REVIEW ARTICLE e-ISSN: 2349-0659 p-ISSN; 2350-0964

Disease Monitoring Parameters for Autoimmune Diseases

B. Karikalan[1]*, A. G. Mathialagan[2], T. H. Sasongko[3], K. Karisnan[3], K. Kademane[2], M. H. M. Nazmul[4]

Abstract

Autoimmune diseases are complex chronic multisystem disorders that are potentially life threatening. The etiology of autoimmune diseases is not known but genetic, hormonal, and environmental factors are found to be involved in their pathogenesis. The clinical course is usually very long and patients have circulating autoantibodies in their serum before the appearance of clinical signs and symptoms. Seventy-five percent of the autoimmune diseases occur in women and it is one of the top ten causes of death in women below the age of 65 years. Many women may possess irregular non-specific symptoms such fatigue, muscle pain, and joint pain because of the genes and may or may not progress to one or the other symptomatic autoimmune diseases leading to severe complications including organ failure and death. Increased death rates in women because of autoimmune diseases have been recently reported in the US and UK. Researchers have also reported a steep rise in economic burden due to autoimmune diseases. Early diagnosis of the autoimmune diseases may play an important role in modifying the course of disease progression. Following up of patients with autoimmune diseases on a regular basis with available prognostic tests will greatly reduce morbidity and possibly mortality in these patients. In this comprehensive review article, we have summarized available prognostic strategies and recommendations for common autoimmune disorders.

Keywords: Autoimmune diseases, Prognosis, Parameters, Biomarkers

Asian Pac. J. Health Sci., (2021); DOI: 10.21276/apjhs.2021.8.1.6

Introduction

Dramatic increase in autoimmune diseases (AD) has been reported recently especially in industrialized countries. Experts from the US reported an alarming 8.8% rise in frequency of AD yearly, over the past three decades.[1] About 16% of the US population (24–50 million) suffer from autoimmune diseases. This prevalence equals combined incidence of cancer and heart disease. Seventy-five percent of the autoimmune diseases occur in women and it is one of the top ten causes of death in women below the age of 65 years. It has been attributed to the possibility of predisposing genetic variants being housed in the X chromosome. Many women may possess irregular non-specific symptoms such fatigue, muscle pain, and joint pain because of the genes and may or may not progress to one or the other symptomatic autoimmune diseases leading to severe complications including organ failure and death. Increased death rates in women because of autoimmune diseases have been recently reported in the US and UK. Researchers have also reported a steep rise in economic burden due to autoimmune diseases.[2,3] Autoimmune diseases are complex chronic multisystem disorders that are potentially life threatening. The etiology of autoimmune diseases is not known but genetic, hormonal, and environmental factors are found to be involved in their pathogenesis. The clinical course is usually very long and patients have circulating autoantibodies in their serum before the appearance of clinical signs and symptoms.

Early diagnosis of the autoimmune diseases may play an important role in modifying the course of disease progression. Following up of patients with autoimmune diseases on a regular basis with available prognostic tests will greatly reduce morbidity and possibly mortality in these patients.[4-6] The aim of this article is to summarize available prognostic strategies and recommendations for common autoimmune disorders.

Materials and Methods

This is a traditional review based on studies that were done to summarize available prognostic strategies and recommendations for common autoimmune disorders. The search engines that were utilized for electronic data from the Internet were MEDLINE, PUBMED, GOOGLE SCHOLAR, OVID, EBSCOHOST, and EMBASE using the search items autoimmune diseases, patient follow-up and prognostic biomarkers. All studies that mentioned patient follow-up strategies for any autoimmune disease worldwide on all time periods were included in the study.

[1]Department of Pathology, Perdana University, Kuala Lumpur, Malaysia
[2]DepartmentofPharmacology,PerdanaUniversity,KualaLumpur,Malaysia
[3]Department of Physiology, Perdana University, Kuala Lumpur, Malaysia
[4]Department of Microbiology, Perdana University, Kuala Lumpur, Malaysia
Corresponding Author: B. Karikalan, Department of Pathology, Perdana University, 50490 Kuala Lumpur, Malaysia. E-mail: baranisri@gmail.com

How to cite this article: Karikalan B, Mathialagan AG, Sasongko TH, Karisnan K, Kademane K, Nazmul MHM. Disease Monitoring Parameters for Autoimmune Diseases. Asian Pac. J. Health Sci., 2021;8(1):24-31

Source of support: Nil

Conflicts of interest: None

Received: 29/09/2020 **Revised:** 28/10/2020 **Accepted:** 19/11/2020

Results and Discussion

Autoimmune Thyroid Disease (ATD)

ATD affect 2–5% of the population. ATD constitutes one of the most prevalent organ-specific autoimmune diseases.[6] Grave's disease and Hasimoto's thyroiditis constitute STD and are the major reasons for clinical hyperthyroidism and hypothyroidism, respectively.[7] The presence of anti-thyroid peroxidase (TPO), anti-thyroglobulin (Tg), or anti-thyroid-stimulating hormone receptor (TSHR) antibodies indicate either of these auto-immune thyroid diseases. TSHR antibodies are molecules with the same action of TSH and are called as long-acting thyroid stimulator (LATS) due to its prolonged action. About 90% of Grave's disease patients and 0–20% of Hashimoto's disease patients

have elevated anti-TSHR antibodies.[8] Anti-TPO antibodies are seen in 90–95% of ATD patients, about 80% of Grave's disease patients and 10–15% of non-ATD patients.[3] There is evidence of increased oxidative stress due to decreased antioxidant levels, advanced glycation end products, and oxygen metabolites in blood.[9]

The production of antibodies against Tg can be induced by massive destruction of the thyroid gland, but high Tg levels in blood do not *per se* induce antibody production.[4] The functional consequence of anti-Tg antibodies is not clear as they do not cause thyroid cell destruction. Circulating antibodies could be detected in about 10% of healthy young subjects and 15% of people >60 years of age. Among HT patients, antibody prevalence was 60–80% and in 50–60% in GD patients. Another study identified anti-Tg antibodies in 70–80% of AITD patients, 30–40% of GD patients, and 10–15% of patients with non-thyroid immune disorders.

About 50–60% of grave's disease patients and 60–80% of Hashimoto's disease patients have elevated anti-Tg antibodies. Anti-Tg antibodies were also detected in 10% of healthy young patients and in patients with non-thyroid immune disorders. The role of anti-Tg antibodies is unclear. They do not cause thyroid cell destruction. They can be induced by excessive destruction of the thyroid gland but high blood Tg levels do not increase antibody production.[10,11]

Long-term follow-up of all autoimmune anti-thyroid disease by assessing thyroid status is important. The majority of long-term follow-up studies including quantitative thyroid antibody measurements showed fluctuating unpredicting results. Hence, assessing levels of antibodies in autoimmune thyroiditis patients are unreliable especially for long-term follow-up plans.

Thyroid status must be monitored in ATD patients by assessing serum TSH levels. Secretion of the thyroid hormones is regulated by the TSH regulates secretion of thyroid hormones, thyroxine (T4) and T3. In turn, thyroid hormones control TSH secretion. There lies a negative feedback relationship between free T4 (fT4) and TSH. Even small changes in fT4 concentration induce very large reciprocal changes in TSH secretion.[5] This means that serum levels of TSH are the best indicators for assessing thyroid function. TSH levels at the time of presentation are also important in signaling the clinical course of the disease. Assessing thyroid status by TSH and T4 is required in all patients with autoimmune thyroiditis.[12]

Pernicious Anemia

Long-term autoimmune attack of gastric mucosa results in a condition called pernicious anemia (PA). Preventing lifelong complications of this condition by understanding its pathogenesis has been an important fascinating scientific endeavor. Identifying autoantibodies responsible for the clinical effects of the disease and using them to develop animal models of the disease has been extremely helpful in understanding underlying immunopathology of this disease. Although clinical diagnosis can be done by measuring autoantibodies in patients serum, due to low specificity and sensitivity, sometimes endoscopic examination is essential to make a diagnosis.[13]

Monitoring patients with pernicious anemia, although complex, needs to be complete. PA patients must be monitored, yearly, for full blood count and serum ferritin and cobalamin levels for early detection and treatment of anemia. PA patients should meet with the clinician yearly for clinical evaluation (dysphagia, epigastric pain, dyspeptic symptoms, loss of body weight, and/or iron-deficiency). Presence of any of the above symptoms requires immediate endoscopic evaluation. Annual incidence of gastric cancer in pernicious anemia patients range from 0.1 to 0.5%.[14-16]

Different studies have recommended different intervals for endoscopic evaluation of pernicious anemia patients, ranging from 1 year to 5 years.[17] One recent study that compared 2 and 4 years endoscopic follow-up of pernicious anemia, suggested that a 4-year follow-up to be safe and effective in the detection of pre-neoplastic and neoplastic lesions.[18] Considering the risk for developing neoplastic lesions over time in some PA patients, all PA patients should be monitored regularly by gastroscopy with antral and corporal biopsies at 4-year intervals. However, this approach lacks prospective data on cost-effectiveness.[19]

Primary Biliary Cirrhosis

Primary biliary cirrhosis (PBC) is an ideal autoimmune disease with the presence of its specific serologic signature of antimicrobial antibodies (AMA) and bile duct pathology. Along with measuring AMA levels and alkaline phosphatase levels (indicating cholestasis), histology of non-infective cholangitis, and destruction of bile ducts aid in diagnosing PBC. Follow-up of PBC patients include liver function tests (every 3–6 months), thyroid function tests (annually), bone mineral density (every 3–4 years), vitamin levels (for Vtamins A, D, and K annually if bilirubin >2), and upper endoscopy (every 1–3 years, if cirrhosis is present or Mayo risk score is > 4.1). Ultrasound and AFP levels are done in patients with known or suspected cirrhosis.[20]

Liver functions tests indicate disease progression and activity. Thyroid function tests and bone mineral density are done because PBC patients are prone to coexisting other autoimmune diseases such as rheumatoid arthritis, ATD, and Sjogren's syndrome. Regular upper endoscopy is needed, since PBC patients are known to develop esophageal varices even in the absence of cirrhosis. Abdominal ultrasound and AFP levels are required for patients with definite or suspected cirrhosis. Although asymptomatic PBC has an excellent prognosis, about 25% of PBC patients develop symptoms over duration of 10 years. Hence, PBC patients need to be monitored at required intervals with above-mentioned investigations.[21]

Multiple Sclerosis

Multiple sclerosis (MS) is an autoimmune disorder of the nervous system. There is T cell mediated immune response causing destruction of myelin sheaths.[22] Diagnosis of MS is based on McDonald's 2010 criteria using clinical evidence including number of attacks, number of lesions in MRI scan, and CSF evaluation for oligoclonal bands and/or elevated IgG index.[23] A follow-up brain MRI is recommended in all diagnosed MS patients in the following conditions: (1) Demonstrate dissemination in time of diagnosis, (2) detect clinically silent disease activity while on treatment, (3) safety monitoring including progressive multifocal leukoencephalopathy surveillance while on treatment, (4) unexpected clinical worsening, (5) reassess the original diagnosis, (6) as a new baseline MRI before starting or modifying therapy, and (7) every 6 months to 2 years for patients with relapsing MS. A brain MRI with gadolinium is recommended for the diagnosis of MS. However, the use of gadolinium should be restricted to specific circumstances in follow-up to avoid its accumulation in the brain.[24]

Myasthenia Gravis (MG)

MG is an autoimmune neuromuscular disease characterized by fluctuating muscle weakness, worsening with exertion, and improving with rest.[25] MG is classified into five subtypes based on clinical evaluation and severity of muscle involvement by The Myasthenia Gravis Foundation of America (MGFA). Nearly 100% of patients have circulating acetylcholine receptor (AChR) antibodies. The levels of AChR antibodies do not correlate with severity of the disease. Hence, it is not considered as a relevant prognostic marker.[26]

Quality of life in MG patients can be measured by validated questionnaires such as 15 item MG-QOL 15 and other MG-specific scales. The questionnaire can either be done by the patient himself and/or could be completed by any trained clinic personnel or physician. The scores correlate well with the quality of life of MG patients. It is very useful for physicians to assess MG patients regularly, investigate the influencing factors, and administer corresponding interventions to improve the patients' quality of life.[27,28]

Sjogren's Syndrome (SjS)

SjS is an immune mediated chronic inflammatory disease that is characterized by lymphocytic destruction of the exocrine salivary glands resulting in the progressive impairment of gland function manifesting as sicca syndrome.[29,30] Gold standard test for diagnosing SjS is histopathological examination of minor salivary glands. However, the test is painful with occasional unreliable results.[31] B-cell hyperactivity leads to hypergammaglobulinemia and production of autoantibodies, namely, rheumatoid factor (RF) and anti-Ro and anti-La antibodies.[30]

2016 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria involving clinical features and tests, minor salivary gland biopsy, and specific autoantibodies for SjS classification have been widely used. The EULAR task force on SjS has proposed and validated two new instruments for evaluating disease activity and outcome measure. The ESSDAI (EULAR SjS Disease Activity Index) involves scoring systems according to severity and contains multiple domains involving various organ systems. A second tool, the EULAR Sjögren's syndrome patient-reported index (ESSPRI), serves for the purpose of evaluating the subjective symptoms of patients such as fatigue, dryness, and pain scored using lykert's numerical scale. Although the ESSDAI and ESSPRI are increasingly being used as inclusion criteria and endpoints in clinical trials evaluating innovative therapies for SjS, their use in clinical practice could also be recommended. A modified ESSDAI scoring system, the so-called ClinESSDAI has been derived from the ESSDAI by exclusion of the biological domain for the purpose of eliminating problems of collinearity in trials, in which biomarkers included in the biological domain of the original ESSDAI were analyzed as separate outcome measures.[30]

Goodpasture's Syndrome

Anti-glomerular basement membrane (GBM) antibody disease is a rare autoimmune disorder manifested as crescentic rapidly progressive glomerulonephritis. The term Goodpasture syndrome is used if pulmonary hemorrhage is also present.[32] Linear deposits of immunoglobulins along the glomerular basement membrane through direct immunofluorescence test determines anti-GBM disease. However, since kidney biopsy cannot always be easily and/or promptly performed in ill patients, diagnosis is made by detecting circulating anti-GBM antibodies in patients serum by immunoassay-based anti-GBM antibody analysis.[33,34] Patients on treatment for this syndrome need to be constantly monitored for disease recurrence by regular measurement of anti-GBM antibody titers. Patients should also be evaluated for any decline in renal function through regular renal function tests.[35]

Rheumatoid Arthritis (RA)

RA is a chronic inflammatory disease with autoimmune pathogenesis, characterized by joint involvement (that leads to deforming and destructive arthritis), and multiple systemic manifestations.[36] At present, the ACR/ EULAR 2010 criteria for the RA diagnosis use the rheumatoid factor (RF) and antibodies against cyclic citrullinated proteins (anti-CCP). Besides them, other diagnostic biomarkers such as anti-citrullinated peptide antibodies (ACPA), antibodies against mutated citrullinated vimentin (anti-MCV), and antibodies against carbamylated proteins (Anti-Carp) that can help the early diagnosis of RA were identified.[37]

Three composite scores for disease monitoring include disease activity score (DAS 28), simple disease activity index (SDAI), and clinical disease activity index (CDAI). The parameters used in the above scores are tender joints, swollen joints, patient global assessment of disease activity, clinician global assessment of disease activity, and ESR and CRP levels. The disadvantage of these scores is the degree of subjectivity of some of the criteria. Moreover, a significant proportion of the patients with negative inflammatory tests, still have active disease.[38,39] For better monitoring of the disease activity, a test that includes several biomarkers under the name "multi-biomarkers disease activity test (MBDA) has been developed. It uses the determination of some biomarkers involved in the pathogenesis of the RA chain, and it is available for clinicians under the name VectraDA.[40]

Systemic Lupus Erythematosus (SLE)

SLE is a chronic multisystem disease, involving complex immunopathogenic mechanisms.[41] The disease usually has a relapsing and remitting course. The disease can result in considerable morbidity due to flare-ups and also due to accumulated damage. There is also an increased risk of premature death because of infection or cardiovascular disease.[42]

According to the modified criteria by American Rheumatism Association for SLE published in 1997 modification, SLE is diagnosed and classified if the patient had any 4 or more of 11 criteria mentioned.[43] However, in reality, diagnosis is made only on the basis of either autoantibodies or hematological features even when the criteria are not fully filled.[44] Revised versions of the BILAG-2004 index, SLEDAI-2K, and SELENA-SLEDAI index are some of the most reliable ways for evaluating disease activity. These methods involve manifestations/items of disease activity to be recorded and that the data collection forms to be used in accordance with relevant glossary and scoring systems.[45-52] The SLICC/ACR damage index (SDI) is another validated tool for evaluating disease activity.[53] Furthermore, patients' perception of their disease can be assessed using quality of life questionnaires such as the generic Short-form36 (SF-36), which has been validated to be used by SLE patients.[54] Lupus-specific questionnaires such as the Lupus Quality of Life (LupusQoL)[55] can also be used to assess the quality of life in SLE patients.

Table 1: List of common autoimmune diseases with their disease monitoring parameters

Disease	*Disease monitoring parameters*
Hashimoto's thyroiditis	TSH
Grave's Disease	T4, TSH
Pernicious anemia	Complete blood count, and serum cobalamin and ferritin levels 4-year-interval gastroscopy
Primary biliary cirrhosis	Albumin, total bilirubin, AST, ALT, ALP, GGT, PT every 3–6 months Thyroid function (TSH, free T4) Every 1 year, Bone mineral density testing Every 2–4 year, Upper GI endoscopy Every 1–2 years, Abdominal ultrasound and serum AFP Every 1 year (every 3–6 months in liver cirrhosis)
Multiple sclerosis	MRI – 6 months to 2 years; Contrast MRI - highly active disease; OR when there is rapidly declining and unexplained and unexpected clinical worsening;
Myasthenia gravis	Myasthenia Gravis Foundation of America (MGFA) clinical classification
Sjogren's syndrome	2016 ACR/EULAR classification criteria; ESSDAI; ESSPRI), ClinESSDAI
Goodpasture syndrome	Anti-GBM Ab, ANCA, Serum creatinine
Rheumatoid Arthritis	Disease activity score (DAS 28), simple disease activity index (SDAI) and clinical disease activity index (CDAI).; "multi-biomarkers disease activity test (MBDA)"; Rheumatoid factor (FR), Antibodies directed to cyclic citrullinated peptides (Anti-CCP), Antibodies against mutated citrullinated vimentin (Anti-MCV), Cartilage oligomeric matrix protein (COMP), calprotectin, survivin
SLE (Follow up every 1–3 months for active disease every 6–12 months for stable disease)	History and examination Focused history Clinical examination Vital signs (Blood pressure, heart rate, weight) Drug review including vaccination status Bloods Full blood count Other tests for anemia Renal function Bone profile Liver function tests Creatine kinase CRP Vitamin D3 (annually) Thyroid function Immunology Anti-dsDNA titer, C3/C4 level aPL (LA, aCL, anti-beta2-glycoptroteinI) Immunoglobulins (annually) Direct Coombs' test Urine Urinalysis (screen for proteinuria, haematuria, leucocyturia and nitrites to exclude infection) Urine random protein:creatinine ratio Or 24-h urine collection for protein Urine microscopy (and culture) Other investigations Microbiology (other) Biopsy (e.g. skin, kidney) Lung function tests Neurophysiology ECG Imaging Chest X-ray Other imaging (US, CT, MRI) Modifiable cardiovascular risk factors (Annually) Hypertension Dyslipidemia Diabetes mellitus High BMI Smoking Disease activity and damage scores (Annually) BILAG (BILAG 2004 index) or SLEDAI (SLEDAI–2K or SELENA SLEDAI) SLICC/ACR Damage Index Quality of life questionnaires (annually) Short-form 36 or LupusQoL
AI hepatitis	Serum ALT; IgG
Dermatomyositis	Myositis intention to treat index (MITAX) and the myositis disease activity assessment visual analogue scale (MYOACT), the myositis damage index (MDI)

(Contd...)

Table 1: (*Continued*)

Disease	*Disease monitoring parameters*
	(Evaluate the presence and extent of involvement in the constitutional, articular, cardiac, pulmonary, gastrointestinal, cutaneous and skeletal muscle organ/systems)
Systemic Sclerosis	Lung – a pulmonary function test with diffusing capacity (DLCo); annually, HRCT if lung fn decline Skin disease activity-modified Rodnan skin score Others – blood pressure (echo if necessary), complete blood count, metabolic state, and renal function
Pemphigus vulgaris	Pemphigus Disease Area Index (PDAI) and the Autoimmune Bullous Skin Disorder Intensity Score (ABSIS); oral disease severity index
Pemphigus foliaceus	Pemphigus Disease Area Index (PDAI) and the Autoimmune Bullous Skin Disorder Intensity Score (ABSIS);
Bullous pemphigoid	BPDAI consists of two components: Objective and pruritus.

Autoimmune Hepatitis (AIH)

AIH is a chronic immune mediated disorder of unknown etiology. It affects people of all ages and has usually a progressive and occasionally fluctuating course. Diagnostic criteria are based on presence of circulating autoantibodies, degree of serum hypergammaglobulinemia, interface lymphocytic infiltration on liver histology, and exclusion of viral hepatitis.[56,57] Disease activity measures should ideally be done by liver histology to monitor AI patients on treatment. Since, liver biopsy is invasive, regular monitoring is usually done using serological markers. Out of all serological markers that are used to assess liver function, ALT, and IgG are more relevant. They have 99% sensitivity in representing inflammatory activity in the liver. Remission is determined by normalization of the serological parameters. Sometimes, patients with normal serum parameters also showed inflammatory activity in histology. Having said that, disease monitoring by serological markers seems to be suitable for regular follow-up.[58]

Dermatomyositis (DM)

DM is a chronic immune mediated inflammatory disease of the skin and muscles. Fifty to 70% of DM patients show myositis specific autoantibodies in their serum.[59] Criteria for diagnosis and classification of DM defined by Bohan and Peter in 1975 are still most widely used.[60] Patients have elevated muscle enzymes (creatine kinase [CK], aldolase, aspartate aminotransferase [AST], alanine aminotransferase [ALT], and/or lactate dehydrogenase [LDH]) in addition to proximal muscle weakness and skin manifestations. Electromyogram (EMG) studies show abnormal but non-specific. Some of the specific findings include increased activity with fibrillation potentials, sharp positive waves, repetitive complex discharges, early recruitment, and tiny polyphasic motor potentials.[61] MRI seems to be more sensitive for evaluation of myositis with muscle edema and muscle atrophy becomes evident in later disease. Muscle biopsy is essential to confirm diagnosis.[62]

Myositis intention to treat index (MITAX) and the myositis disease activity assessment visual analog scale (MYOACT) are the two tools that have been developed to measure disease activity in these patients. Myositis damage index (MDI) is another index that has been devised to evaluate the extent of disease damage in different organs and systems. Myositis experts participating in the International Myositis Assessment and Clinical Studies (IMACS) group have found these indices to have good face validity and comprehensiveness in their review.[63] MITAX and MYOACT measures include evaluation of the constitutional, articular, cardiac, pulmonary, gastrointestinal, cutaneous, and skeletal muscle systems. The MDI is more comprehensive and assesses the severity and extent of damage in different organs and systems. The MDI is composed of two portions. One portion accounts for the damage in organ systems and the other portion is the myositis damage score (MYODAM) that consists of visual analog scales series to evaluate the severity of damage in various organ systems.[63]

Systemic Sclerosis (SSc)

SSc is a chronic multisystem connective tissue disorder caused by activation cellular as well as humoral immune systems. The disease is characterized by fibrosis of internal organs and skin, and microangiopathy. Diagnosis and also classification are established by American College of Rheumatology (ACR) classification criteria based on detection of disease specific autoantibodies in the serum and identification of typical microvascular changes.[64,65] Many tools are available for monitoring disease activity in systemic sclerosis. Skin severity can be measured by modified Rodnan skin score. Skin severity combined with a patient assessment of skin activity can determine overall disease severity. Measuring various autoantibody levels do not correlate with disease activity.[66]

Follow-up protocol for systemic sclerosis patients should include the following:[67]

1. Pulmonary function tests to be done annually and if found abnormal should be followed by HRCT.
2. Yearly echocardiography to determine right heart function.
3. Malignancy screening due to increased risk in these patients
4. Overall physical and psychological evaluation every 6 months.

A European Scleroderma Study Group has proposed a composite index including clinical examination, laboratory measures, patient assessment, and lung function to determine scleroderma disease activity in clinical practice. Special measures are helpful in the research setting including health assessment questionnaire-disability index modified for scleroderma, SF-36, Medsger severity index, the United Kingdom Function Scoreland various organ specific measures.[66] A composite disease activity measurement index was developed by an European scleroderma study group. The index includes clinical evaluation, laboratory investigations, and lung function tests and is being used in clinical practice.[68,69]

Pemphigus Vulgaris and Pemphigus Foliaceus

Pemphigus vulgaris is a humoral autoimmune disease with mucocutaneous blistering lesions due to the presence of

anti-desmoglein 3 or 1 IgG autoantibodies. Pemphigus foliaceus is also caused by humoral autoimmune response with blistering skin lesions sparing the oral mucosa due to anti-desmoglein 1 IgG autoantibodies. Biopsy of lesions from both pemphigus vulgaris and pemphigus foliaceus shows acantholysis that progress to intraepithelial blisters. The presence of residual basal keratinocytes at the basement membrane zone termed as tombstone effect can be seen in pemphigus vulgaris. Although intraepithelial blisters in both the diseases are non-inflammatory, mild neutrophilic or eosinophilic distribution can occasionally be seen in superficial dermis and epidermis. Direct immunofluorescence study of both diseases shows IgG antibodies and occasional complement C3 lining the cell surface in a honeycomb pattern. Although reliable and sensitive, immunofluorescence might yield false negative results in occasional cases due to reactants being inside acantholytic keratinocytes.[70]

Circulating pemphigus autoantibodies can be analyzed using enzyme-linked immunosorbent assays (ELISAs) that are highly sensitive and specific. Nearly, all pemphigus patients have anti-desmoglein antibodies.[71] On rare occasions, active skin lesions might be seen even in the absence of circulating antibodies and in 20–40% of patients in remission where known to have detectable circulating autoantibodies. Furthermore, very low levels of these autoantibodies can also be detected in normal individuals.[72-76]

The Pemphigus Disease Area Index (PDAI) and the Autoimmune Bullous Skin Disorder Intensity Score (ABSIS) are two indices used to measure pemphigus disease activity that has gained world-wide acceptance. PDAI takes into account the number and size of the lesions, while ABSIS is a scoring system involving body surface area and type of the lesions. Pemphigus diseases are identified as under different sub groups according to severity measured by both the indices.[77-81]

Other than disease severity, quality of life can be measured in these patients. Autoimmune Bullous Disease Quality of Life (ABQOL) and Treatment of Autoimmune Bullous Disease Quality of Life (TABQOL) are two reliable and valid tools for the measurement of quality of life of pemphigus patients. Both methods contain 17 questions to measure life quality-related parameters.[82-84]

Bullous Pemphigoid

Bullous pemphigoid (BP) is one of the rare but potentially fatal groups of autoimmune blistering skin diseases.[85] The disease manifests clinically as large and tense skin blisters preceded by intense pruritus and urticarial plaques, and immunopathological by the presence of subepidermal BP autoantibodies that affect adhesion substances promoting dermo-epidermal cohesion.[86]

A combination of clinical, histopathological, and immunological criteria are used to make a diagnosis of BP.[87] In addition to presence of tense bullae with histological evidence of dermal-epidermal separation and immunofluorescence positivity for IgG or C3, BP is diagnosed if three out of four following criteria are present: age > 70 years, absence of mucosal lesions, absence of atrophic lesions, and non-involvement of neck and head.[88,89]

Bullous Pemphigoid Disease Area Index (BPDAI) is the first BP specific disease severity outcome measure developed by the BP definitions group that consisted of worldwide autoimmune blistering disease experts.[90] BPDAI consists of objective and subjective pruritis components. Objective components include blisters or erosions, urticarial or erythematous lesions, and mucosal involvement while subjective components include severity of pruritus in the last 1 day, week, and month. The BPDAI index has been validated in terms of sensitivity, accuracy, external validity, inter-rater, and intra-rater reliability.[91-93] Other than disease severity by BPDAI, Autoimmune Bullous Disease Quality of Life (ABQOL) and Treatment of Autoimmune Bullous Disease Quality of Life (TABQOL) questionnaires may also be used to measure quality of life of BP patients. The two questionnaires have also been validated in terms of reliability and consistency.[77,94]

Conclusion

This review paper describes current disease monitoring parameters for patients on treatment for commonly occurring autoimmune diseases [Table 1]. Many have adequate markers and tests for predicting complications. However, some diseases such as Myasthenia gravis, Sjogren's syndrome, and advanced Systemic lupus erythematosus still require ideal predictive markers to be identified by further research. For these diseases, where ideal markers defining prognosis are not available, quality of life questionnaires are used as instruments to assess disease severity and progression.

Acknowledgments

The authors would like to thank Perdana University e-library resources for their services.

References

1. Lerner A, Jeremia P, Matthias T. The world incidence and prevalence of autoimmune diseases is increasing. Int J Celiac Dis 2015;3:151-5.
2. American Autoimmune Related Diseases Association. The Cost Burden of Autoimmune Disease: The Latest Front in the War on Healthcare Spending. Eastpointe, MI: American Autoimmune Related Diseases Association; 2011. Available from: http://www.aarda.org. [Last accessed on 2019 Novermber 09].
3. Walsh SJ, Rau LM. Autoimmune diseases: A leading cause of death among young and middle-aged women in the United States. Am J Public Health 2000;90:1463-6.
4. Shepshelovich D, Shoenfeld Y. Prediction and prevention of autoimmune diseases: Additional aspects of the mosaic of autoimmunity. Lupus 2006;15:183-90.
5. Beecham JE, Seneff S. Autoimmune disease: Budget-buster or enlightened solutions? (The coming epidemic and the new administration in Washington). Arch Community Med Public Health 2017;3:32-40.
6. Thomas SL, Griffiths C, Smeeth L, Rooney C, Hall AJ. Burden of mortality associated with autoimmune diseases among females in the United Kingdom. Am J Public Health 2010;100:2279-87.
7. Simmonds MJ, Gough SC. Unravelling the genetic complexity of autoimmune thyroid disease: HLA, CTLA-4 and beyond. Clin Exp Immunol 2004;136:1-10.
8. Dayan CM, Daniels GH. Chronic autoimmune thyroiditis. N Engl J Med 1996;335:99-107.
9. de Carvalho G, Perez C, Ward L. The clinical use of thyroid function tests. Arq Bras Endocrinol Metabol 2013;57:193-204.
10. Fröhlich E, Wahl R. Thyroid autoimmunity: Role of anti-thyroid antibodies in thyroid and extra-thyroidal diseases. Front Immunol 2017;8:521.
11. Franco JS, Amaya-Amaya J, Anaya JM. Thyroid disease and autoimmune diseases. In: Anaya JM, Shoenfeld Y, Rojas-Villarraga A, Levy RA, Cervera C, editors. Autoimmunity: From Bench to Bedside. Ch. 30. Bogota, Colombia: El Rosario University Press; 2013.

12. Özen S, Berk Ö, Şimşek DG, Darcan S. Clinical course of Hashimoto's thyroiditis and effects of levothyroxine therapy on the clinical course of the disease in children and adolescents. J Clin Res Pediatr Endocrinol 2011;3:192-7.
13. van Driel IR, Gleeson ET. Autoimmune gastritis and pernicious anemia. In: The Autoimmune Diseases. 5th ed., Ch. 44. London, United Kingdom: Academic Press; 2014. p. 619-31.
14. Sjöblom SM, Sipponen P, Miettinen M, Karonen SL, Jrvinen HJ. Gastroscopic screening for gastric carcinoids and carcinoma in pernicious anemia. Endoscopy 1988;20:52-6.
15. Kokkola A, Sjöblom SM, Haapiainen R, Sipponen P, Puolakkainen P, Järvinen H. The risk of gastric carcinoma and carcinoid tumours in patients with pernicious anaemia. A prospective follow-up study. Scand J Gastroenterol 1998;33:88-92.
16. Schafer LW, Larson DE, Melton LJ 3rd, Higgins JA, Zinsmeister AR. Risk of development of gastric carcinoma in patients with pernicious anemia: A population-based study in Rochester, Minnesota. Mayo Clin Proc 1985;60:444-8.
17. Sjöblom SM, Sipponen P, Järvinen H. Gastroscopic follow up of pernicious anaemia patients. Gut 1993;34:28-32.
18. Lahner E, Caruana P, D'Ambra G, Ferraro G, Di Giulio E, Fave GD, *et al*. First endoscopic-histologic follow-up in patients with body-predominant atrophic gastritis: When should it be done? Gastrointest Endosc 2001;53:443-8.
19. Lahner E, Annibale B. Pernicious anemia: New insights from a gastroenterological point of view. World J Gastroenterol 2009;15:5121-8.
20. Lindor KD, Gershwin ME, Poupon R, Kaplan M, Bergasa NV, Heathcote EJ. Primary biliary cirrhosis. Hepatology 2009;50:291-308.
21. Working Subgroup (English version) for Clinical Practice Guidelines for Primary Biliary Cirrhosis. Guidelines for the Management of Primary Biliary Cirrhosis: The Intractable Hepatobiliary Disease Study Group Supported by the Ministry of Health, Labour and Welfare of Japan2014), Guidelines for PBC. Hepatol Res 2014;44:71-90.
22. Lassmann H, Brück W, Lucchinetti C. Heterogeneity of multiple sclerosis pathogenesis: Implications for diagnosis and therapy. Trends Mol Med 2001;7:115-21.
23. Polman CH, Reingold SC, Banwell B, Clanet M, Cohen JA, Filippi M, *et al*. Diagnostic criteria for multiple sclerosis: 2010 Revisions to the McDonald criteria. Ann Neurol 2011;69:292-302.
24. Consortium of MS Centers MRI Protocol and Clinical Guidelines for the Diagnosis and Follow-up of MS. Revised Guidelines; 2018.
25. Trouth AJ, Dabi A, Solieman N, Kurukumbi M, Kalyanam J. Myasthenia gravis: A review. Autoimmune Dis 2012;2012:874680.
26. Heldal AT, Eide GE, Romi F, Owe JF, Gilhus NE. Myasthenia gravis foundation of America clinical classification. (Version 1). PLoS One 2014;9:e114060.
27. Xiao-Hui M, Zhiyun L, Ju L, Hong-Xi C, Zi-Yan S, Hong-Yu Z, *et al*. Investigation and analysis of health-related quality of life in myasthenia gravis patients with myasthenia gravis quality of life-15 Chinese version. J Peking Univ 2018;50:514-20.
28. Li KK, Qian K, Feng YG, Guo W, Tan QY, Deng B. Predictive factors of prolonged mechanical ventilation, overall survival, and quality of life in patients with post-thymectomy myasthenic crisis. World J Surg Oncol 2017;15:150.
29. Ito I, Nagai S, Kitaichi M, Nicholson AG, Johkoh T, Noma S, *et al*. Pulmonary manifestations of primary Sjogren's syndrome: A clinical, radiologic, and pathologic study. Am J Respir Crit Care Med 2005;171:632-8.
30. Del Papa N, Vitali C. Management of primary Sjögren's syndrome: Recent developments and new classification criteria. Ther Adv Musculoskelet Dis 2018;10:39-54.
31. Versura P, Frigato M, Cellini M, Mulè R, Malavolta N, Campos EC. Diagnostic performance of tear function tests in Sjogren's syndrome patients. Eye 2007;21:229-37.
32. Levy JB, Lachman RH, Pusey CD. Goodpasture's disease. Lancet 2001;358:917-20.
33. Wilson CB, Dixon FJ. Diagnosis of immunopathologic renal disease. Kidney Int 1974;5:389-401.
34. Sinico RA, Radice A, Corace C, Sabadini E, Bollini B, Anti-glomerular basement membrane antibodies in the diagnosis of Goodpasture syndrome: A comparison of different assays. Nephrol Dial Transplant 2006;21:397-401.
35. Zhang YY, Tang Z, Chen DM, Gong DH, Ji DX, Liu ZH. Comparison of double filtration plasmapheresis with immunoadsorption therapy in patients with anti-glomerular basement membrane nephritis. BMC Nephrol 2014;15:128.
36. Balanescu A. Poliartritareumatoidasiboliinrudite. In: Ionescu R editor. Esentialul in Reumatologie. Bucureşti: Medicala Amaltea; 2006.
37. Gavrilă BI, Ciofu C, Stoica V. Biomarkers in rheumatoid arthritis, what is new? J Med Life 2016;9:144-8.
38. Landewé R. Barriers to effective disease activity monitoring in rheumatoid arthritis clinical practice and implications for treat-to-target guidelines. Eur Musculoskelet Rev 2011;6:88-93.
39. Dewing KA, Fritz J, Kortan JM, Ruffing V. Personalized medicine in rheumatology: The nursing perspective. Rheumatol Nurse Newsl 2013;6:1-15.
40. Centola M, Cavet G, Shen Y, Ramanujan S, Knowlton N, Swan KA, *et al*. Development of a multi-biomarker disease activity test for rheumatoid arthritis. PLoS One 2013;8:e60635.
41. Rahman A, Isenberg DA. Systemic lupus erythematosus. N Engl J Med 2008;358:929-39.
42. Pons-Estel GJ, Alarcon GS, Scofield L, Reinlib L, Cooper GS. Understanding the epidemiology and progression of systemic lupus erythematosus. Semin Arthritis Rheum 2010;39:257-68.
43. Hochberg MC. Updating the American college of rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1997;40:1725.
44. Petri M. Review of classification criteria for systemic lupus erythematosus. Rheum Dis Clin North Am 2005;31:245-54.
45. Nuttall A, Isenberg DA. Assessment of disease activity, damage and quality of life in systemic lupus erythematosus: New aspects. Best Pract Res Clin Rheumatol 2013;27:309-18.
46. Rao V, Gordon C. Advances in the assessment of lupus disease activity and damage. Curr Opin Rheumatol 2014;26:510-9.
47. NHS England. Interim Clinical Commissioning Policy Statement: Rituximab for the Treatment of Systemic Lupus Erythematosus in Adults (Reference NHS England A13/PS/a). Available from: https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2013/10/a13-ps-a.pdf. [Last accessed on 2017 May 01].
48. Yee CS, Farewell V, Isenberg DA, Griffiths B, The LS, Bruce IN, *et al*. The BILAG-2004 index is sensitive to change for assessment of SLE disease activity. Rheumatology 2009;48:691-5.
49. Yee CS, Cresswell L, Farewell V, Rahman A, The LS, Griffiths B, *et al*. Numerical scoring for the BILAG-2004 index. Rheumatology 2010;49:1665-9.
50. Gladman DD, Ibanez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000. J Rheumatol 2002;29:288-91.
51. Buyon JP, Petri MA, Kim MY, Kalunian KC, Grossman J, Hahn BH, *et al*. The effect of combined estrogen and progesterone hormone replacement therapy on disease activity in systemic lupus erythematosus: A randomized trial. Ann Intern Med 2005;142:953-62.
52. The Selena-Sledai Index, (Appendix B). In: Tsokos G, Gordon C, Smolen J, editors. Systemic Lupus Erythematosus: A Companion to Rheumatology. 1st ed. Amsterdam, Netherlands: Elsevier; 2007. p. 525.
53. Gladman DD, Urowitz MB, Goldsmith CH, Fortin P, Ginzler E, Gordon C, *et al*. The reliability of the systemic lupus international collaborating clinics/American college of rheumatology damage index in patients with systemic lupus erythematosus. Arthritis Rheum 1997;40:809-13.
54. Stoll T, Gordon C, Seifert B, Richardson K, Malik J, Bacon PA, *et al*. Consistency and validity of patient administered assessment of quality of life by the MOS SF-36; its association with disease activity

and damage in patients with systemic lupus erythematosus. J Rheumatol 1997;24:1608-14.
55. McElhone K, Abbott J, Shelmerdine J, Bruce IN, Ahmad Y, Gordon C, *et al*. Development and validation of a disease-specific health-related quality of life measure, the LupusQol, for adults with systemic lupus erythematosus. Arthritis Rheum 2007;57:972-9.
56. Lowe D, John S. Autoimmune hepatitis: Appraisal of current treatment guidelines. World J Hepatol 2018;10:911-23.
57. Hennes EM, Zeniya M, Czaja AJ, Parés A, Dalekos GN, Krawitt EL, *et al*. Simplified criteria for the diagnosis of autoimmune hepatitis. Hepatology 2008;48:169-76.
58. Lüth S, Herkel J, Kanzler S, Frenzel C, Galle PR, Dienes HP, *et al*. Serologic markers compared with liver biopsy for monitoring disease activity in autoimmune hepatitis. J Clin Gastroenterol 2008;42:926-30.
59. Marvi U, Chung L, Fiorentino DF. Clinical presentation and evaluation of dermatomyositis. Indian J Dermatol 2012;57:375-81.
60. Bohan A, Peter JB. Polymyositis and dermatomyositis (first of two parts). N Engl J Med 1975;292:344-7.
61. Briani C, Doria A, Sarzi-Puttini P, Dalakas MC. Update on idiopathic inflammatory myopathies. Autoimmunity 2006;39:161-70.
62. Kimball AB, Summers RM, Turner M, Dugan EM, Hicks J, Miller FW, *et al*. Magnetic resonance imaging detection of occult skin and subcutaneous abnormalities in juvenile dermatomyositis. Implications for diagnosis and therapy. Arthritis Rheum 2000;43:1866-73.
63. Isenberg DA, Allen E, Farewell V, Ehrenstein MR, Hanna MG, Lundberg IE, *et al*. International consensus outcome measures for patients with idiopathic inflammatory myopathies. Development and initial validation of myositis activity and damage indices in patients with adult onset disease. Rheumatology (Oxford) 2004;43:49-54.
64. Lambova S, Müller-Ladner U. Systemic sclerosis. In: Ginsburg GS, Willard HF, Tsalik EL, Woods CW, editors. Genomic and Precision Medicine. 3rd ed., Ch. 17. Academic Press; 2019. p. 291-329.
65. Lonzetti LS, Joyal F, Raynauld J, Roussin A, Goulet J, Rich É, *et al*. Updating the American College of Rheumatology preliminary classification criteria for systemic sclerosis: Addition of severe nailfold capillaroscopy abnormalities markedly increases the sensitivity for limited scleroderma. Arthritis Rheum 2001;44:735-6.
66. Shah AA, Wigley FM. My approach to the treatment of scleroderma. Mayo Clin Proc 2013;88:377-93.
67. Khanna D, Denton CP. Evidence-based management of rapidly progressing systemic sclerosis. Best Pract Res Clin Rheumatol 2010;24:387-400.
68. Valentini G, Rossa AD, Bombardieri S, Bencivelli W, Silman AJ, D'Angelo S, *et al*. European multicentre study to define disease activity criteria for systemic sclerosis. II. Identification of disease activity variables and development of preliminary activity indexes. Ann Rheum Dis 2001;60:592-8.
69. Valentini G, D'Angelo S, Rossa AD, Bencivelli W, Bombardieri S. European scleroderma study group to define disease activity criteria for systemic sclerosis. IV. Assessment of skin thickening by modified rodnan skin score. Ann Rheum Dis 2003;62:904-5.
70. Kasperkiewicz M, Ellebrecht CT, Takahashi H, Yamagami J, Zillikens D, Payne AS, *et al*. Pemphigus. Nat Rev Dis Primers 2017;3:17026.
71. Amagai M, Komai A, Hashimoto T, Shirakata Y, Hashimoto K, Yamada T, *et al*. Usefulness of enzyme-linked immunosorbent assay using recombinant desmogleins 1 and 3 for serodiagnosis of pemphigus. Br J Dermatol 1999;140:351-7.
72. Schmidt E, Zillikens D. Modern diagnosis of autoimmune blistering skin diseases. Autoimmun Rev 2010;10:84-9.
73. Kwon EJ, Yamagami J, Nishikawa T, Amagai M. Anti-desmoglein IgG autoantibodies in patients with pemphigus in remission. J Eur Acad Dermatol Venereol 2008;22:1070-5.
74. Naseer SY, Seiffert-Sinha K, Sinha AA. Detailed profiling of anti-desmoglein autoantibodies identifies anti-Dsg1 reactivity as a key driver of disease activity and clinical expression in pemphigus vulgaris. Autoimmunity 2015;48:231-41.
75. Anzai H, Stanley JR, Amagai M. Production of low titers of anti-desmoglein 1 IgG autoantibodies in some patients with staphylococcal scalded skin syndrome. J Invest Dermatol 2006;126:2139-41.
76. Prussmann W, Prüßmann J, Koga H, Recke A, Iwata H, Juhl D, *et al*. Prevalence of pemphigus and pemphigoid autoantibodies in the general population. Orphanet J Rare Dis 2015;10:63.
77. Zhao CY, Murrell DF. Outcome measures for autoimmune blistering diseases. J Dermatol 2015;42:31-6.
78. Rosenbach M, Murrell DF, Bystryn JC, Dulay S, Dick S, Fakharzadeh S, *et al*. Reliability and convergent validity of two outcome instruments for pemphigus. J Invest Dermatol 2008;129:2404-10.
79. Pfütze M, Niedermeier A, Hertl M, Eming R. Introducing a novel autoimmune bullous skin disorder intensity score (ABSIS) in pemphigus. Eur J Dermatol 2007;17:4-11.
80. Shimizu T, Takebayashi T, Sato Y, Niizeki H, Aoyama Y, Kitajima Y, *et al*. Grading criteria for disease severity by pemphigus disease area index. J Dermatol 2014;41:969-73.
81. Boulard C, Lehembre SD, Picard-Dahan C, Kern JS, Zambruno G, Feliciani C, *et al*. Calculation of cutoff values based on the ABSIS and PDAI pemphigus scoring systems for defining moderate, significant, and extensive types of pemphigus. Br J Dermatol 2016;175:142-9.
82. Sebaratnam DF, Hanna AM, Chee SN, Frew JW, Venugopal SS, Daniel BS, *et al*. Development of a quality-of-life instrument for autoimmune bullous disease: The autoimmune bullous disease quality of life questionnaire. JAMA Dermatol 2013;149:1186-91.
83. Tjokrowidjaja A, Daniel BS, Frew JW, Sebaratnam DF, Hanna AM, Chee S, *et al*. The development and validation of the treatment of autoimmune bullous disease quality of life questionnaire, a tool to measure the quality of life impacts of treatments used in patients with autoimmune blistering disease. Br J Dermatol 2013;169:1000-6.
84. Sebaratnam DF, Okawa J, Payne A, Murrell DF, Werth VP. Reliability of the autoimmune bullous disease quality of life (ABQOL) questionnaire in the USA. Qual Life Res 2015;24:2257-60.
85. Marazza G, Pham HC, Schärer L, Pedrazzetti PP, Hunziker T, Trüeb RM, *et al*. Incidence of bullous pemphigoid and pemphigus in Switzerland: A 2-year prospective study. Br J Dermatol 2009;161:861-8.
86. Labib RS, Anhalt GJ, Patel HP, Mutasim DF, Diaz LA. Molecular heterogeneity of the bullous pemphigoid antigens as detected by immunoblotting. J Immunol 1986;136:1231-5.
87. Di Zenzo G, Torre RD, Zambruno G, Borradori L. Bullous pemphigoid: From the clinic to the bench. Clin Dermatol 2012;30:3-16.
88. Vaillant L, Bernard P, Joly P, Prost C, Labeille B, Bedane C, *et al*. Evaluation of clinical criteria for diagnosis of bullous pemphigoid. French Bullous Study Group. Arch Dermatol 1998;134:1075-80.
89. Joly P, Courville P, Lok C, Bernard P, Saiag P, Dreno B, *et al*. Clinical criteria for the diagnosis of bullous pemphigoid: A reevaluation according to immunoblot analysis of patient sera. Dermatology. 2004;208:16-20.
90. Murrell DF, Daniel BS, Joly P, Borradori L, Amagai M, Hashimoto T, *et al*. Definitions and outcome measures for bullous pemphigoid: Recommendations by an international panel of experts. J Am Acad Dermatol 2012;66:479-85.
91. Patsatsi A, Kyriakou A, Giannakou A, Pavlitou-Tsiontsi A, Lambropoulos A, Sotiriadis D. Clinical significance of anti-desmoglein-1 and-3 circulating autoantibodies in pemphigus patients measured by area index and intensity score. Acta DermVenereol 2014;94:203-6.
92. Lévy-Sitbon C, Barbe C, Plee J, Goeldel AL, Antonicelli F, Reguiaï Z, *et al*. Assessment of bullous pemphigoid disease area index during treatment: A prospective study of 30 patients. Dermatology 2014;229:116-22.
93. Wijayanti A, Zhao CY, Boettiger D, Chiang YZ, Ishii N, Hashimoto T, *et al*. The Validity, Reliability and Responsiveness of the Bullous Pemphigoid Disease Area Index (BPDAI). North Stradbroke Island, Australia: Cutaneous Biologic Meeting; 2014.
94. Finlay AY, Khan GK, Luscombe DK, Salek MS. Validation of sickness impact profile and psoriasis disability index in psoriasis. Br J Dermatol 1990;123:751-6.