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# Connective Tissue Diseases on the Elderly Population in Dakar Hospital Setting

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## Abstract

**Introduction:** Immunosenescence contributes to the development of autoantibodies. However, while the prevalence of some autoantibodies increases with age, the incidence of connective tissue diseases decreases with age. This study aims to determine the clinical and paraclinical characteristics of connective tissue diseases in the elderly population. **Materials and Methods:** We conducted a retrospective and descriptive study, from March 2010 to March 2021, in the Internal Medicine Department of Aristide Le Dantec Hospital, including all the medical records of patients followed up for connective tissue disease and whose symptomatology began at an age greater than or equal to 65 years. Epidemiological, clinical, paraclinical, therapeutic and evolutionary data were collected from a pre-established survey form and then processed using SPSS software. **Results:** Overall, 22 cases were collected out of 275 seen on consultation. They involved 16 women and 6 men, aged between 65 and 85 years with a median of 70 years. The mean duration of the clinical picture was 15.7 months with extremes of 1 and 96 months. The clinical symptoms were joint pain in 21 patients associated with dry eye and mouth syndrome in seven cases and one patient underwent isolated dry eye and mouth syndrome. Joint involvement was deforming in 13 patients. Poor general condition was noted in 20 patients. Biology showed anemia in 14 patients, hyperleukocytosis (2 patients) and thrombocytosis (5 patients). The sedimentation rate (SR) was accelerated in 9 patients and the C-reactive protein (CRP) was positive in 12 patients. Immunology showed a positive Latex test (3 patients/6), Waaler-Rose reaction (8 patients/13), anti-cyclic citrullinated peptides (anti-CCP) antibodies (11 patients/11), anti-nuclear antibodies (2 patients/4). Anti-extractable nuclear antigens (anti-ENA) antibody testing in 4 patients showed positive

anti-U1RNP (1 case), anti-SSA and anti-SSB (1 case). Plain X-Rays of the hands, wrists and feet showed destructive lesions in 16 patients. The diagnosis of rheumatoid arthritis (RA) was set in 21 patients, one of which was associated with Sjogren's syndrome (SS) and one with primary Sjogren's syndrome. Treatment was based on prednisone (21 cases), methotrexate (17 patients), and hydroxychloroquine (9 patients). The evolution was remarkable in 10 patients. **Conclusion:** Autoimmune diseases in the elderly are uncommon compared to the young adult population. In our study, we only found cases of rheumatoid arthritis and Sjogren's syndrome. As the population ages, connective tissue diseases may be increasingly diagnosed.

## Keywords

Connective Tissue Disease, Elderly, Rheumatoïd Polyarthritis, Sjögren's Syndrome, Dakar

## 1. Introduction

Immunosenescence or aging of the immune system contributes to the increased occurrence of autoantibodies [1]. However, while the prevalence of some autoantibodies increases with age, the incidence of systemic autoimmune diseases called connective tissue diseases, on the contrary, decreases with age [2]. To our knowledge, few studies have focused on systemic diseases in the elderly [2] [3] [4]. In Senegal, a study in a rheumatology department reported 74 cases of connective tissue disease in the elderly in 5 years [5]. Several studies have been carried out on the particularities of RA in the elderly [6] [7] [8] [9] and other studies have concerned SS [10] [11] [12] and systemic lupus erythematosus in the elderly [13] [14] [15] [16] and often the aspects of these affections were compared with those of the adults [17] [18] [19]. Our present study aimed to determine the clinical and paraclinical characteristics of systemic autoimmune diseases in the elderly in internal medicine in Dakar.

## 2. Materials and Methods

We conducted a retrospective and descriptive study, from 2010 to 2021 in the Internal Medicine Department of Aristide Le Dantec Hospital, included all the medical records of patients followed for a systemic autoimmune disease and whose symptomatology began at an age greater than or equal to 65 years according to the WHO definition of the elderly population. We didn't include medical records with insufficient data to make a positive diagnosis and those of elderly patients but on whom the condition started before the age of 65. The diagnosis of connectivitis was established on epidemiological, clinical, paraclinical arguments, in agreement with their usual international criteria, in particular the criteria for the ACR-EULAR 2010 for rheumatoid arthritis (RA), the criteria of American-European consensus of 2002 for the Sjogren's syndrome (SS). Epide-

miological, clinical, paraclinical, therapeutic and evolutionary data were collected from a pre-established survey form and processed using SPSS software. The outcome was considered remarkable if a low level of activity or remission of the disease was observed over 6 months or more and unfavourable if the clinical picture didn't improve and/or in case complications occur.

## 3. Results

22 cases were collected out of 275 seen on consultation, representing 8%. They included 16 women and 6 men, aged between 65 and 85 years with a median of 70 years.

The conditions associated with these connective tissue diseases were: hypertension (n = 7), diabetes (n = 2), asthma (n = 1), gout (n = 1), peptic ulcer (n = 1), uterine myoma (n = 1) and thyroid carcinoma (1 case).

The mean duration of the symptomatology was 15.7 months with extremes of 1 and 96 months. The clinical symptoms were inflammatory joint pain in 21 patients and one patient underwent isolated dry eye and mouth. This pain was polyarticular and symmetrical in 20 patients and monoarticular in one patient. Joint involvement was deforming in 13 patients. Extra-articular signs included dry eyes (n = 3), dry mouth (n = 2), dry eye and mouth syndrome (n = 1), rheumatoid nodules (n = 2) and basal lung crackles (n = 1). Poor general condition was noted in 20 patients featuring weight loss, physical asthenia and general anorexia (Table 1).

Anemia was noted in 14 patients. Leukocytes were normal in 16 patients. Two cases of hyperleukocytosis, two cases of leukopenia, two cases of neutropenia, one case of lymphopenia and one case of lymphocytosis were observed. Thrombocytosis was observed in 5 patients. The SR was not performed in 5 patients. However it was normal in 8 patients and was accelerated in 9 patients with levels ranging from 45 to 110 mm at the first hour. CRP was not performed in 2 cases, negative in 8 cases and positive in 12 cases ranging from 6 to 768 mg/L (Table 1).

The Latex test, performed in 6 patients, was positive in 3 patients. The Waaler-Rose test, performed in 13 patients, was positive in 8 patients. Anti-CCP antibodies were positive in all 11 patients. Anti-nuclear antibodies were present in 2/4 patients. Anti-ECT antibodies were positive in 4 patients, anti-U1RNP in 1, anti-SSA and anti-SSB in 1, and negative for anti-Sm, anti-Jo1, anti-ScL70 and anti-centromeres (Table 1).

Plain X-rays of hands, wrists and feet were abnormal in 16 patients, normal in 2 patients and not carried out in 4 patients. Isolated bone demineralisation was found in 3 patients. In the remaining 13 patients, the X-Rays showed destructive lesions combining pinching, demineralisation, geodes and erosions with fusing carpitis in 8 patients, erosion of the 5th metatarsal head in 5 patients and bilateral coxitis in 1 patient.

The diagnosis of rheumatoid arthritis (RA) was set in 21 patients, one of which was associated with Sjogren's syndrome (SS) and one case of primary SS (Figure 1).

**Table 1.** Clinical and immuno-biological data of patients.

| Clinique | Weight loss, asthenia, anorexia N = 20 | Polyarthritis N = 20 | Monoarthritis N = 1 | Joint deformities N = 13 | Oculo-oral dryness N = 6 | Rheumatoid nodules N = 1 |
|---|---|---|---|---|---|---|
| **Biologie** | | Results | | | Effective | |
| | SR | | Normale | | 8 | |
| | | | Accelerated | | 9 | |
| | CRP | | Positive | | 12 | |
| | | | Negative | | 8 | |
| | hemoglobin | | Normale | | 6 | |
| | | | Anemia | | 14 | |
| | Leukocytes | | Normale | | 16 | |
| | | | Hyperleukocytosis | | 2 | |
| | | | Leukopenia | | 2 | |
| | Neutrophils | | Normale | | 17 | |
| | | | Neutropenia | | 2 | |
| | Lymphocytes | | Normale | | 18 | |
| | | | Lymphopenia | | 1 | |
| | | | Lymphocytosis | | 1 | |
| | Platelets | | Normale | | 14 | |
| | | | Thrombocytosis | | 5 | |
| **Immunologie** | | Results | | | Effective | |
| | Latex | | Positive | | 3 | |
| | | | Negative | | 3 | |
| | Waaler rose | | Positive | | 8 | |
| | | | Negative | | 5 | |
| | Anti-CCP | | Positive | | 11 | |
| | | | Negative | | 2 | |
| | AAN | | Positive | | 2 | |
| | | | Negative | | 2 | |
| | U1RNP | | Positive | | 1 | |
| | | | Negative | | 3 | |
| | ANTI-SSA/Ro-SSB/La | | Positive | | 1 | |
| | | | Negative | | 3 | |
| | Autres (anti-Sm, Jo1, Scl70, centromères | | Positive | | 0 | |
| | | | Negative | | 4 | |

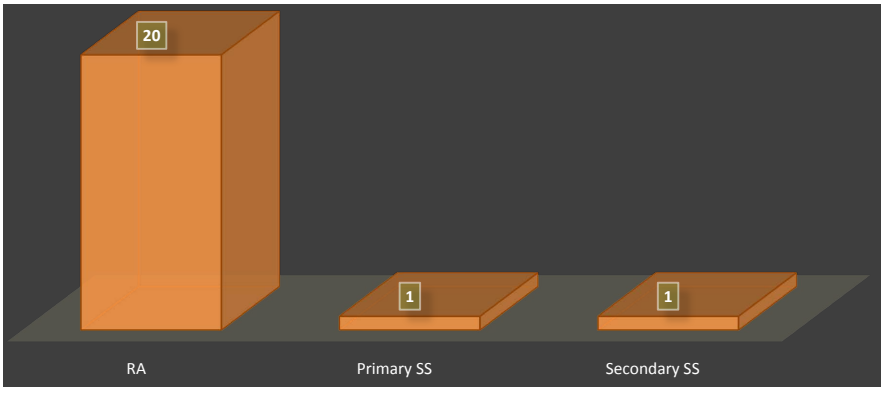


**Figure 1.** Distribution of patients according to type of connectivity.

Symptomatic treatment was based on prednisone (21 cases) and analgesics (3 cases). The core treatment was based on methotrexate (17 patients), hydroxychloroquine (9 patients) and azathioprine (1 case).

The outcome was remarkable in 10 patients, stationary in three patients. Six patients were lost of sight and two patients didn't undergo an assessment.

## 4. Discussion

An age greater than or equal to 65 years defines the elderly population according to the WHO. Advancing age is associated with a dysregulation of the immune system called immunosenescence [20] [21]. Physiological autoimmunity is more common in healthy elderly people and contrasts with the rarity of connective tissue diseases in this population. An increased prevalence of anti-double-stranded DNA, antithyroglobulin, anticardiolipin, antinuclear and rheumatoid factor autoantibodies has been reported in the serum of healthy elderly people [22] [23]. However, these data are still controversial [24] [25]. The prevalence of autoimmune diseases in the elderly was 8% in our study; RA and SS being the two ADIs found, while various connective tissue diseases were found in the other medical records investigated. This rate is similar to the literature data. According to Dubost JJ, RA is the most frequently diagnosed AD after the age of 60 [2]; it represents 10% to 33% of all AD according to the literature [6]. There was a clear predominance of women (72.72%), even though this predominance is lower than in the adult population, with a sex ratio of around 1.5 to 2, compared with 4 to 4.5 for RA in young people. The incidence of RA increases with age with a peak between the 4th and 6th decade [7]. Cases of elderly people with RA are with an estimated prevalence of 2% from the age of 60 onwards [26]. Late-onset RA is characterised by an acute onset, and evident general signs with common shoulder involvement [10]. It is often associated with poor general condition and may mimic paraneoplastic polyarthritis. In our cohort, 20 patients underwent poor general condition but shoulder involvement was not predominant. According to the literature, the level of rheumatoid factors is highly variable [8]. The frequency of anti-CCP in elderly patients with RA is 71% and 65% respectively in the studies reported by Dubost JJ and Lopez-Hoyos M [2] [27]. This frequency reaches 83% in the KORONA cohort [28]. However, another study reports that RA in the elderly is less frequently associated with rheumatoid factors and anti-CCP [17].

In Diallo's work in Senegal, the 74 cases of connective tissue diseases were divided into isolated RA (22 cases), primary SS (40 cases), SS secondary to RA (18 cases), SS associated with vitiligo (2 cases) and systemic lupus (2 cases) [5]. Dubost et al report that SS is the most common connective tissue disease, 28%, followed by scleroderma (20%), myositis (20%) and lupus (16%) [2]. Another study of 443 patients with inflammatory rheumatism hospitalised between 1990 and 1991 showed that 104 patients started their disease after the age of 60 [3]. RA was the most common, followed by PPR, Horton's disease and less frequently

connective tissue diseases and spondyloarthritis [2]. In this series, some patients underwent RA after 75 years of age [9]. SS can occur at any age but peaks in the 40s and 50s [11]. Its prevalence increases with age with a variable rate according to the literature. Indeed, the frequency was 30% according to Haga and [12] and was higher with 6% to 20% in other studies [10] [18] [19]. SS predominates in women with a female/male sex ratio of 9/1 or more [10] [11] [18] [19]. This female predominance was noted in our series. All the studies agree on the long delay in diagnosis of primary SS in the elderly. It was 38.6 ± 26.8 months in our study. This delay was relatively short compared to that found by Botsios (116.4 months ± 40.8) [19]. This long diagnosis delay can be explained by the alleviation of the functional signs of dry syndrome at the beginning and by the ubiquity of the systemic attacks, which are sometimes misleading, mixed with other pathologies. The existence of a biological inflammatory syndrome, a positive anti-nuclear antibody test, and the presence of anti-SSA/Ro and anti-SSB/La antibodies are the arguments in favour of SS that allow it to be differentiated from a simple dry syndrome that is common in the elderly. The presentation of SS in the elderly does not differ from that of the young. Glandular manifestations are common in primary SS in the elderly, with a frequency varying from 76.1 to 100% according to the studies [10] [18] [19]. Joint involvement is the most frequent extraglandular involvement in primary SS in the elderly, with a frequency ranging from 29% to 66.7% according to the studies [10] [18] [19]. It was 88.8% in the study carried by Chebbi [12].

Biological features are frequent in primary SS in the elderly [19]. The prevalence of ANAs in primary SS in the elderly varies from 36% to 85.7% according to the studies [10] [18] [19]. Our two patients were positive for antinuclear, anti-SSA and anti-SSB at levels greater than 16 times the normal range. In the studies performed by Garcia-Carrasco [10] and Botsios [10], the immunological expression of SS in elderly patients was similar to that in young population. However, other studies, notably those of Chebbi, Tishler and Haga [12] [18] [29], have reported significantly higher frequencies of anti-SSA and anti-SSB antibodies in Sjögren's syndrome in young population. In contrast to the study by Botsios [19], Haga and Jonsson [29] found a significant influence of age on serological abnormalities in primary SS, but not on disease manifestations. It has been suggested that older and younger patients with systemic AID may have different genetic determinants and respond to different triggering mechanisms [13] [14] [15] [16]. The slightly less excessive expression of immunological features in elderly patients with primary SS may reflect senescence of the immune system [4]. The study by Botsios, conducted on a cohort of 336 Italian patients with primary SS, shows a minimal effect of age of onset on the main clinical and immunological manifestations of such a disease. The treatment of connective tissue diseases in the elderly population must be cautious because it must consider the fragility of the patient. Thus, in elderly RA, treatment must be less aggressive than in the young because of the frequency of liver and kidney function impairment, the

presence of polymedication increasing the risk of drug interactions, comorbidities and the increased risk of infection [30]. Age over 75 years is a recognised factor in non-prescription of core treatment [31]. However, this population is more often exposed to glucocorticoids [31] [32]. NSAIDs should be used cautiously, taking into account renal function, risk of drug interaction, increased risk of cardiovascular, renal and gastrointestinal adverse effects.

Our study acknowledges some limitations in relation to the small size of our cohort and unusable medical records due to missing and/or paraclinical data. Thus we could not make an analytical approach and we limited ourselves to a descriptive study.

## 5. Conclusion

Systemic autoimmune diseases in the elderly are uncommon compared to the adult population. In our study, we only found cases of rheumatoid arthritis and Sjögren's syndrome and the clinical symptomatology was comparable to that of the adult population.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

## References

[1] Hurme, M., Korkki, S., Lehtimäki, T., Karhunen, P.J., Jylhä, M., Hervonen, A., *et al.* (2007) Autoimmunity and Longevity: Presence of Antinuclear Antibodies Is Not Associated with the Rate of Inflammation or Mortality in Nanogenarians. *Mechanisms of Ageing and Development*, **128**, 407-408. https://doi.org/10.1016/j.mad.2007.03.001

[2] Dubost, J.J., Pereira, B., Mathieu, S., Tournadre, A., Malochet Guinamand, S., Couderc, M., *et al.* (2014) Répartition des rhumatismes du sujet âgé: Enquête auprès des rhumatologues de la région Auvergne. *Revue du Rhumatisme*, **81**, 69-73. https://doi.org/10.1016/j.rhum.2013.04.011

[3] Dubost, J.J. and Sauvezie, B. (1992) Current Aspects of Inflammatory Rheumatic Diseases in Elderly Patients. *Revue du rhumatisme et des maladies osteo-articulaires*, **59**, 37S-42S. https://doi.org/10.1016/S0307-742X(21)00618-4

[4] Stevens, M.B. (1986) Connective Tissue Disease in the Elderly. *Clinics in Rheumatic Diseases*, **12**, 11-32.

[5] Diallo, S., Niasse, M. and Guèye, Y.A.N. (2020) Connectivites du sujet âgé: Étude de 74 observations. *Revue du Rhumatisme*, **87**, A253. https://doi.org/10.1016/j.rhum.2020.10.454

[6] Olivieri, I., Palazzi, C., Peruz, G. and Padula, A. (2005) Management Issues with Elderly-Onset Rheumatoid Arthritis: An Update. *Drugs & Aging*, **22**, 809-822. https://doi.org/10.2165/00002512-200522100-00002

[7] Daien, C., Hua, C., Gaujoux-Viala, C., Cantagrel, A., Dubremetz, M., Dougados, M., *et al.* (2019) Update of French Society for Rheumatology Recommendations for Managing Rheumatoid Arthritis. *Joint Bone Spine*, **86**, 135-150. https://doi.org/10.1016/j.jbspin.2018.10.002

[8] Soubrier, M., Mathieu, S., Payet, S., Dubost, J.J. and Ristori, J.M. (2010) Elderly Onset-Rheumatoid Arthritis. *Joint Bone Spine*, **77**, 290-296. https://doi.org/10.1016/j.jbspin.2010.04.004

[9] Chiba, H., Matsushita, K., Shibakawa, A. and Aoki, H. (2003) Rheumatoid Arthritis in Patients Aged above 75-Years-Old at Onset. *Ryumachi*, **43**, 557-563. https://doi.org/10.1191/096120399678847353

[10] García-Carrasco, M., Cervera, R., Rosas, J., Ramos-Casals, M., Ramos-Casals, M., Morlà, R.M., Sisó, A., *et al.* (1999) Primary Sjögren's Syndrome in the Elderly: Clinical and Immunological Characteristics. *Lupus*, **8**, 20-23. https://doi.org/10.1007/s00393-009-0518-3

[11] Westhoff, G. and Zink, A. (2010) Epidemiology of Primary Sjögren's Syndrome. *Zeitschrift für Rheumatologie*, **69**, 41-49. https://doi.org/10.11604/pamj.2015.20.8.5042

[12] Chebbi, W., Ben Salem, W., Klii, R., Kessomtini, W., Jerbi, S., Habib Sfar, M. (2015) Syndrome de Gougerot-Sjögren primitif du sujet âgé: Caractéristiques cliniques et immunologiques. *Pan African Medical Journal*, **20**, Article No. 8.

[13] Catoggio, L.J., Skinner, R.P., Smith, G. and Maddison, P.J. (1984) Systemic Lupus Erythematosus in the Elderly: Clinical and Serological Characteristics. *The Journal of Rheumatology*, **11**, 175-181.

[14] Bell, D.A. (1998) SLE in the Elderly. Is It Really SLE or Systemic Sjögren's Syndrome? *The Journal of Rheumatology*, **15**, 723-724.

[15] Rovensky, J. and Tuchynová, A. (2008) Systemic Lupus Erythematosus in the Elderly. *Autoimmunity Reviews*, **7**, 235-239. https://doi.org/10.1016/j.autrev.2007.11.014

[16] Lazaro, D. (2007) Elderly-Onset Systemic Lupus Erythematosus: Prevalence, Clinical Course and Treatment. *Drugs & Aging*, **24**, 701-715. https://doi.org/10.2165/00002512-200724090-00001

[17] Spinel-Bejarano, N., Quintana, G., Heredia, R., *et al.* (2013) Comparative Study of Elderly-Onset Rheumatoid Arthritis and Young-Onset Rheumatoid Arthritis in a Colombian Population: Clinical Laboratory and HLA DRB1 Findings. *Clinical and Experimental Rheumatology*, **31**, 40-46.

[18] Tishler, M., Yaron, I., Shirazi, I. and Yaron, M. (2001) Clinical and Immunological Characteristics of Elderly Onset Sjögren's Syndrome: A Comparison with Younger Onset Disease. *The Journal of Rheumatology*, **28**, 795-797.

[19] Botsios, C., Furlan, A., Ostuni, P., Sfriso, P., Andretta, M., Ometto, F., *et al.* (2011) Elderly Onset of Primary Sjögren's Syndrome: Clinical Manifestations, Serological Features and Oral/Ocular Diagnostic Tests-Comparison with Adult and Young Onset of the Disease in a Cohort of 336 Italian Patients. *Joint Bone Spine*, **78**, 171-174. https://doi.org/10.1016/j.jbspin.2010.05.008

[20] Lang, P.O. and Aspinall, R. (2012) Immunosenescence and Herd Immunity: With an Ever-Increasing Aging Population Do We Need to Rethink Vaccine Schedules? *Expert Review of Vaccines*, **11**, 167-176. https://doi.org/10.1586/erv.11.187

[21] Weiskopf, D., Weinberger, D. and Grubeck-Loebenstein, B. (2009) The Aging of the Immune System. *Transplant International*, **22**, 1041-1050. https://doi.org/10.1111/j.1432-2277.2009.00927.x

[22] Hallgren, H.M., Buckley, C.E., Gilbertsen, V.A. and Yunis, E.J. (1973) Lymphocyte Phytohemagglutinin Responsiveness Immunoglobulins and Autoantibodies in Aging Humans. *The Journal of Immunology*, **111**, 1101-1107.

[23] Moulias, R., Proust, J., Wang, A., Congy, F., Marescot, M.R., Deville Chabrolle, A., *et al.* (1984) Age-Related Increase in Autoantibodies. *Lancet*, **1**, 1128-1129.

https://doi.org/10.1016/s0140-6736(84)92547-9

[24] Gordon, J. and Rosenthal, M. (1984) Failure to Detect Age-Related Increase of Non-Pathological Autoantibodies. *Lancet*, **323**, 231. https://doi.org/10.1016/S0140-6736(84)92157-3

[25] Franceschi, C., Monti, D., Sansoni, P. and Cossarizza, A. (1995) The Immunology of Exceptional Individuals: The Lesson of Centenarians. *Immunology Today*, **16**, 12-16. https://doi.org/10.1016/0167-5699(95)80064-6

[26] Rasch, E.K., Hirsch, R., Paulose-Ram, R. and Hochberg, M.C. (2003) Prevalence of Rheumatoid Arthritis in Persons 60 Years of Age and Older in the United States: Effect of Different Methods of Case Classification. *Arthritis & Rheumatology*, **48**, 917-926. https://doi.org/10.1002/art.10897

[27] Lopez-Hoyos, M., Ruiz De Alegria, C., Blanco, R., Crespo, J., Peña, M., Rodriguez-Valverde, V., *et al.* (2004) Clinical Utility or Anti-CCP Antibodies in the Differential Diagnosis of Elderly-Onset Rheumatoid Arthritis and Polymyalgia Rheumatic. *Rheumatology*, **43**, 655-657. https://doi.org/10.1093/rheumatology/keh143

[28] Cho, S.K., Sung, Y.K., Choi, C.B., Cha, H.S., Choe, J.Y., Chung, W.T., *et al.* (2012) Do Patients with Elderly Onset-Rheumatoid Arthritis Have Severe Functional Disability? *Seminars in Arthritis and Rheumatism*, **42**, 23-31. https://doi.org/10.1016/j.semarthrit.2012.02.004

[29] Haga, H.J. and Jonsson, R. (1999) The Influence of Age on Disease Manifestations and Serological Characteristics in Primary Sjögren's Syndrome. *Scandinavian Journal of Rheumatology*, **28**, 227-232. https://doi.org/10.1080/03009749950155599

[30] Tutuncu, Z., Reed, G., Kremer, J. and Kavanaugh, A. (2006) Do Patients with Older-Onset Rheumatoid Arthritis Receive Less Aggressive Treatment? *Annals of the Rheumatic Diseases*, **65**, 1226-1229. https://doi.org/10.1136/ard.2005.051144

[31] Solomon, D.H., Yelin, E., Katz, J.N., Lu, B., Shaykevich, T. and Ayanian, J.Z. (2013) Treatment of Rheumatoid Arthritis in the Medicare Current Beneficiary Survey. *Arthritis Research & Therapy*, **15**, Article No. R43. https://doi.org/10.1186/ar4201

[32] Dixon, W.G., Abrahamowicz, M., Beauchamp, M.E., Ray, D.W., Bernatsky, S., Suissa, S., *et al.* (2012) Immediate and Delayed Impact of Oral Glucocorticoid Therapy on Risk of Serious Infection in Older Patients with Rheumatoid Arthritis: A Nested Case-Control Analysis. *Annals of the Rheumatic Diseases*, **71**, 1128-1133. https://doi.org/10.1136/annrheumdis-2011-200702