



Systemic lupus erythematosus in the intensive care unit

Rishi Raj, MD, Susan Murin, MD, Richard A. Matthay, MD,
Herbert P. Wiedemann, MD*

*Department of Pulmonary and Critical Care Medicine, Cleveland Clinic Foundation, Desk A-90,
9500 Euclid Avenue, Cleveland, OH 44195, USA*

Systemic lupus erythematosus (SLE) is an inflammatory autoimmune disorder that affects multiple organ systems and causes significant morbidity and mortality. Although the 5-year survival rate in most recent studies exceeds 90% [1], its high incidence (124 cases per 100,000) makes the disease responsible for a significant mortality [2]. Infection, cardiovascular disease, and organ failure are among the leading causes of death in almost all the studies looking at mortality in SLE [3]. Although the disease affects virtually all organ systems with varying degrees of severity, this article focuses on clinical manifestations of the disease that are severe enough to necessitate admission to the intensive care unit (ICU) (Table 1).

Pulmonary involvement in SLE

This section updates and revises the authors' earlier reviews of the respiratory complications of SLE [4,7]. Infection is the most common form of pulmonary involvement in patients with SLE [4]. Infections in patients with SLE can be confused with exacerbation of the underlying disease process, and empiric therapy with broad-spectrum antimicrobial agents is warranted until infection is conclusively ruled out. Bronchoscopy or open-lung biopsy may be needed in addition to routine cultures to exclude an infectious origin.

Acute lupus pneumonitis

A diagnosis of acute lupus pneumonitis can be made after rigorously excluding infections in patients presenting with features resembling infectious

* Corresponding author.

E-mail address: wiedemh@ccf.org (H.P. Wiedemann).

Table 1
Systemic lupus erythematosus in the ICU

-
- Pulmonary/airway complications
 - Lupus pneumonitis
 - Diffuse alveolar hemorrhage
 - Shrinking-lung syndrome
 - Upper airway complications
 - Cardiovascular complications
 - Coronary artery disease
 - Premature atherosclerosis
 - Vasculitis
 - Myocarditis
 - Pericarditis
 - Miscellaneous complications
 - Neuropsychiatric complications
 - Lupus cerebritis
 - Cerebrovascular accidents
 - Aseptic meningitis
 - Seizures
 - Miscellaneous complications
 - Gastrointestinal complications
 - Bowel perforation
 - Pancreatitis
 - Miscellaneous complications
 - Infectious complications
 - Viruses
 - Bacteria
 - Fungi
 - Protozoa
 - Mycobacteria
-

pneumonia. The reported incidence of this syndrome varies from 0.9% to 11.7% [5], but the exact incidence is difficult to determine because the literature on acute lupus pneumonitis consists largely of case reports and small case series. Dyspnea, cough, fever, and, occasionally, hemoptysis are the usual presenting symptoms [5]. Unilateral or bilateral alveolar infiltrates are seen on the chest radiograph [6,7], although one case of biopsy-proven lupus pneumonitis presenting with a normal chest radiograph has been reported [8]. Clinical and radiographic evidence of pleural involvement is common. Hypoxemia and respiratory alkalosis may be seen on arterial blood gas studies, and ventilatory assistance may be required in severe cases [5,9].

Although lupus pneumonitis was the initial manifestation of SLE in half of the 12 patients in one series [5], most patients with lupus pneumonitis have established SLE at presentation. Mortality in patients with lupus pneumonitis may be as high as 50% [5], and a prompt diagnosis and institution of appropriate therapy early in the course of disease are crucial. A high index of suspicion should be maintained for the young female patient presenting with unexplained pulmonary infiltrates. Pregnant patients are at a high risk of developing lupus pneumonitis in the postpartum period [10], because approximately 30% to 50%

of women with SLE will have an exacerbation of SLE from 2 days to 8 weeks postpartum [11].

Blood and sputum cultures are necessary, and bronchoscopy or open-lung biopsy may be needed to exclude other conditions, such as pneumonia, alveolar hemorrhage, and other acute pulmonary processes that resemble lupus pneumonitis clinically and radiographically [12].

Pathologic findings in lupus pneumonitis are not specific [12,13] except for hematoxylin-eosin bodies or lupus erythematosus cells that in rare cases can be seen on light microscopy [14]. Inflammation and tissue injury are common, but vascular abnormalities are not usually seen. Alveolitis, alveolar necrosis, alveolar hemorrhage, edema, interstitial pneumonitis, hyaline membranes, interstitial pneumonitis, capillary thrombosis, and deposition of immunoglobulin and complement may be seen on histopathologic examination [15,16].

Reports of efficacy of various therapeutic options for acute lupus pneumonitis are largely anecdotal, and there are no controlled trials evaluating one therapy versus another. Response to high-dose corticosteroids (equivalent of prednisone, 1–2 mg/kg/day) is generally favorable [5,13,17–21]. In patients who do not respond to corticosteroids, azathioprine is the best-studied of the adjunctive agents, which include pulse cyclophosphamide, methotrexate, and plasmapheresis in various combinations [5,22–28]. Three of the seven patients reported by Matthay et al responded to azathioprine and survived after failing to respond to high-dose corticosteroid therapy [26]. Therapy should first be initiated with corticosteroids; azathioprine or other immunosuppressive agents should be added if there is no response to corticosteroids or in critically ill patients [4].

Alveolar hemorrhage

Alveolar hemorrhage is a rare but serious complication of SLE with high morbidity and mortality. Two percent of patients with SLE will develop alveolar hemorrhage; it accounts for 1.5% to 3.7% of total hospitalizations and for one out of five hospital admissions for pulmonary involvement in SLE [29–32]. The severity of alveolar hemorrhage in SLE may range from an uncommon mild and chronic form [33–35] to massive bleeding resulting in death. The report by Zamora et al [32] of their experience with 15 patients admitted with 19 episodes of alveolar hemorrhage is the single largest case series of patients with alveolar hemorrhage and SLE. More recently, Santos-Ocampo et al recently reported seven patients who were admitted for 11 episodes of alveolar hemorrhage [36], and Lee et al reported seven patients with 9 episodes of diffuse alveolar hemorrhage [37,38].

Most patients with diffuse alveolar hemorrhage and SLE are young women [32,36,37]. Patients present with an abrupt onset of symptoms of cough and dyspnea, sometimes accompanied with fever. The classic triad of hemoptysis, falling hematocrit, and pulmonary infiltrates is not uniformly present in all patients [32,36,37]. Hemoptysis usually occurs during the course of illness, and 25% [29] to 100% [31] of patients have hemoptysis at presentation [22,32,36]. Some patients never develop hemoptysis [36,39]. Bilateral diffuse alveolar

infiltrates are seen on the chest radiograph, but they may be patchy, with lower lobe predominance [32]. Most patients have new pulmonary infiltrates on presentation, but up to 17% of patients in one series did not have new pulmonary infiltrates on presentation [29]. Respiratory failure may occur, and more than half of affected patients in most series required mechanical ventilation [22,31,32,36,37,40].

A decrease in hematocrit is characteristic of this syndrome and occurs in 75% [31] to 100% [29,41,42] of patients on presentation. Antinuclear antibodies (ANAs) are universally present, and complement levels are usually decreased [22,40,43]. A higher prevalence of anticardiolipin antibodies reported in one series [31] has not been confirmed by other authors [32].

Patients with alveolar hemorrhage usually have lupus nephritis as a pre-existing condition [22,31,32]. Lupus nephritis was present in 93% of patients in the series reported by Zamora et al [32] and in 83% of patients in the series reported by Lee et al [38]. This proportion was higher than the incidences of 60% reported previously by Zamora et al [32] and 75% in the series reported by Santos-Ocampo et al [36].

Fever in combination with new pulmonary infiltrates on presentation may make distinction from infectious pneumonia difficult. Fever (oral temperature > 102.2°F) was present in 82% [36] and 83% [38] of patients in the more recent series but in only 26% [32] of patients reported by Zamora et al.

Thirty-two percent of the patients reported by Zamora et al [32] and 1 of the 10 patients reported by Lee et al [38] had a viral or bacterial pneumonia on presentation. Cytomegalovirus, herpes simplex virus, and *Legionella*, *Aspergillus*, *Klebsiella* species, and *Staphylococcus* species were among the infectious agents at presentation in these patients [22,31,32,38]. Mechanical ventilation in these patients predisposes them to nosocomial pneumonias, which occurred in 16% [32] of patients in the largest series, and 33% [38] of the series from Korea. Interestingly, none of the patients in the series reported by Santos-Ocampo et al had primary or nosocomial infection [36]. Patients developing nosocomial infections were found to have a mortality rate of 100%, despite aggressive treatment [32,38].

Most patients with SLE-associated alveolar hemorrhage have established SLE on presentation, but alveolar hemorrhage was the presenting manifestation of SLE in more than 12% of the 72 cases reported in the literature and reviewed by Zamora et al, in 20% of the cases from the University of Colorado [32], and in 14% in Santos-Ocampo's series [36]. A diagnosis of SLE is established during hospitalization in most of these patients presenting with alveolar hemorrhage. The diagnosis may be delayed in some cases, however, particularly in cases initially diagnosed as idiopathic pulmonary hemosiderosis [31,33] or presenting as iron-deficiency anemia from chronic blood loss [35].

Patients without a pre-existing diagnosis of SLE should undergo serologic testing for SLE and to exclude alternate diagnoses as Wegener's granulomatosis or Goodpasture's syndrome. Early bronchoscopy with bronchoalveolar lavage (BAL) is recommended to demonstrate alveolar hemorrhage and to collect

specimens for culture. Gross bleeding or bloody lavage fluid is usually seen during an acute event. Hemosiderin-laden macrophages suggest the diagnosis of alveolar hemorrhage in the absence of gross bleeding [30]. Open-lung biopsy may be necessary in the absence of classic manifestations and serologic evidence of the disease [4].

Mononuclear and polymorphonuclear cell interstitial infiltration, hyaline membranes, alveolar necrosis, edema, microvascular thrombosis, hemosiderin-laden macrophages, vascular intimal proliferation, and organized intramural thrombi [22] may be seen on histopathologic studies in patients undergoing lung biopsy [12,44]. Electron microscopy shows granular electron-dense material [33,45] that corresponds to the granular deposits of IgG, other antibodies, and C3 along alveolar, interstitial, or capillary endothelial cells seen on immunofluorescence study [22,25,40,43,44]. Capillaritis is being increasingly noted in this condition since the description by Myers and Katzenstein in 1986 [44]. Capillaritis was detected in 80% of the patients who underwent lung biopsy (N = 8) in the series reported by Zamora [32] et al and in both patients who underwent lung biopsy in the series reported by Santos-Ocampo et al [36].

Mortality in patients with alveolar hemorrhage is high. Most series report mortality rates ranging from 40% to more than 90% [9,20,22,25,29,32,38,44,46]. Mechanical ventilation, associated infection at presentation, nosocomial infection, and treatment with cyclophosphamide were associated with a higher mortality rate in earlier studies [32]. Cyclophosphamide therapy and respiratory failure necessitating mechanical ventilation are probably markers of more severe disease; these variables were not analyzed independently for their effect on mortality. The need for mechanical ventilation and cyclophosphamide did not adversely affect mortality in the case series reported by Santos-Ocampo et al [36]. Although the excellent survival rates in this group may have resulted from patients' being less ill than in the previous studies, the therapy, which included antibiotics even in the absence of positive cultures and a combination of cyclophosphamide and plasmapheresis in patients not responding adequately to corticosteroids, may have contributed to the improved outcomes [36].

There are no randomized studies comparing the efficacy of various available therapeutic options. High-dose corticosteroids are the first line of therapy [31,32,36], with adjunctive immunosuppressive agents added for critically ill patients or lack of response to corticosteroids [22,31,36,47]. Cyclophosphamide is the most frequently used agent [22,36]. Cyclophosphamide, along with other therapeutic modalities, was used in 70% of patients reported by Santos-Ocampo et al, with 100% survival [36]. This survival rate contrasts with the 46% survival rate in the series reported by Zamora et al, who used cyclophosphamide in 68% of patients [32]. Azathioprine and 6-mercaptopurine have been used sporadically [22]. Plasmapheresis has also been used with success in some patients with alveolar hemorrhage and SLE [32,36,40,48]. Plasmapheresis results in clinical improvement, as noted in a patient with recurrent episodes of alveolar hemorrhage responding to plasmapheresis on every occasion [49]. In the case series reported by Santos-Ocampo et al [36], plasmapheresis was used with excellent

overall results in patients not responding to corticosteroids and cyclophosphamide, but the exact contribution of plasmapheresis to improved survival rates can be debated [32,36,49].

Acute, reversible hypoxemia

In 1991, Abramson et al [50] reported acute, reversible hypoxemia in lupus patients hospitalized with SLE exacerbation but without significant pulmonary involvement. Alveolar-arterial oxygen gradients were elevated in 6 of 10 patients with normal or nearly normal chest radiographs. Pleuritic chest pain, dyspnea, and chest discomfort were present in all six patients. Pulmonary function testing showed a reduced vital capacity and diffusing capacity of carbon monoxide. Complement degradation products were significantly elevated in these patients. Corticosteroid therapy resulted in improved A-a gradient (mean, 30.4 to 11.6 mmHg), pulmonary function tests, and complement degradation product levels. Martinez-Taboada et al [51] subsequently reported a similar clinical picture in four patients with SLE. Complement-mediated aggregation and activation of neutrophils similar to the sequestration of activated neutrophils in lungs of hemodialysis patients may be responsible for this syndrome [50].

Shrinking-lung syndrome

Shrinking-lung syndrome occurs in patients with established SLE, but two cases have been reported in which this syndrome was the presenting manifestation of SLE [52]. Patients with shrinking-lung syndrome have dyspnea, respiratory muscle dysfunction, characteristic chest radiographic findings of small lung volumes, elevated hemidiaphragms, and basilar atelectasis in the absence of significant pulmonary parenchymal or pulmonary vascular involvement [53]. Respiratory function may worsen to the point of requiring mechanical ventilation. Respiratory muscle weakness is common in patients with SLE, and sophisticated physiologic testing has shown that this muscle weakness, and not pleural adhesions and lupus pleurisy, as hypothesized in the earlier reports [53,56], is the cause of most cases of pulmonary restriction in patients with lupus [54,55]. Diaphragmatic dysfunction is present in patients with shrinking-lung syndrome [56]. This dysfunction characteristically results in orthopnea, which should suggest the diagnosis [56,57]. Most patients with shrinking-lung syndrome do not have generalized muscle weakness or evidence of myositis or vasculitis, although these conditions may be present in some patients [58]. Steroid myopathy is not likely to be the cause of muscle dysfunction, because shrinking-lung syndrome has been documented in patients before initiation of steroid therapy, and corticosteroids have been shown to result in clinical improvement in case reports and small case series [52,54,59]. In anecdotal case reports, treatment with β -adrenergic agonists and theophylline [60] have resulted in improved pulmonary functions. Response to therapy is variable, and many patients will stabilize over time [56] despite the presence of significant dyspnea and muscle weakness [54].

Upper airway involvement

Unlike other connective tissue disorders such as rheumatoid arthritis, Wegener's granulomatosis, and relapsing polychondritis, the upper airway is involved only rarely in SLE [61]. Hypopharyngeal ulceration, laryngeal inflammation, epiglottitis, subglottic stenosis, and vocal cord paralysis have been reported [62–66] in patients with SLE. Patients with SLE may be excessively prone to postintubation complications. Two of the four patients with upper airway involvement who had clinically and serologically active SLE developed subglottic stenosis after brief (3-to 48-hour) periods of endotracheal intubation. One patient improved with corticosteroids, but the other patient required tracheostomy [4].

Hypopharyngeal ulceration was the initial manifestation of SLE in one patient who needed intubation [67]. Rarely, the larynx may be involved by SLE vasculitis [67].

Neuropsychiatric manifestations of lupus

The central nervous system (CNS) is commonly involved in SLE. The following section discusses the acute manifestations of SLE including lupus cerebritis, cerebrovascular accidents, aseptic meningitis, seizures, and transverse myelitis. Although neuropsychiatric lupus erythematosus (NPLE) may be the initial manifestation of SLE, studies suggest that NPLE is more likely to occur when SLE is clinically and serologically active [68–73].

Cerebrovascular accidents

Analysis of data from the Canadian lupus population reveals that after controlling for risk factors (sex, age, systolic blood pressure, diastolic blood pressure, smoking, diabetes, cholesterol levels, and left ventricular hypertrophy), the relative risk for stroke in lupus patients is 7.9 (95% confidence interval [CI], 4.0–13.6) [74]. During the past decade, several investigators have emphasized the association of antiphospholipid antibodies and emboli from cardiac valvular lesions with thrombotic occlusion [75–83]. Stroke syndromes secondary to NPLE can affect any area of the brain [84–87]. Patients can present acutely with transient ischemic attacks, hemiplegia, aphasia, cerebral dysfunction, cortical blindness, or other deficits of cerebral function. Symptoms can be caused by intracranial hemorrhage from aneurysms [88,89], thrombotic strokes from vasculitis or vasculopathy, or embolic strokes from cardiac emboli.

Transverse myelitis

Spinal cord myelopathy is an infrequent but devastating manifestation of NPLE. Patients present with weakness or paralysis (paraplegia or quadriplegia), bilateral sensory deficits, and impaired sphincter control [90,91]. Transverse

myelitis is often the initial or an early manifestation of SLE [91]. Symptoms usually evolve over a matter of hours or days. The diagnosis is established clinically and is supported by characteristic laboratory abnormalities, including elevated protein levels in the cerebrospinal fluid (CSF) (82%), pleocytosis (70%), and a CSF glucose level less than 30 mg/dL (50%) [92]. Magnetic resonance imaging of the spinal cord may show characteristic abnormalities of cord edema if obtained early [93]. Transverse myelitis is caused by vasculitis in some patients [90] and is associated with antiphospholipid antibodies in others [94]. Because of the poor prognosis, early diagnosis and aggressive therapy of transverse myelitis are important [95,96]. Success in a limited number of cases has been reported with the use of combination of prednisone, cyclophosphamide, and plasmapheresis [97,98]

Seizures

Seizures are common manifestations of NPLE. They may occur before the development of other symptoms of SLE or at any time during the disease course [70]. Any kind of seizure can occur, giving diffuse or focal symptoms. Grand mal seizures are most common, although focal, petit mal, and temporal lobe seizures have also been observed. Seizure episodes are usually limited, although status epilepticus can occur frequently, signaling a preterminal event [99]. Seizures may occur in isolation or accompanying other neurologic symptoms such as strokes or intracranial hemorrhage. Consequently, the etiology of seizures in NPLE is multifactorial. Indeed, antineuronal antibodies, focal ischemia, and infarcts caused by vasculitis or antiphospholipid antibodies, embolic phenomenon, and hemorrhage have all been implicated [73].

Aseptic meningitis

SLE patients with aseptic meningitis present with headache, meningeal signs, and CSF pleocytosis [100]. The pleocytosis is most commonly less than 200 to 300 cells/mm³, predominantly lymphocytes. Rarely, significantly higher cell counts with a neutrophil predominance can occur in severely ill patients. Infectious meningitis of any cause [101] and aseptic meningitis secondary to medications such as nonsteroidal anti-inflammatory drugs, particularly ibuprofen, and azathioprine need to be excluded [102,103]. Aseptic meningitis caused by NPLE responds to corticosteroid therapy [73].

Other CNS involvement

Thrombotic thrombocytopenic purpura [73], atherosclerotic or embolic strokes, subdural hematoma [104], and intracerebral hemorrhage occur with increased frequency in SLE patients and may cause CNS dysfunction unrelated to NPLE [73].

Diagnostic and therapeutic considerations

Although not specific for lupus cerebritis, elevated CSF IgG, IgM, and IgA indices or the presence of oligoclonal bands have been observed in NPLE patients, particularly those with diffuse manifestations [105,106]. Antineuronal antibodies have been noted to be concentrated in the CSF and found more frequently in patients with nonfocal NPLE presentations [107]. Although conventional MR imaging is the diagnostic technique of choice for patients with neuropsychiatric symptoms of SLE [108], computed tomographic (CT) scanning is used more frequently because of practical considerations.

Immunosuppressive therapy should be considered after infections have been rigorously excluded. There have been no controlled clinical trials proving the value of corticosteroids or cytotoxic medications in the treatment of NPLE. Clearly some patients may improve without these medications [70]. Many clinicians use pulse methylprednisolone for severe cases, followed by addition of cytotoxic medications or plasmapheresis when there is no response to high-dose corticosteroids [109]. High-dose corticosteroids should be used for suspected vasculitis, and cytotoxic medications should be considered early during the course of disease, but the value of corticosteroids in thrombosis or emboli associated with antiphospholipid antibodies is debated [110]. Neuwelt et al reported a significant improvement in 69% of 31 patients with severe NPLE who were administered pulse cyclophosphamide after not responding to high-dose steroid therapy [111]. In patients with antiphospholipid antibodies, antiplatelet drugs and anticoagulation therapy seem beneficial; however, these agents should be used with caution in patients with large or cardioembolic strokes [73].

Infections in SLE

Immunosuppression resulting from the disease process or its therapy predisposes patients with SLE to a higher risk of infections than the general population. Infections complicate the course of illness in more than half of the patients with SLE [112]. Infection is the leading cause of mortality in patients with SLE [112] and is an important cause for admission to the ICU. The clinical presentation of patients with infection may resemble the exacerbation of underlying disease, sometimes leading to escalation of immunosuppressive therapy, often with disastrous consequences.

The underlying disease process and its therapy significantly increase the risk for infection, but the exact contribution of each factor is difficult to define. Corticosteroids and other immunosuppressive drugs increase the risk of infection in SLE patients [113], and patients with SLE have a higher risk of dying from infection within 3 months following cytotoxic therapy [114]. The presence of pyogenic pneumonia found on autopsy in 76% of patients dying of SLE in 1955, before the use of immunosuppressive medications for the disease, suggests that SLE is an independent risk factor for infection [115].

Phagocytic dysfunction [116], lymphopenia [117–121], CD4 lymphocytopenia, decreased cytokine production, reduction in the production of immunoglobulins and in complement levels [122–124], and reduced elimination of microorganisms secondary to functional asplenia [125] predispose patients with SLE to infections [126,127].

Viral infections

Patients with SLE have a higher rate of viral infections than the general population, but there are no data to show that these infections are more aggressive, more resistant to therapy, or follow a more chronic course [112]. Varicella-zoster virus (VZV) causes infections more frequently in patients with SLE. In one series, disseminated VZV accounted for 11% of infections [128], but this finding was not confirmed in other series [129], and aggressive clinical presentations are exceptional [114]. Cytomegalovirus was responsible for two deaths in a large series of fatal infections in patients with SLE [114]. Coinfection with HIV is largely coincidental and has been shown to result in clinical and serologic improvement [130,131].

Bacterial infections

In some series, bacteria cause more than 90% of infections in patients with SLE [114,132–135]. *Staphylococcus aureus*, Enterobacteriaceae, and nonfermentative gram-negative organisms are common causes of infection. Gram-negative sepsis was one of the most common causes of severe infection in one series of 544 patients with SLE [132].

Salmonella causes significant morbidity and mortality in patients with SLE. Patients with SLE are predisposed to *Salmonella* infections because of impaired mononuclear phagocytic system function, steroid administration, hypocomplementemia, and low splenic function [136]. Before the advent of HIV, SLE was the most common comorbid condition in patients with *Salmonella* bacteremia, and *Salmonella* is the most frequent cause of bacteremia in SLE patients [137,138]. *Salmonella* infection in these patients may present as bacteremia and extraintestinal syndromes such as urinary tract infection, mycotic aneurysms, pericarditis, soft tissue abscesses, arthritis, and osteomyelitis [139–143]. Typhoid fever is uncommon in patients with SLE [144]. The fatality rate in severe *Salmonella* infections in SLE patients may be as high as 25% [145].

Low levels of complement, hyposplenism, and opsonization and chemotaxis deficit predispose patients with SLE to pneumococcal infections. *Streptococcus pneumoniae* is a common cause of community-acquired pneumonia and of occasionally severe sepsis in patients with SLE [146–149].

Patients with SLE treated with corticosteroids are at a high risk for lung and brain disease caused by *Nocardia* species [150]. The incidence of *Nocardia* infection has decreased significantly since the widespread use of cotrimoxazole prophylaxis in patients receiving chronic corticosteroid therapy. Pulmonary

nocardiosis presents as lung nodules that are often cavitated, as air-space consolidation, or as pleural effusions; chest wall extension should suggest the diagnosis. Extrapulmonary manifestations are common, and CNS abscesses, meningitis, subcutaneous nodules, and endophthalmitis have been reported [151–156]. In one series, 2.8% of more than 200 patients had infection with *Nocardia* species [157]. Pulmonary involvement was common, and the overall mortality rate was 35%. Mortality was 75% in the 10% of patients who had CNS nocardiosis [157]. Prompt therapy with sulfonamides and surgical intervention, if necessary, may cure this infection that may be fatal if untreated.

Yersinia species, *Neisseria meningitidis*, *Campylobacter* species, *Pasteurella multocida*, *Rhodococcus* species, *Pseudomonas* species, and *Tropheryma whipplei* have been reported in the literature as causing infections of varying severity.

Infections caused by *Legionella* species or *Listeria monocytogenes* should be considered in SLE patients, particularly those taking corticosteroids, but there is no definite evidence that SLE patients have an increased susceptibility to these infections [158–161].

Systemic mycoses

In SLE patients, unlike HIV patients, *Pneumocystis carinii* infection causes a rapidly progressive disease with a short prodromal course [114]. *P. carinii* was responsible for 12.5% of lethal infections in a classic series of opportunistic infections in patients with SLE [114]. *P. carinii* pneumonia almost always occurs in patients receiving immunosuppressive medications [162].

Invasive fungal infections are less common than might be expected, considering the predisposing factors in patients with SLE [163]. *Candida* species caused 25% of lethal infections in a series of opportunistic infections in SLE patients [114]. Candidiasis should be considered in patients with indwelling catheters and in those receiving immunosuppressive medications and broad-spectrum antibiotics. Management of candidiasis in patients with SLE does not differ from that in patients with other clinical conditions.

Invasive aspergillosis is uncommon in patients with SLE and presents as nodular pulmonary lesions in patients receiving high doses of corticosteroids. *Aspergillus fumigatus* is the most common species [164].

Meningeal cryptococcosis is quite uncommon but was responsible for 2 of the 24 cases reviewed in one series [114]. Insidious clinical presentation and nonspecific neurologic findings may be mistaken for NPLE [101]. *Microsporium canis*, *Penicillium marneffeii*, *Histoplasma capsulatum*, *Coccidioides immitis*, and *Zygomycoses* [165] occasionally cause infections in patients with SLE [166–169].

Mycobacterial infections

Patients with SLE, especially those treated with corticosteroids, living in endemic areas, or with a suggestive history or a positive tuberculin skin test are at

a high risk for developing tuberculosis. In a series of 311 SLE patients, 16 developed tuberculosis, a number consistent with the high incidence of 5000 per 100,000 population [170]. Severe extrapulmonary or miliary disease was common in this subgroup. In five of the seven patients who died, death was directly attributable to tuberculosis [170], a far greater percentage than expected in the general population. Among Filipino patients in one study, 10 of 54 patients with tuberculosis had miliary disease, and 3 had CNS involvement. Eight of 10 patients with disseminated or miliary disease died of respiratory failure [171].

Parasitic infections

Case reports of paragonimiasis [172], toxoplasmosis in different locations [173–175], disseminated strongyloidiasis [176,177], visceral leishmaniasis [178], and *Acanthamoeba* meningitis [179] in patients with SLE have been described in the literature, but systemic parasitic infections in patients with SLE are uncommon.

Cardiovascular disease in SLE

Cardiac involvement in SLE includes pericarditis, pericardial effusion, Libman-Sacks endocarditis, myocarditis, coronary artery disease, and myocardial infarction. Cases of left ventricular free wall rupture [180], acute mitral regurgitation following rupture of chordae tendinae [181], and aortic dissection [182] have been reported in the literature. Cardiovascular disease secondary to accelerated atherosclerosis is increasingly recognized as a cause of morbidity and mortality in patients with SLE. Mortality from cardiovascular disease in patients with SLE varies from 3% [183] to 45% [184], depending on the population characteristics in a given series. Female lupus patients in the 35- to 44-year-old age group in the SLE Cohort at Pittsburgh were 52.4 times more likely to have a myocardial infarction than the age-matched control group from the Framingham Offspring Study [185]. Analysis of data from the Canadian lupus population revealed that, after controlling for the Framingham risk factors (sex, age, systolic blood pressure, diastolic blood pressure, smoking, diabetes, cholesterol levels, and left ventricular hypertrophy), the increase in relative risk conferred by SLE was 10.1 for nonfatal myocardial infarction (95% CI, 5.8–15.6), 17.0 for death caused by coronary heart disease (95% CI, 8.1–29.7), and 7.5 for overall coronary heart disease (95% CI, 5.1–10.4) [74].

Although patients with SLE are often concerned about vasculitis, almost all coronary occlusive disease in SLE results from atherosclerosis or thrombosis [186,187]. The mean age of first myocardial infarction among SLE patients has been reported to be 49 years, which is 20 years younger than in the general population [188]. Among SLE patients younger than 35 years, acute myocardial infarction is the most common initial manifestation of coronary artery disease, followed by congestive heart failure, sudden death, and angina [189]. The

coronary arteries may be affected in SLE by several mechanisms, the most prominent of which are premature atherosclerosis, with or without hyperlipidemia; hyperhomocystinemia; coagulopathy, especially related to antiphospholipid antibodies; and coronary artery aneurysms [187].

Coronary artery disease among SLE patients with antiphospholipid antibodies is presumably mediated by the associated coagulopathy [187]. Patients with myocardial infarctions may present with angiographically normal coronary arteries [190,191], perhaps because of the spontaneous breakup of a significant clot in the epicardial vessel or spasm [192] or thrombosis of small cardiac vessels [190,191]. Because myocardial infarction may occur with antiphospholipid antibodies in the absence of significant structural disease and even in the absence of angiographically detectable thrombi, the diagnosis is frequently made based on clinical criteria. The diagnosis is further complicated because patients with a very high titer of antiphospholipid antibodies have a greater than 50% risk of reocclusion after revascularization [193].

Vasculitis of coronary arteries has been well described in SLE [186,190, 194,195], although it accounts for only small number of deaths from myocardial infarction [187]. Pathologically, affected vessels are typically narrowed by cellular intimal fibrosis [196] with areas of aneurysmal dilatation. Like other arteritides of muscular arteries, the radiographic diagnosis depends on the identification of aneurysms by angiography. In the case of coronary artery disease, however, the detection of a single aneurysm on an angiogram may be compatible with a diagnosis of atherosclerosis or vasculitis; coronary artery aneurysms were detected by angiography in 4.9% of 978 patients with atherosclerosis in the study Coronary Artery Surgery Study (CASS) [197]. More convincing evidence of vasculitis may be provided by the demonstration of aneurysm formation followed by rapid stenosis [198]. Although coronary vasculitis is likely to be seen in patients with active SLE, there have been reports of pathologically proven coronary artery vasculitis in serologically and clinically inactive patients [195]; coronary artery aneurysms have also been reported in SLE patients in the absence of detectable disease activity [198].

Medical treatment of active coronary artery disease caused by atherosclerosis in patients with SLE does not differ from that in patients without lupus. The various coronary revascularization strategies have not been systematically evaluated in SLE. Complication rates have been reported to be high [199]. Both angioplasty and coronary artery bypass grafting are routinely performed in patients with SLE [200,201].

Lupus myocarditis is treated with high-dose steroids. A few patients have been treated with cyclophosphamide or azathioprine [202,203].

Gastrointestinal emergencies in SLE

Patients with SLE may present with acute abdomen from mesenteric arterial thrombosis [204]; ischemic bowel [205]; ruptured hepatic aneurysms [206];

cholecystitis [207]; perforated rectal ulcer [208], appendix, cecum [209], or colon [210]; and pancreatitis [211,212]. In addition, diverticulitis, gastroenteritis, duodenitis, and inflammatory bowel disease may cause abdominal pain [210].

Patients with active SLE presenting with acute abdomen and a high SLE Disease Activity Index (SLEDAI) scores are more likely to have active intra-abdominal vasculitis than patients with active SLE but low SLEDAI scores. The former group, in view of high mortality in this subgroup [213], should undergo early laparotomy. In one series, 59% of emergency room visits by SLE patients with abdominal pain were for ischemic bowel disease [205].

Medication use [214] was believed to be the most common cause of pancreatitis in patients with SLE, followed by hypertriglyceridemia, alcohol use, cholelithiasis, and vasculitis. Steroid therapy in pancreatitis caused by SLE results in improved clinical and laboratory values [212,215].

Steroids and cytotoxic medications should be considered early in acute abdomen secondary to vasculitis. Surgical and supportive treatment otherwise is similar to that of patients without SLE.

Summary

SLE causes significant morbidity and mortality by multisystem organ involvement. Infections are the leading cause of morbidity and mortality in patients with SLE. Meticulous exclusion of infection is mandatory in patients with SLE, because infections may masquerade as exacerbation of underlying disease; and the immunosuppression used to treat severe forms of exacerbation of lupus can have catastrophic consequences in patients with infections. Corticosteroids are the first-line therapy for most noninfectious complications of SLE, with various adjuvant immunosuppressive agents such as cyclophosphamide being increasingly used in combination with plasmapheresis. Some recent series have shown an improved survival rate, but this improvement needs to be confirmed by further studies. Controlled trials comparing various therapeutic options are lacking, and optimal therapy has not been defined.

References

- [1] Ruiz-Irastorza G, Khamashta MA, Castellino G, et al. Systemic lupus erythematosus. *Lancet* 2001;357(9261):1027–32.
- [2] Hochberg MC, Perlmuter DL, Medsger TA, et al. Prevalence of self-reported physician-diagnosed systemic lupus erythematosus in the USA. *Lupus* 1995;4(6):454–6.
- [3] Trager J, Ward MM. Mortality and causes of death in systemic lupus erythematosus. *Curr Opin Rheumatol* 2001;13(5):345–51.
- [4] Murin S, Wiedemann HP, Matthay RA. Pulmonary manifestations of systemic lupus erythematosus. *Clin Chest Med* 1998;19(4):641–65 [viii].
- [5] Matthay RA, Schwarz MI, Petty TL, et al. Pulmonary manifestations of systemic lupus erythematosus: review of twelve cases of acute lupus pneumonitis. *Medicine (Baltimore)* 1975;54(5):397–409.

- [6] Byrd RB, Trunk G. Systemic lupus erythematosus presenting as pulmonary hemosiderosis. *Chest* 1973;64(1):128–9.
- [7] Wiedemann HP, Matthay RA. Pulmonary manifestations of systemic lupus erythematosus. *J Thorac Imaging* 1992;7(2):1–18.
- [8] Susanto I, Peters JI. Acute lupus pneumonitis with normal chest radiograph. *Chest* 1997;111(6):1781–3.
- [9] Carette S, Macher AM, Nussbaum A, et al. Severe, acute pulmonary disease in patients with systemic lupus erythematosus: ten years of experience at the National Institutes of Health. *Semin Arthritis Rheum* 1984;14(1):52–9.
- [10] Myers SA, Podczaski E, Freese U. Acute lupus pneumonitis in the puerperium. A case report and literature review. *J Reprod Med* 1980;25(5):285–9.
- [11] Cryer PE, Kissane JM. Systemic lupus erythematosus with post-partum pulmonary disease. *Am J Med* 1978;64:1047.
- [12] Haupt HM, Moore GW, Hutchins GM. The lung in systemic lupus erythematosus. Analysis of the pathologic changes in 120 patients. *Am J Med* 1981;71(5):791–8.
- [13] Hunninghake GW, Fauci AS. Pulmonary involvement in the collagen vascular diseases. *American Review of Respiratory Disease* 1979;119(3):471–503.
- [14] Schleissner LA, Sheehan WW, Orselli RC. Lupus erythematosus in a patient with amyloidosis, adrenal insufficiency, and subsequent immunoblastic sarcoma: demonstration of the LE phenomenon in the lung. *Arthritis Rheum* 1976;19(2):249–55.
- [15] Inoue T, Kanayama Y, Ohe A, et al. Immunopathologic studies of pneumonitis in systemic lupus erythematosus. *Ann Intern Med* 1979;91(1):30–4.
- [16] Lyon MG, Bewtra C, Kenik JG, et al. Tubuloreticular inclusions in systemic lupus pneumonitis. Report of a case and review of the literature. *Arch Pathol Lab Med* 1984;108(7):599–600.
- [17] Churg A, Franklin W, Chan KL, et al. Pulmonary hemorrhage and immune-complex deposition in the lung. Complications in a patient with systemic lupus erythematosus. *Arch Pathol Lab Med* 1980;104(7):388–91.
- [18] Domingo-Pedrol P, Rodriguez DLS, Mancebo-Cortes J, et al. Adult respiratory distress syndrome caused by acute systemic lupus erythematosus. *Eur J Respir Dis* 1985;67(2):141–4.
- [19] Holgate ST, Glass DN, Haslam P, et al. Respiratory involvement in systemic lupus erythematosus. A clinical and immunological study. *Clin Exp Immunol* 1976;24(3):385–95.
- [20] Mintz G, Galindo LF, Fernandez-Diez J, et al. Acute massive pulmonary hemorrhage in systemic lupus erythematosus. *J Rheumatol* 1978;5(1):39–50.
- [21] Urman JD, Rothfield NF. Corticosteroid treatment in systemic lupus erythematosus. Survival studies. *JAMA* 1977;238(21):2272–6.
- [22] Eagen JW, Memoli VA, Roberts JL, et al. Pulmonary hemorrhage in systemic lupus erythematosus. *Medicine (Baltimore)* 1978;57(6):545–60.
- [23] Fink SD, Kremer JM. Successful treatment of interstitial lung disease in systemic lupus erythematosus with methotrexate. *J Rheumatol* 1995;22(5):967–9.
- [24] Isbister JP, Ralston M, Hayes JM, et al. Fulminant lupus pneumonitis with acute renal failure and RBC aplasia. Successful management with plasmapheresis and immunosuppression. *Arch Intern Med* 1981;141(8):1081–3.
- [25] Marino CT, Pertschuk LP. Pulmonary hemorrhage in systemic lupus erythematosus. *Arch Intern Med* 1981;141(2):201–3.
- [26] Matthay RA, Hudson LD, Petty TL. Acute lupus pneumonitis: response to azathioprine therapy. *Chest* 1973;63(1):117–20.
- [27] Matthay RA, Petty TL. Treatment of acute lupus pneumonitis with azathioprine [letter]. *Chest* 1974;66(2):219–20.
- [28] Orens JB, Martinez FJ, Lynch III JP. Pleuropulmonary manifestations of systemic lupus erythematosus. *Rheum Dis Clin North Am* 1994;20(1):159–93.
- [29] Abud-Mendoza C, Diaz-Jouanen E, Alarcon-Segovia D. Fatal pulmonary hemorrhage in systemic lupus erythematosus. Occurrence without hemoptysis. *J Rheumatol* 1985;12(3):558–61.

- [30] Leatherman JW, Davies SF, Hoidal JR. Alveolar hemorrhage syndromes: diffuse microvascular lung hemorrhage in immune and idiopathic disorders. *Medicine (Baltimore)* 1984;63(6):343–61.
- [31] Schwab EP, Schumacher Jr. HR, Freundlich B, et al. Pulmonary alveolar hemorrhage in systemic lupus erythematosus. *Semin Arthritis Rheum* 1993;23(1):8–15.
- [32] Zamora MR, Warner ML, Tuder R, et al. Diffuse alveolar hemorrhage and systemic lupus erythematosus. Clinical presentation, histology, survival, and outcome. *Medicine (Baltimore)* 1997;76(3):192–202.
- [33] Kuhn C. Systemic lupus erythematosus in a patient with ultrastructural lesions of the pulmonary capillaries previously reported in the review as due to idiopathic pulmonary hemosiderosis. *American Review of Respiratory Disease* 1972;106(6):931–2.
- [34] Carr DT, Lillington GA, Mayne JG. Pleural-fluid glucose in systemic lupus erythematosus. *Mayo Clin Proc* 1970;45(6):409–412.
- [35] Blanche P, Krebs S, Renaud B, et al. Systemic lupus erythematosus presenting as iron deficiency anemia due to pulmonary alveolar hemorrhage. *Clin Exp Rheumatol* 1996;14(2):228.
- [36] Santos-Ocampo AS, Mandell BF, Fessler BJ. Alveolar hemorrhage in systemic lupus erythematosus: presentation and management. *Chest* 2000;118(4):1083–90.
- [37] Lee JG, Joo KW, Chung WK, et al. Diffuse alveolar hemorrhage in lupus nephritis. *Clin Nephrol* 2001;55(4):282–8.
- [38] Lee CK, Koh JH, Cha HS, et al. Pulmonary alveolar hemorrhage in patients with rheumatic diseases in Korea. *Scand J Rheumatol* 2000;29(5):288–94.
- [39] Ahmad S. Lovastatin-induced lupus erythematosus. *Arch Intern Med* 1991;151(8):1667–8.
- [40] Roark JH, Kuntz CL, Nguyen KA, et al. Breakdown of B cell tolerance in a mouse model of systemic lupus erythematosus. *J Exp Med* 1995;181(3):1157–67.
- [41] Koh WH, Thumboo J, Boey ML. Pulmonary haemorrhage in Oriental patients with systemic lupus erythematosus. *Lupus* 1997;6(9):713–6.
- [42] Liu MF, Lee JH, Weng TH, et al. Clinical experience of 13 cases with severe pulmonary hemorrhage in systemic lupus erythematosus with active nephritis. *Scand J Rheumatol* 1998; 27(4):291–5.
- [43] Desnoyers MR, Bernstein S, Cooper AG, et al. Pulmonary hemorrhage in lupus erythematosus without evidence of an immunologic cause. *Arch Intern Med* 1984;144(7):1398–400.
- [44] Myers JL, Katzenstein AA. Microangiitis in lupus-induced pulmonary hemorrhage. *Am J Clin Pathol* 1986;85(5):552–6.
- [45] Gould DB, Soriano RZ. Acute alveolar hemorrhage in lupus erythematosus. *Ann Intern Med* 1975;83(6):836–7.
- [46] Onomura K, Nakata H, Tanaka Y, et al. Pulmonary hemorrhage in patients with systemic lupus erythematosus. *J Thorac Imaging* 1991;6(2):57–61.
- [47] Fukuda M, Kamiyama Y, Kawahara K, et al. The favourable effect of cyclophosphamide pulse therapy in the treatment of massive pulmonary haemorrhage in systemic lupus erythematosus. *Eur J Pediatr* 1994;153(3):167–70.
- [48] Millman RP, Cohen TB, Levinson AI, et al. Systemic lupus erythematosus complicated by acute pulmonary hemorrhage: recovery following plasmapheresis and cytotoxic therapy. *J Rheumatol* 1981;8(6):1021–3.
- [49] Erickson RW, Franklin WA, Emlen W. Treatment of hemorrhagic lupus pneumonitis with plasmapheresis. *Semin Arthritis Rheum* 1994;24(2):114–23.
- [50] Abramson SB, Dobro J, Eberle MA, et al. Acute reversible hypoxemia in systemic lupus erythematosus. *Ann Intern Med* 1991;114(11):941–7.
- [51] Martinez-Taboada VM, Blanco R, Armona J, et al. Acute reversible hypoxemia in systemic lupus erythematosus: a new syndrome or an index of disease activity? *Lupus* 1995;4(4): 259–62.
- [52] Stevens WM, Burdon JG, Clemens LE, et al. The ‘shrinking lungs syndrome’ – an infrequently recognised feature of systemic lupus erythematosus. *Aust N Z J Med* 1990;20(1):67–70.
- [53] Chick TW, DeHoratius RJ, Skipper BE, et al. Pulmonary dysfunction in systemic lupus erythematosus without pulmonary symptoms. *J Rheumatol* 1976;3(3):262–8.

- [54] Martens J, Demedts M, Vanmeenen MT, et al. Respiratory muscle dysfunction in systemic lupus erythematosus. *Chest* 1983;84(2):170–5.
- [55] Wilcox PG, Stein HB, Clarke SD, et al. Phrenic nerve function in patients with diaphragmatic weakness and systemic lupus erythematosus. *Chest* 1988;93(2):352–8.
- [56] Gibson CJ, Edmonds JP, Hughes GR. Diaphragm function and lung involvement in systemic lupus erythematosus. *Am J Med* 1977;63(6):926–32.
- [57] Hoffbrand BJ, Beck ER. “Unexplained” dyspnea and shrinking lungs in systemic lupus erythematosus. *BMJ* 1965;1:1273 [Ref Type: Generic].
- [58] Warrington KJ, Moder KG, Brutinel WM. The shrinking lungs syndrome in systemic lupus erythematosus. *Mayo Clin Proc* 2000;75(5):467–472.
- [59] Walz-Leblanc BA, Urowitz MB, Gladman DD, et al. The “shrinking lungs syndrome” in systemic lupus erythematosus—improvement with corticosteroid therapy. *J Rheumatol* 1992;19(12):1970–2.
- [60] Van Veen S, Peeters AJ, Sterk PJ, et al. The “shrinking lung syndrome” in SLE, treatment with theophylline. *Clin Rheumatol* 1993;12(4):462–5.
- [61] Martin L, Edworthy SM, Ryan JP, et al. Upper airway disease in systemic lupus erythematosus: a report of 4 cases and a review of the literature. *J Rheumatol* 1992;19(8):1186–90.
- [62] Asherson RA, Zulman J, Hughes GR. Pulmonary thromboembolism associated with procainamide induced lupus syndrome and anticardiolipin antibodies. *Ann Rheum Dis* 1989;48(3):232–5.
- [63] Burgess ED, Render KC. Hypopharyngeal obstruction in lupus erythematosus. *Ann Intern Med* 1984;100(2):319.
- [64] Scarpelli DG, McCoy FW, Scott JK. Acute lupus erythematosus with laryngeal involvement. *N Engl J Med* 1959;261:691.
- [65] Smith GA, Ward PH, Berci G. Laryngeal involvement by systemic lupus erythematosus. *Transactions of the American Academy of Ophthalmology and Otolaryngology* 1977;84(1):124–8.
- [66] Toomey JM, Snyder III GG, Maenza RM, et al. Acute epiglottitis due to systemic lupus erythematosus. *Laryngoscope* 1974;84(4):522–7.
- [67] Smith RR, Ferguson GB. Systemic lupus erythematosus causing subglottic stenosis. *Laryngoscope* 1976;86(5):734–8.
- [68] Abel T, Gladman DD, Urowitz MB. Neuropsychiatric lupus. *J Rheumatol* 1980;7(3):325–33.
- [69] Buchbinder R, Hall S, Littlejohn GO, et al. Neuropsychiatric manifestations of systemic lupus erythematosus. *Aust N Z J Med* 1988;18(5):679–84.
- [70] Feinglass EJ, Arnett FC, Dorsch CA, et al. Neuropsychiatric manifestations of systemic lupus erythematosus: diagnosis, clinical spectrum, and relationship to other features of the disease. *Medicine (Baltimore)* 1976;55(4):323–39.
- [71] Gibson T, Myers AR. Nervous system involvement in systemic lupus erythematosus. *Ann Rheum Dis* 1975;35(5):398–406.
- [72] Lee P, Urowitz MB, Bookman AA, et al. Systemic lupus erythematosus. A review of 110 cases with reference to nephritis, the nervous system, infections, aseptic necrosis and prognosis. *Q J Med* 1977;46(181):1–32.
- [73] West SG. Neuropsychiatric lupus. *Rheum Dis Clin North Am* 1994;20(1):129–58.
- [74] Esdaile JM, Abrahamowicz M, Grodzicky T, et al. Traditional Framingham risk factors fail to fully account for accelerated atherosclerosis in systemic lupus erythematosus. *Arthritis Rheum* 2001;44(10):2331–7.
- [75] Asherson RA, Khamashta MA, Gil A, et al. Cerebrovascular disease and antiphospholipid antibodies in systemic lupus erythematosus, lupus-like disease, and the primary antiphospholipid syndrome. *Am J Med* 1989;86(4):391–9.
- [76] Chartash EK, Lans DM, Paget SA, et al. Aortic insufficiency and mitral regurgitation in patients with systemic lupus erythematosus and the antiphospholipid syndrome. *Am J Med* 1989;86(4):407–12.
- [77] Fields RA, Sibbitt WL, Toubbeh H, et al. Neuropsychiatric lupus erythematosus, cerebral infarctions, and anticardiolipin antibodies. *Ann Rheum Dis* 1990;49(2):114–7.

- [78] Fishman P, Kamashta M, Ehrenfeld M, et al. Interleukin-3 immunoassay in systemic lupus erythematosus patients: preliminary data. *Int Arch Allergy Immunol* 1993;100(3):215–8.
- [79] Nihoyannopoulos P, Gomez PM, Joshi J, et al. Cardiac abnormalities in systemic lupus erythematosus. Association with raised anticardiolipin antibodies. *Circulation* 1990;82(2):369–75.
- [80] Pope JM, Canny CL, Bell DA. Cerebral ischemic events associated with endocarditis, retinal vascular disease, and lupus anticoagulant. *Am J Med* 1991;90(3):299–309.
- [81] Asherson RA, Hughes GR. The expanding spectrum of Libman Sacks endocarditis: the role of antiphospholipid antibodies. *Clin Exp Rheumatol* 1989;7(3):225–8.
- [82] Levine SR, Welch KM. The spectrum of neurologic disease associated with antiphospholipid antibodies. Lupus anticoagulants and anticardiolipin antibodies. *Arch Neurol* 1987;44(8):876–83.
- [83] Asherson RA, Baguley E, Pal C, et al. Antiphospholipid syndrome: five year follow up. *Ann Rheum Dis* 1991;50(11):805–10.
- [84] Eustace S, Hutchinson M, Bresnihan B. Acute cerebrovascular episodes in systemic lupus erythematosus. *Q J Med* 1991;80(293):739–50.
- [85] Futrell N, Millikan C. Frequency, etiology, and prevention of stroke in patients with systemic lupus erythematosus. *Stroke* 1989;20(5):583–91.
- [86] Kitagawa Y, Gotoh F, Koto A, et al. Stroke in systemic lupus erythematosus. *Stroke* 1990;21(11):1533–9.
- [87] Tsokos GC, Tsokos M, le Riche NG, et al. A clinical and pathologic study of cerebrovascular disease in patients with systemic lupus erythematosus. *Semin Arthritis Rheum* 1986;16(1):70–8.
- [88] Nagayama Y, Kusudo K, Imura H. A case of central nervous system lupus associated with ruptured cerebral berry aneurysm. *Jpn J Med* 1989;28(4):530–3.
- [89] Trentham DE. Berry aneurysms and lupus [letter]. *N Engl J Med* 1976;295(2):114.
- [90] Andrianakos AA, Duffy J, Suzuki M, et al. Transverse myelopathy in systemic lupus erythematosus. Report of three cases and review of the literature. *Ann Intern Med* 1975;83(5):616–24.
- [91] Warren RW, Kredich DW. Transverse myelitis and acute central nervous system manifestations of systemic lupus erythematosus. *Arthritis Rheum* 1984;27(9):1058–60.
- [92] van Dam AP. Diagnosis and pathogenesis of CNS lupus. *Rheumatol Int* 1991;11(1):1–11.
- [93] Boumpas DT, Patronas NJ, Dalakas MC, et al. Acute transverse myelitis in systemic lupus erythematosus: magnetic resonance imaging and review of the literature. *J Rheumatol* 1990;17(1):89–92.
- [94] Lavalle C, Pizarro S, Drenkard C, et al. Transverse myelitis: a manifestation of systemic lupus erythematosus strongly associated with antiphospholipid antibodies. *J Rheumatol* 1990;17(1):34–7.
- [95] Barile L, Lavalle C. Transverse myelitis in systemic lupus erythematosus—the effect of IV pulse methylprednisolone and cyclophosphamide. *J Rheumatol* 1992;19(3):370–2.
- [96] Propper DJ, Bucknall RC. Acute transverse myelopathy complicating systemic lupus erythematosus. *Ann Rheum Dis* 1989;48(6):512–5.
- [97] Mok CC, Lau CS, Chan EY, et al. Acute transverse myelopathy in systemic lupus erythematosus: clinical presentation, treatment, and outcome. *J Rheumatol* 1998;25(3):467–73.
- [98] Kovacs B, Lafferty TL, Brent LH, et al. Transverse myelopathy in systemic lupus erythematosus: an analysis of 14 cases and review of the literature. *Ann Rheum Dis* 2000;59(2):120–4.
- [99] Albert DA, Hadler NM, Ropes MW. Does corticosteroid therapy affect the survival of patients with systemic lupus erythematosus? *Arthritis Rheum* 1979;22(9):945–53.
- [100] Welsby P, Smith C. Recurrent sterile meningitis as a manifestation of systemic lupus erythematosus. *Scand J Infect Dis* 1977;9(2):149–50.
- [101] Zimmermann III B, Spiegel M, Lally EV. Cryptococcal meningitis in systemic lupus erythematosus. *Semin Arthritis Rheum* 1992;22(1):18–24.
- [102] Codding C, Targoff IN, McCarty GA. Aseptic meningitis in association with diclofenac treatment in a patient with systemic lupus erythematosus. *Arthritis Rheum* 1991;34(10):1340–1.

- [103] Hoppmann RA, Peden JG, Ober SK. Central nervous system side effects of nonsteroidal anti-inflammatory drugs. Aseptic meningitis, psychosis, and cognitive dysfunction. *Arch Intern Med* 1991;151(7):1309–13.
- [104] Futran J, Shore A, Urowitz MB, et al. Subdural hematoma in systemic lupus erythematosus: report and review of the literature. *J Rheumatol* 1987;14(2):378–81.
- [105] Emerudh J, Olsson T, Lindstrom F, et al. Cerebrospinal fluid immunoglobulin abnormalities in systemic lupus erythematosus. *J Neurol Neurosurg Psychiatry* 1985;48(8):807–13.
- [106] Seibold JR, Buckingham RB, Medsger Jr. TA, et al. Cerebrospinal fluid immune complexes in systemic lupus erythematosus involving the central nervous system. *Semin Arthritis Rheum* 1982;12(1):68–76.
- [107] Bluestein HG, Woods Jr. VL. Antineuronal antibodies in systemic lupus erythematosus. *Arthritis Rheum* 1982;25(7):773–8.
- [108] Huizinga TW, Steens SC, Van Buchem MA. Imaging modalities in central nervous system systemic lupus erythematosus. *Curr Opin Rheumatol* 2001;13(5):383–8.
- [109] Guthrie JA, Turney JH. Plasma exchange for cerebral lupus erythematosus. *Lancet* 1987;1(8531):506–7.
- [110] Goldberger E, Elder RC, Schwartz RA, et al. Vasculitis in the antiphospholipid syndrome. A cause of ischemia responding to corticosteroids. *Arthritis Rheum* 1992;35(5):569–72.
- [111] Neuwelt CM, Lacks S, Kaye BR, et al. Role of intravenous cyclophosphamide in the treatment of severe neuropsychiatric systemic lupus erythematosus. *Am J Med* 1995;98(1):32–41.
- [112] Bouza E, Moya JG, Munoz P. Infections in systemic lupus erythematosus and rheumatoid arthritis. *Infect Dis Clin North Am* 2001;15(2):335–61 [vii.].
- [113] Ginzler E, Diamond H, Kaplan D, et al. Computer analysis of factors influencing frequency of infection in systemic lupus erythematosus. *Arthritis Rheum* 1978;21(1):37–44.
- [114] Hellmann DB, Petri M, Whiting-O'Keefe Q. Fatal infections in systemic lupus erythematosus: the role of opportunistic organisms. *Medicine (Baltimore)* 1987;66(5):341–8.
- [115] Purnell DC, Baggenstos AH, Olsen AM. Pulmonary lesions in disseminated lupus erythematosus. *Ann Intern Med* 1955;42:619.
- [116] Al Hadithy H, Isenberg DA, Addison IE, et al. Neutrophil function in systemic lupus erythematosus and other collagen diseases. *Ann Rheum Dis* 1982;41(1):33–8.
- [117] Boswell J, Schur PH. Monocyte function in systemic lupus erythematosus. *Clin Immunol Immunopathol* 1989;52(2):271–8.
- [118] Gyimesi E, Kavai M, Kiss E, et al. Triggering of respiratory burst by phagocytosis in monocytes of patients with systemic lupus erythematosus. *Clin Exp Immunol* 1993;94(1):140–4.
- [119] Keeling DM, Isenberg DA. Haematological manifestations of systemic lupus erythematosus. *Blood Rev* 1993;7(4):199–207.
- [120] Bernas BL, Petri M, Goldman D, et al. T helper cell dysfunction in systemic lupus erythematosus (SLE): relation to disease activity. *J Clin Immunol* 1994;14(3):169–77.
- [121] Tsokos GC, Balow JE. Cellular immune responses in systemic lupus erythematosus. *Prog Allergy* 1984;35:93–161.
- [122] Cronin ME, Balow JE, Tsokos GC. Immunoglobulin deficiency in patients with systemic lupus erythematosus. *Clin Exp Rheumatol* 1989;7(4):359–64.
- [123] Lipnick RN, Karsh J, Stahl NI, et al. Pneumococcal immunization in patients with systemic lupus erythematosus treated with immunosuppressives. *J Rheumatol* 1985;12(6):1118–21.
- [124] Mitchell SR, Nguyen PQ, Katz P. Increased risk of neisserial infections in systemic lupus erythematosus. *Semin Arthritis Rheum* 1990;20(3):174–84.
- [125] Dillon AM, Stein HB, English RA. Splenic atrophy in systemic lupus erythematosus. *Ann Intern Med* 1982;96(1):40–3.
- [126] Piliero P, Furie R. Functional asplenia in systemic lupus erythematosus. *Semin Arthritis Rheum* 1990;20(3):185–9.
- [127] McCune WJ, Golbus J, Zeldes W, et al. Clinical and immunologic effects of monthly administration of intravenous cyclophosphamide in severe systemic lupus erythematosus. *N Engl J Med* 1988;318(22):1423–31.

- [128] Kahl LE. Herpes zoster infections in systemic lupus erythematosus: risk factors and outcome. *J Rheumatol* 1994;21(1):84–6.
- [129] Moga I, Formiga F, Canet R, et al. [Herpes-zoster virus infection in patients with systemic lupus erythematosus] *Rev Clin Esp* 1995;195(8):530–3.
- [130] Contreras G, Green DF, Pardo V, et al. Systemic lupus erythematosus in two adults with human immunodeficiency virus infection. *Am J Kidney Dis* 1996;28(2):292–5.
- [131] Fox RA, Isenberg DA. Human immunodeficiency virus infection in systemic lupus erythematosus. *Arthritis Rheum* 1997;40(6):1168–72.
- [132] Kim WU, Min JK, Lee SH, et al. Causes of death in Korean patients with systemic lupus erythematosus: a single center retrospective study. *Clin Exp Rheumatol* 1999;17(5):539–45.
- [133] Nived O, Sturfelt G, Wollheim F. Systemic lupus erythematosus and infection: a controlled and prospective study including an epidemiological group. *QJM* 1985;55(218):271–87.
- [134] Petri M. Infection in systemic lupus erythematosus. *Rheum Dis Clin North Am* 1998;24(2):423–56.
- [135] Petri M, Genovese M. Incidence of and risk factors for hospitalizations in systemic lupus erythematosus: a prospective study of the Hopkins Lupus Cohort. *J Rheumatol* 1992;19(10):1559–65.
- [136] Lovy MR, Ryan PF, Hughes GR. Concurrent systemic lupus erythematosus and salmonellosis. *J Rheumatol* 1981;8(4):605–12.
- [137] Abramson S, Kramer SB, Radin A, et al. Salmonella bacteremia in systemic lupus erythematosus. Eight-year experience at a municipal hospital. *Arthritis Rheum* 1985;28(1):75–9.
- [138] Roberts FJ. Nontyphoidal, nonparatyphoidal salmonella septicemia in adults. *Eur J Clin Microbiol Infect Dis* 1993;12(3):205–8.
- [139] Frayha RA, Jizi I, Saadeh G. Salmonella typhimurium bacteriuria. An increased infection rate in systemic lupus erythematosus. *Arch Intern Med* 1985;145(4):645–7.
- [140] Howe HS, Wong JS, Ding ZP, et al. Mycotic aneurysm of a coronary artery in SLE—a rare complication of salmonella infection. *Lupus* 1997;6(4):404–7.
- [141] Sanchez-Guerrero J, Alarcon-Segovia D. Salmonella pericarditis with tamponade in systemic lupus erythematosus. *Br J Rheumatol* 1990;29(1):69–71.
- [142] Shamiss A, Thaler M, Nussinovitch N, et al. Multiple Salmonella enteritidis leg abscesses in a patient with systemic lupus erythematosus. *Postgrad Med J* 1990;66(776):486–8.
- [143] van de Laar MA, Meenhorst PL, van Soesbergen RM, et al. Polyarticular Salmonella bacterial arthritis in a patient with systemic lupus erythematosus. *J Rheumatol* 1989;16(2):231–4.
- [144] Juega J, Pedreira JD, Adegá M, et al. [Infection in systemic lupus erythematosus]. *Rev Clin Esp* 1989;184(5):245–6.
- [145] Shahram F, Akbarian M, Davatchi F. Salmonella infection in systemic lupus erythematosus. *Lupus* 1993;2(1):55–9.
- [146] Mackenzie AR, Laing RB, MacDonald AG, et al. Pneumococcal septicaemia in a patient with systemic lupus erythematosus. *Ann Rheum Dis* 1997;56(7):403–4.
- [147] Shalit M, Gross DJ, Levo Y. Pneumococcal epiglottitis in systemic lupus erythematosus on high-dose corticosteroids. *Ann Rheum Dis* 1982;41(6):615–6.
- [148] Van der SC, Wei N, Rothschild J et al. Rapidly fatal pneumococcal septicemia in systemic lupus erythematosus. *J Rheumatol* 1987;14(6):1177–80.
- [149] DiNubile MJ, Alborno MA, Stumacher RJ, et al. Pneumococcal soft-tissue infections: possible association with connective tissue diseases. *J Infect Dis* 1991;163(4):897–900.
- [150] Pina BR, Lopez de Letona JM, Frieyro SE, et al. [Systemic lupus erythematosus associated with nocardiosis]. *Rev Clin Esp* 1978;149(2):177–9.
- [151] Balbir-Gurman A, Schapira D, Nahir AM. Primary subcutaneous nocardial infection in a SLE patient. *Lupus* 1999;8(2):164–7.
- [152] Gorevic PD, Katler EI, Agus B. Pulmonary nocardiosis. Occurrence in men with systemic lupus erythematosus. *Arch Intern Med* 1980;140(3):361–3.
- [153] Ishibashi Y, Watanabe R, Hommura S, et al. Endogenous Nocardia asteroides endophthalmitis in a patient with systemic lupus erythematosus. *Br J Ophthalmol* 1990;74(7):433–6.

- [154] Mok CC, Lau CS, Poon SP. Primary nocardial meningitis in systemic lupus erythematosus. *Br J Rheumatol* 1995;34(2):178–81.
- [155] Petri M, Katzenstein P, Hellmann D. Laryngeal infection in lupus: report of nocardiosis and review of laryngeal involvement in lupus. *J Rheumatol* 1988;15(6):1014–5.
- [156] Wang SM, Liu CC, Chen CT, et al. Pulmonary nocardiosis in a child with systemic lupus erythematosus: report of a case. *J Formos Med Assoc* 1995;94(8):506–8.
- [157] Mok CC, Yuen KY, Lau CS. Nocardiosis in systemic lupus erythematosus. *Semin Arthritis Rheum* 1997;26(4):675–83.
- [158] Kraus A, Cabral AR, Sifuentes-Osornio J, et al. Listeriosis in patients with connective tissue diseases. *J Rheumatol* 1994;21(4):635–8.
- [159] Merrell WH, Moritz A, Butt HL, et al. Isolation of *Legionella maceachemii* from an immunocompromised patient with severe underlying lung disease. *Med J Aust* 1991;155(6):415–7.
- [160] Nomura S, Hatta K, Iwata T, et al. *Legionella pneumophila* isolated in pure culture from the ascites of a patient with systemic lupus erythematosus. *Am J Med* 1989;86(6 Pt 2):833–4.
- [161] Senecal JL, St Antoine P, Beliveau C. *Legionella pneumophila* lung abscess in a patient with systemic lupus erythematosus. *Am J Med Sci* 1987;293(5):309–14.
- [162] Porges AJ, Beattie SL, Ritchlin C, et al. Patients with systemic lupus erythematosus at risk for *Pneumocystis carinii* pneumonia. *J Rheumatol* 1992;19(8):1191–4.
- [163] Pillay VK, Wilson DM, Ing TS, et al. Fungus infection in steroid-treated systemic lupus erythematosus. *JAMA* 1968;205(5):261–5.
- [164] Collazos J, Martinez E, Flores M, et al. *Aspergillus* pneumonia successfully treated with itraconazole in a patient with systemic lupus erythematosus. *Clin Investig* 1994;72(11):920–1.
- [165] Andersen FG, Guckian JC. Systemic lupus erythematosus associated with fatal pulmonary coccidioidomycosis. *Tex Rep Biol Med* 1968;26(1):93–9.
- [166] Fingerote RJ, Seigel S, Atkinson MH, et al. Disseminated zygomycosis associated with systemic lupus erythematosus. *J Rheumatol* 1990;17(12):1692–4.
- [167] Hansen KE, St Clair EW. Disseminated histoplasmosis in systemic lupus erythematosus: case report and review of the literature. *Semin Arthritis Rheum* 1998;28(3):193–9.
- [168] Lo CY, Chan DT, Yuen KY, et al. *Penicillium marneffei* infection in a patient with SLE. *Lupus* 1995;4(3):229–31.
- [169] Sieving RR, Kauffman CA, Watanakunakorn C. Deep fungal infection in systemic lupus erythematosus—three cases reported, literature reviewed. *J Rheumatol* 1975;2(1):61–72.
- [170] Feng PH, Tan TH. Tuberculosis in patients with systemic lupus erythematosus. *Ann Rheum Dis* 1982;41(1):11–4.
- [171] Victorio-Navarra ST, Dy EE, Arroyo CG, et al. Tuberculosis among Filipino patients with systemic lupus erythematosus. *Semin Arthritis Rheum* 1996;26(3):628–34.
- [172] Kraus A, Guerra-Bautista G, Chavarria P. Paragonimiasis: an infrequent but treatable cause of hemoptysis in systemic lupus erythematosus. *J Rheumatol* 1990;17(2):244–6.
- [173] Baykal Y, Saglam K, Caliskaner Z. *Toxoplasma* infection in patients with systemic lupus erythematosus. *J Rheumatol* 1998;25(10):2038–9.
- [174] Deleze M, Mintz G, del Carmen MM. *Toxoplasma gondii* encephalitis in systemic lupus erythematosus. A neglected cause of treatable nervous system infection. *J Rheumatol* 1985;12(5):994–6.
- [175] D'Ercole C, Boubli L, Franck J, et al. Recurrent congenital toxoplasmosis in a woman with lupus erythematosus. *Prenat Diagn* 1995;15(12):1171–5.
- [176] Setoyama M, Fukumaru S, Takasaki T, et al. SLE with death from acute massive pulmonary hemorrhage caused by disseminated strongyloidiasis. *Scand J Rheumatol* 1997;26(5):389–91.
- [177] Wachter RM, Burke AM, MacGregor RR. Strongyloides stercoralis hyperinfection masquerading as cerebral vasculitis. *Arch Neurol* 1984;41(11):1213–6.
- [178] Fernandez-Guerrero ML, Aguado JM, Buzon L, et al. Visceral leishmaniasis in immunocompromised hosts. *Am J Med* 1987;83(6):1098–102.
- [179] Grunnet ML, Cannon GH, Kushner JP. Fulminant amebic meningoencephalitis due to *Acanthamoeba*. *Neurology* 1981;31(2):174–6.

- [180] Saga T, Iemura J, Oku H, et al. [Successful surgical management of postinfarction left ventricular free wall rupture in a case of systemic lupus erythematosus]. *Jpn J Thorac Cardiovasc Surg* 1993;41(12):2395–9.
- [181] Tsuji K, Kino K, Sogabe O, et al. Urgent mitral valve replacement for acute mitral regurgitation due to ruptured chordae tendineae in systemic lupus erythematosus. *Jpn J Thorac Cardiovasc Surg* 1993;46(9):795–7.
- [182] Lansman SL, Raissi S, Ergin MA, et al. Urgent operation for acute transverse aortic arch dissection. *J Thorac Cardiovasc Surg* 1989;97(3):334–41.
- [183] Rosner S, Ginzler EM, Diamond HS, et al. A multicenter study of outcome in systemic lupus erythematosus. II. causes of death. *Arthritis Rheum* 1982;25(6):612–7.
- [184] Urowitz MB, Bookman AA, Koehler BE, et al. The bimodal mortality pattern of systemic lupus erythematosus. *Am J Med* 1976;60(2):221–5.
- [185] Manzi S, Meilahn EN, Rairie JE, et al. Age-specific incidence rates of myocardial infarction and angina in women with systemic lupus erythematosus: comparison with the Framingham Study. *Am J Epidemiol* 1997;145(5):408–15.
- [186] Haider YS, Roberts WC. Coronary arterial disease in systemic lupus erythematosus; quantification of degrees of narrowing in 22 necropsy patients (21 women) aged 16 to 37 years. *Am J Med* 1981;70(4):775–81.
- [187] Karrar A, Sequeira W, Block JA. Coronary artery disease in systemic lupus erythematosus: a review of the literature. *Semin Arthritis Rheum* 2001;30(6):436–43.
- [188] Bruce IN, Gladman DD, Urowitz MB. Premature atherosclerosis in systemic lupus erythematosus. *Rheum Dis Clin North Am* 2000;26(2):257–78.
- [189] Doherty NE, Siegel RJ. Cardiovascular manifestations of systemic lupus erythematosus. *Am Heart J* 1985;110(6):1257–65.
- [190] Kattwinkel N, Villanueva AG, Labib SB, et al. Myocardial infarction caused by cardiac microvasculopathy in a patient with the primary antiphospholipid syndrome. *Ann Intern Med* 1992;116(12 Pt 1):974–6.
- [191] Rangel A, Lavalle C, Chavez E, et al. Myocardial infarction in patients with systemic lupus erythematosus with normal findings from coronary arteriography and without coronary vasculitis—case reports. *Angiology* 1999;50(3):245–53.
- [192] Takatsu Y, Hattori R, Sakaguchi K, et al. Acute myocardial infarction associated with systemic lupus erythematosus documented by coronary arteriograms. *Chest* 1985;88(1):147–9.
- [193] Morton KE, Gavag TP, Krilliss SA. Coronary artery graft failure—an autoimmune phenomenon? *Lancet* 1986;2:1353–7.
- [194] Englund JA, Lucas Jr. RV. Cardiac complications in children with systemic lupus erythematosus. *Pediatrics* 1983;72(5):724–30.
- [195] Bonfiglio TA, Botti RE, Hagstrom JW. Coronary arteritis, occlusion, and myocardial infarction due to lupus erythematosus. *Am Heart J* 1972;83(2):153–8.
- [196] Bulkley BH, Roberts WC. The heart in systemic lupus erythematosus and the changes induced in it by corticosteroid therapy. A study of 36 necropsy patients. *Am J Med* 1975;58(2):243–64.
- [197] Swaye PS, Fisher LD, Litwin P, et al. Aneurysmal coronary artery disease. *Circulation* 1983;67:134–8.
- [198] Wilson VE, Eck SL, Bates ER. Evaluation and treatment of acute myocardial infarction complicating systemic lupus erythematosus. *Chest* 1992;101(2):420–4.
- [199] Papa MZ, Shiloni E, Vetto JT, et al. Surgical morbidity in patients with systemic lupus erythematosus. *Am J Surg* 1989;157(3):295–8.
- [200] Ura M, Sakata R, Nakayama Y, et al. Coronary artery bypass grafting in patients with systemic lupus erythematosus. *Eur J Cardiothorac Surg* 1999;15(5):697–701.
- [201] Rinaldi RG, Carballido J, Betancourt B, et al. Coronary artery bypass grafting in patients with systemic lupus erythematosus. Report of 2 cases. *Tex Heart Inst J* 1995;22(2):185–8.
- [202] Fairfax MJ, Osborn TG, Williams GA, et al. Endomyocardial biopsy in patients with systemic lupus erythematosus. *J Rheumatol* 1988;15(4):593–6.

- [203] Borenstein DG, Fye WB, Arnett FC, et al. The myocarditis of systemic lupus erythematosus: association with myositis. *Ann Intern Med* 1978;89(5 Pt 1):619–24.
- [204] Kojima E, Naito K, Iwai M, et al. Antiphospholipid syndrome complicated by thrombosis of the superior mesenteric artery, co-existence of smooth muscle hyperplasia. *Intern Med* 1997;36(7):528–31.
- [205] Min J, Park J, Kim S. Acute abdominal pain in patients with systemic lupus erythematosus entered in emergency room [abstract]. *Arthritis Rheum* 1997;40:S106.
- [206] McCollum CN, Sloan ME, Davison AM, et al. Ruptured hepatic aneurysm in systemic lupus erythematosus. *Ann Rheum Dis* 1979;38(4):396–8.
- [207] Fitzgerald RC, Triadafilopoulos G. Esophageal manifestations of rheumatic disorders. *Semin Arthritis Rheum* 1997;26(4):641–66.
- [208] Teramoto J, Takahashi Y, Katsuki S, et al. Systemic lupus erythematosus with a giant rectal ulcer and perforation. *Intern Med* 1999;38(8):643–9.
- [209] Schmidt WA, Schneider W, Gromnica-Ihle EJ. [Necrotizing vasculitis of the appendix and cecum in systemic lupus erythematosus]. *Z Rheumatol* 1996;55(4):267–71.
- [210] Hallegua DS, Wallace DJ. Gastrointestinal manifestations of systemic lupus erythematosus. *Curr Opin Rheumatol* 2000;12(5):379–85.
- [211] Marum S, Veiga MZ, Silva F et al. Lupus pancreatitis. *Acta Med Port* 1998;11(8–9):779–782.
- [212] Saab S, Corr MP, Weisman MH. Corticosteroids and systemic lupus erythematosus pancreatitis: a case series. *J Rheumatol* 1998;25(4):801–6.
- [213] Medina F, Ayala A, Jara LJ, et al. Acute abdomen in systemic lupus erythematosus: the importance of early laparotomy. *Am J Med* 1997;103(2):100–5.
- [214] al Hakeem MS, McMillen MA. Evaluation of abdominal pain in systemic lupus erythematosus. *Am J Surg* 1998;176(3):291–4.
- [215] Kapoor D, Mendez E, Espinoza LR. Corticosteroids and SLE pancreatitis. *J Rheumatol* 1999; 26(4):1011–2.

