
Renal artery	Hypertension, renal infarction
Renal vein	Renal infarction
Intrarenal arteries/arterioles*	Cortical atrophy, hypertension, TMA, CKD
Glomerular capillaries*	Proteinuria, TMA, CKD

*Massive acute thrombosis may be associated with severe acute renal failure and malignant hypertension

TMA = thrombotic microangiopathy; CKD = chronic kidney disease

renal disease (ESRD) due to SLE-related kidney disease should be considered for renal transplantation. Note that the majority of these patients have already received significant immunosuppression and often have associated complications (eg, steroid-induced bone disease). Thus, it seems reasonable to consider such patients for steroid-free protocols.

SLE is often associated with the presence of autoantibodies (usually IgM) in the serum that can cause positive lymphocytotoxicity crossmatches against both recipient and donor lymphocytes. These autoantibodies are not contraindications to transplantation. Treatment of the serum with dithiothreitol (DTT) removes the IgM autoantibodies, converting many of these crossmatches from positive to negative. Other tests such as flow cytometry crossmatching can help determine the clinical significance of these autoantibodies.

As with other glomerular diseases that can recur after transplantation, transplant should not be performed until the SLE is clinically quiescent. In practice, clinically significant recurrence or allograft loss from a recurrence of lupus nephritis is rare.²² Many centers prefer a 6-12 month period of clinical quiescence before proceeding with transplantation to reduce the risk of recurrence. A waiting period is also indicated in patients who have had rapid progression to dialysis dependency because some of these may recover enough renal function to come off dialysis. If a patient is receiving anticoagulation for APS prior to transplantation, anticoagulation should be resumed as soon as safely possible (initially with intravenous heparin) after the transplant surgery. This is to reduce the risk of thrombosis of the allograft or other sites. Less clear is the role of anticoagulation after transplantation in SLE patients with antiphospholipid antibodies, but no history of thrombosis.

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References

1. Houssiau FA. Management of lupus nephritis: an update. *J Am Soc Nephrol* 2004;15(10):2694-704.
2. Weening JJ, D'Agati VD, Schwartz MM, et al. The classification of glomerulonephritis in systemic lupus erythematosus revisited. *J Am Soc Nephrol* 2004;15(2):241-50.
3. Austin HA 3rd, Klippel JH, Balow JE, et al. Therapy of lupus nephritis. Controlled trial of prednisone and cytotoxic drugs. *N Engl J Med* 1986;314(10):614-9.
4. Steinberg AD, Steinberg SC. Long-term preservation of renal function in patients with lupus nephritis receiving treatment that includes cyclophosphamide versus those treated with prednisone only. *Arthritis Rheum* 1991;34(8):945-50.
5. Illei GG, Austin HA, Crane M, et al. Combination therapy with pulse cyclophosphamide plus pulse methylprednisolone improves long-term renal outcome without adding toxicity in patients with lupus nephritis. *Ann Intern Med* 2001;135(4):248-57.
6. Lewis EJ, Hunsicker LG, Lan SP, Rohde RD, Lachin JM. A controlled trial of plasmapheresis therapy in severe lupus nephritis. The Lupus Nephritis Collaborative Study Group. *N Engl J Med* 1992;326(21):1373-9.
7. Boumpas DT, Austin HA 3rd, Vaughn EM, et al. Controlled trial of pulse methylprednisolone versus two regimens of pulse cyclophosphamide in severe lupus nephritis. *Lancet* 1992;340(8822):741-5.
8. Houssiau FA, Vasconcelos C, D'Cruz D, et al. Immunosuppressive therapy in lupus nephritis: the Euro-Lupus Nephritis Trial, a randomized trial of low-dose versus high-dose intravenous cyclophosphamide. *Arthritis Rheum* 2002;46(8):2121-31.
9. Houssiau FA, Vasconcelos C, D'Cruz D, et al. Early response to immunosuppressive therapy predicts good renal outcome in lupus nephritis: lessons from long-term follow-up of patients in the Euro-Lupus Nephritis Trial. *Arthritis Rheum* 2004;50(12):3934-40.
10. Gorman C, Bhatia A, Rahman A. This house believes that low-dose intravenous cyclophosphamide is superior to standard high-dose regimens for treatment of lupus nephritis. *Rheumatology (Oxford)* 2005;44(3):398-401.
11. Neylan JF. Immunosuppressive therapy in high-risk transplant patients: dose-dependent efficacy of mycophenolate mofetil in African-American renal allograft recipients. U.S. Renal Transplant Mycophenolate Mofetil Study Group. *Transplantation* 1997;64(9):1277-82.
12. Chan TM, Li FK, Tang CS, et al. Efficacy of mycophenolate mofetil in patients with diffuse proliferative lupus nephritis. Hong Kong-Guangzhou Nephrology Study Group. *N Engl J Med* 2000;343(16):1156-62.
13. Ginzler EM, Dooley MA, Aranow C, et al. Mycophenolate mofetil or intravenous cyclophosphamide for lupus nephritis. *N Engl J Med* 2005;353(21):2219-28.
14. Contreras G, Pardo V, Leclercq B, et al. Sequential therapies for proliferative lupus nephritis. *N Engl J Med* 2004;350(10):971-80.
15. Burt RK, Traynor A, Statkute L, et al. Nonmyeloablative hematopoietic stem cell transplantation for systemic lupus erythematosus. *JAMA* 2006;295(5):527-35.
16. D'Cruz DP, Hughes GR. The treatment of lupus nephritis. *BMJ* 2005;330(7488):377-8.
17. Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA* 2003;289(19):2560-72.
18. Nakao N, Yoshimura A, Morita H, Takada M, Kayano T, Ideura T. Combination treatment of angiotensin-II receptor blocker and angiotensin-converting-enzyme inhibitor in non-diabetic renal disease (COOPERATE): a randomised controlled trial. *Lancet* 2003; 361(9352):117-24.
19. D'Cruz DP. Systemic lupus erythematosus. *BMJ* 2006;332(7546): 890-4.
20. Nzerue CM, Hewan-Lowe K, Pierangeli S, Harris EN. "Black swan in the kidney": renal involvement in the antiphospholipid antibody syndrome. *Kidney Int* 2002;62(3):733-44.
21. Ward MM. Outcomes of renal transplantation among patients with end-stage renal disease caused by lupus nephritis. *Kidney Int* 2000; 57(5):2136-43.
22. Briganti EM, Russ GR, McNeil JJ, Atkins RC, Chadban SJ. Risk of renal allograft loss from recurrent glomerulonephritis. *N Engl J Med* 2002;347(2):103-9.

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