Results: When compared to sham, control and experimental groups was observed to have reduced connective tissue fibrosis in dermis area, according to Masson Trichrome results. EGCG group showed a significant reduction in fibrosis at the dermal surface area with respect to hematoxylin measurements. MMP-1, MMP-8, p-SMAD 2/3 protein levels and TGF- β mRNA expression were slightly decreased in EGCG Group compared with the other tested groups ($p < 0.05$). Otherwise, MMP-13 wasn't change between groups.

Conclusions: This study contributes to the potential use of EGCG as a treatment for fibrosis in SSc patients. Also, MMP-1&MMP-8 may play an important role in the etiology of SSc.

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AB0169 EVALUATION OF FREQUENCY AND TYPE OF PHYSICAL THERAPY IN MORE THAN 3400 PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a chronic fibrosing autoimmune disease which leads to severe musculoskeletal dysfunction, disability and contractures. Little is known on the type and extent of physical therapy (PT) prescribed to SSc patients in daily practice.

Objectives: To determine the type and frequency of PT received by SSc patients.

Methods: The data of 3430 clinically well defined SSc patients registered in the database of the German Network for Systemic Sclerosis were analyzed using SPSS.

Results: 48,5% (1662/3430) of the patients were treated with PT. The most frequently used form of PT was lymphatic drainage (23,6%/876), followed by physical exercise therapy (22%/817) and paraffin wax bath (10,5%/389). About half of the patients (46,9%) received two or three different forms of PT simultaneously. The prescription of PT did not correlate with the SSc subtype, as 49,5% (503/1016) of dcSSc patients, 50,3% (850/1689) of lcSSc patients and 45,7% (143/313) of SSc-Overlap patients received PT. PT was significantly more often prescribed to patients with pulmonary fibrosis in 51,1% (617/1208), synovitis in 61,6% (299/485) and CK elevation in 61,1% (174/285) ($p = 0,001-0,029$). PT did not correlate with the extent of skin fibrosis as measured by mRSS. Interestingly, patients with joint contractures (45,5%) (388/853) or tendon friction rubs (40,6%) (114/281) received significantly less often PT ($p = 0,006/0,045$). Comparing the prescription of PT during the initial period 2003–2008 (49,1%; 1937/3942) with the follow up period 2009–2013 (45,3%; 2217/4899), a significant decrease of PT prescription was observed ($p < 0,001$). Patterns of PT prescription differed significantly between medical subspecialties ($p < 0,005$) i.e. rheumatologists, dermatologists.

Conclusions: Although SSc is characterized by considerable disability and restriction of motion, less than 50% of patients received PT. The significant decrease in PT prescription during recent years may reflect lack of knowledge how to prescribe PT and more restrictive insurance regulations.

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AB0170 DIMINISHED PERIPHERAL T-CELL ACTIVATION ALONG WITH MARKED TH17 CIRCULATING PROFILE IN SSC

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Background: Systemic sclerosis (SSc) is a rare, debilitating connective tissue disease characterized by immunological alterations, vasculopathy and progressive skin and multiorgan fibrosis. The autoimmune dysregulation in SSc comprises lymphocyte activation that leads to autoantibody production, abnormal production of cytokines and chemokines, and impairment of the innate immunity. Recent research has shown that the T cell activation and especially T helper cells play an important role in the pathogenesis of SSc. Amongst them are the proinflammatory Th17 cells.

Objectives: To investigate T-cell activation, the percentage of Th17 cells and the circulating cytokine profile in SSc.

Methods: We enrolled a total of 24 SSc patients and 16 healthy controls in the study and divided the patients as having diffuse cutaneous SSc (dcSSc, $n=13$) or limited cutaneous SSc (lcSSc, $n=11$). Peripheral venous blood samples were collected from all subjects. We examined the percentage of activated T cells (unstimulated and upon stimulation with PHA-M) and of Th17 cells by flow cytometry in both patients and controls. We used ELISA to quantitate the serum levels of human IL-6, TGF- β 1, and IL-17A.

Results: We identified a decreased percentage of activated T cells (CD3+CD69+) in PHA-stimulated samples from SSc patients in comparison with healthy controls, $p < 0.001$. However, we did not establish a correlation between the down-regulated CD3+CD69+ cells and the SSc phenotype.

With regard to Th17 cells, our patients demonstrated increased percentage as opposed to controls, $p=0.031$. We detected up-regulated Th17 cells within the lcSSc subset against controls, $p=0.025$. However, no difference was found between dcSSc and lcSSc patients. Regarding the peripheral cytokine profile, we detected raised levels of IL-6, $p < 0.001$, TGF- β 1, $p=0.02$, and IL-17A, $p < 0.001$ in patients when compared to controls. Furthermore, we found increased circulating TGF- β , IL-6 and IL-17A in the lcSSc subset versus healthy individuals, as it follows TGF- β 1, $p=0.031$, IL-6, $p < 0.001$, and IL-17A, $p < 0.001$. Furthermore, circulating IL-17A was higher in lcSSc as opposed to dcSSc subset, $p=0.008$. Within the dcSSc phenotype, we detected raised levels of IL-17A and IL-6 versus controls: IL-17A, $p < 0.001$, IL-6, $p < 0.001$.

Conclusions: Our results demonstrate down-regulated T-cell activation upon PHA-stimulation along with pronounced peripheral Th17 profile, and related cytokines in SSc patients, suggesting their implication in the pathogenesis of SSc.

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AB0171 ANTI-CARBAMYLATED PROTEIN ANTIBODIES IN PATIENTS WITH SYSTEMIC SCLEROSIS: AN INTRIGUING ASSOCIATION WITH SKIN INVOLVEMENT

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Background: Systemic sclerosis (SSc), one of the most complex connective tissue disease, is characterized by three pathogenic events namely, vascular damage, autoimmunity and fibroblast activation, leading to a widespread fibrosis of skin and internal organs (1,2). Previous studies showed that 1) carbamylation mainly affects structural proteins undergoing to a low turn-over rate, namely dermal skin and tendons-associated proteins; and that 2) carbamylated proteins accumulate in skin in an age-dependent manner, contributing to tissue alteration (3).

Objectives: As dermis is a disease target and anti-carbamylated protein antibodies (anti-CarP Ab) have been reported in patients with SSc (4), we sought to evaluate any relationship between anti-CarP Ab and clinical parameters reflecting skin involvement in SSc.

Methods: Serum samples and clinical data from 123 patients with SSc were collected. Anti-CarP Ab were detected by indirect ELISA, using carbamylated bovine serum albumin as the antigen. Serum Anti-CarP Ab levels were also measured in 41 healthy aged-matched individuals. Clinical data were retrieved as previously reported (5).

Results: The mean serum levels of anti-CarP Ab did not statistically differ

between healthy and SSc group. In SSc, Spearman analysis showed that anti-CarP inversely correlated with the modified Rodnan skin score (RSS) ($R = -0.325$, $p < 0.001$), independently of patients' age. Receiver operating characteristics (ROC) analysis identified the anti-CarP cutoff that best discriminated dichotomized clinical variables related to skin involvement. This cutoff that was employed to subdivide SSc patients into anti-CarP positive and anti-CarP negative patients. Three SSc skin-related clinical parameters were significantly different between groups: RSS ($p = 0.001$), SI skin ($p = 0.002$), and sclerodema ($p < 0.001$). A worse skin involvement was associated with low anti-CarP levels.

Conclusions: The study shows that anti-CarP Ab serum level inversely associates to the severity of skin involvement in SSc patients. One possible mechanism to explain the inverse association is that the disease-dependent accumulation of carbamylated proteins in the skin may neutralize circulating anti-CarP Ab, thus contributing to their serum levels decrease. However, further investigation is needed to clarify this issue and to assess whether the levels anti-CarP Ab can be useful in the clinical setting of SSc.

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AB0172 PSGL-1 AND ADAM8 ON DENDRITIC CELLS ARE ASSOCIATED WITH SYSTEMIC SCLEROSIS AND COULD ACT AS BIOMARKERS FOR INTERSTITIAL LUNG DISEASE

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Background: Systemic sclerosis (SSc) is a chronic autoimmune disorder with cutaneous, vascular and immune cells abnormalities that lead to extensive cutaneous and visceral fibrosis with high morbidity and mortality. P-Selectin glycoprotein ligand-1 (PSGL-1) is the major ligand for P-selectin. PSGL-1 mediates the initial contacts with endothelial cells during extravasation to inflamed tissues or homing to several tissues in homeostatic conditions. In addition, PSGL-1/P-selectin interaction contributes to the homeostasis of the immune system by generating regulatory T cells¹. Importantly, the metalloprotease ADAM8 interacts with PSGL-1 and proteolytically processes it, what could be a regulatory mechanism to control the expression of PSGL-1². Interestingly, mice lacking PSGL-1 develop a progressive SSc-like syndrome³.

Objectives: To investigate whether PSGL-1 and ADAM8 expression on leukocytes could be implicated in the pathogenesis of SSc.

Methods: PBLs from 47 SSc patients and 35 healthy donors were analyzed by flow cytometry. The percentage of cells expressing PSGL-1, HLA-DR and ADAM8, as well as the membrane (without cell permeabilization) and total (after cell permeabilization) expression were assessed for each leukocyte subset. For cell permeabilization, cells were incubated for 15 min at room temperature with a fixation/permeabilization solution. Positivity was established using isotype control antibodies. Comparisons between groups were analyzed with Student t tests or Mann-Whitney U test. For pairwise multiple comparisons one-way ANOVA with Tukey's post hoc test was applied ($p < 0.05$, 95% CI). To analyze the possible contribution of PSGL-1, ADAM8 and HLA-DR to SSc pathogenesis, and to explore whether they could be used as biomarkers for SSc, we studied the influence of these molecules using a multivariate logistic regression model.

Results: SSc patients showed increased expression of HLA-DR in antigen presenting cells (B cells, monocytes and dendritic cells), indicating a higher activation of these cells. PSGL-1 expression in B cells was decreased in SSc patients but increased in monocytes, dendritic cells (DC) and T cells. ADAM8 was increased in B and T lymphocytes, monocytes and DC from SSc patients. Overall, we have identified three variables that are associated with SSc: high percentage of ADAM8-expressing pDC, high PSGL-1 expression in cDC and high HLA-DR expression in CD16+ monocytes. Remarkably, highest PSGL-1 expression on conventional DC (cDC) and high levels of ADAM8 on plasmacytoid DC (pDC) associate with interstitial lung disease (ILD), one of the most severe SSc clinical manifestations, suggesting that PSGL-1 and ADAM8 could be prognostic markers of ILD.

Conclusions: This study highlights that PSGL-1 and ADAM8 expression on DC, monocytes and lymphocytes could be implicated in SSc pathogenesis and particularly on DC might act as biomarkers for ILD.

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AB0173 MYCOBACTERIAL INFECTION IN SYSTEMIC LUPUS ERYTHEMATOSUS: CLINICAL SIGNIFICANCE AND ASSOCIATED FACTORS. DATA FROM THE REGISTRY OF PATIENTS WITH SLE OF THE SPANISH SOCIETY OF RHEUMATOLOGY (RELESSER)

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Objectives: To study the prevalence of mycobacterial infection (MI), the associated factors and their clinical significance in patients included in a large SLE cohort.

Methods: Retrospective descriptive study of RELESSER patients with a history of MI and analysis of the factors associated with this infection.

Results: In RELESSER 3,658 patients with ≥ 4 ACR SLE criteria were included. 90% are women with a mean age of 32.9 years. 93% are Caucasians. The mean follow-up time ($\pm$ SD) was 120.2 ($\pm$ 87.6) months. 705 (19.3%) patients had ≥ 1 severe infection (defined as requiring admission); 1,227 severe infections occurred. MI were diagnosed in 42 patients (1.2% of all RELESSER patients, 3.4% of all severe infections), 85.7% women. The incidence rate of MI was 1 per 1,000 patients/year (95% CI:0.7–1.4).

MI presentation was pulmonary in 18 (42.9%) patients and extrapulmonary in 24 (57.1%) patients [joints in 8 (19.0%) patients, soft tissue in 6 (14.3%) and other sites in 10 (23.8%)]. The extrapulmonary form was associated with immunosuppressants use: 84.6% of the 13 patients treated with immunosuppressive drugs versus 44.4% of the 27 patients without ($p = 0.01$). We did not observe this association with the use of corticosteroids.

To study the factors associated with MI, we performed a bivariate analysis including the variables associated with severe infection in RELESSER (age, sex, ethnicity, corticosteroids, immunosuppressants, antimalarials, previous admission by SLE activity, rituximab and anti-TNF use, Katz severity index, SDI index, SLEDAI index and Charlson comorbidity index). There is a statistically significant association with previous admission by SLE activity (RR:2.9, 95–95%:1.3–6.2, $p = 0.007$), renal impairment (RR:2.0, CI 95%:1.1–3.7, $p = 0.04$), the Katz score (RR:2.1, 95% CI:1.1–4.0, $p = 0.04$) and the Charlson index (RR: 2.5; 95% CI: 1.3–4.8, $p = 0.009$). Damage (SDI > 0) was closely associated with significance:RR: 2.0; 95% CI: 1.0–4.0, $p = 0.07$. Immunosuppressants use was associated with an important increase in the risk of MI: RR:4.3; 95% CI:2.2–8.3, $p = 0.31$.

Two patients (4.8%) died (1 respiratory and 1 extrapulmonary). Mean survival after MI diagnosis in these cases was 21 days.

Conclusions: MI in RELESSER affects 1.15% of patients. Its incidence rate is 1 per 1,000 patients/year (95% CI:0.7–1.4). Extrapulmonary localization affects more than half of the patients and is associated with immunosuppressants use. Previous admission by SLE activity, renal involvement, SLE severity and increased number of comorbidities are factors associated with MI.

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AB0174 LYMPHOCYTE SUBSETS T, B AND NK CELLS IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a rare multisystem disease with underlying immune mechanisms, whose pathogenesis remains unclear. Few previous reports have evaluated lymphocyte subpopulations in SSc and your results are conflicting.

Objectives: The present study aimed to analyze the lymphocyte subsets in SSc patients in comparison to healthy individuals.

Methods: Peripheral blood (PB) samples to analyze lymphocyte subsets were obtained from a non-random convenience sample of 20 SSc patients. Twenty healthy individuals recruited from the blood bank were used as sex and age-matched controls. Blood samples were analyzed by flow cytometry for total T cells, CD4+ and CD8+ T cells subsets, CD19+ B cells and total NK cells. Statistical analyses were performed using the IBM Statistical Package for Social Sciences (SPSS 18.0). Data are expressed as mean $\pm$ SD and median and range. Non-parametric Mann-Whitney U test was used for analyses of the flow cytometry. A probability $p < 0.05$ was considered statistically significant.

Results: The mean (SD) age of SSc patients was 57.9 (14.2) years, 95% were female and 31.6% presented diffuse cutaneous SSc (dcSSc). Patients presented a lower mean total lymphocyte count compared to healthy controls (23.7% vs.