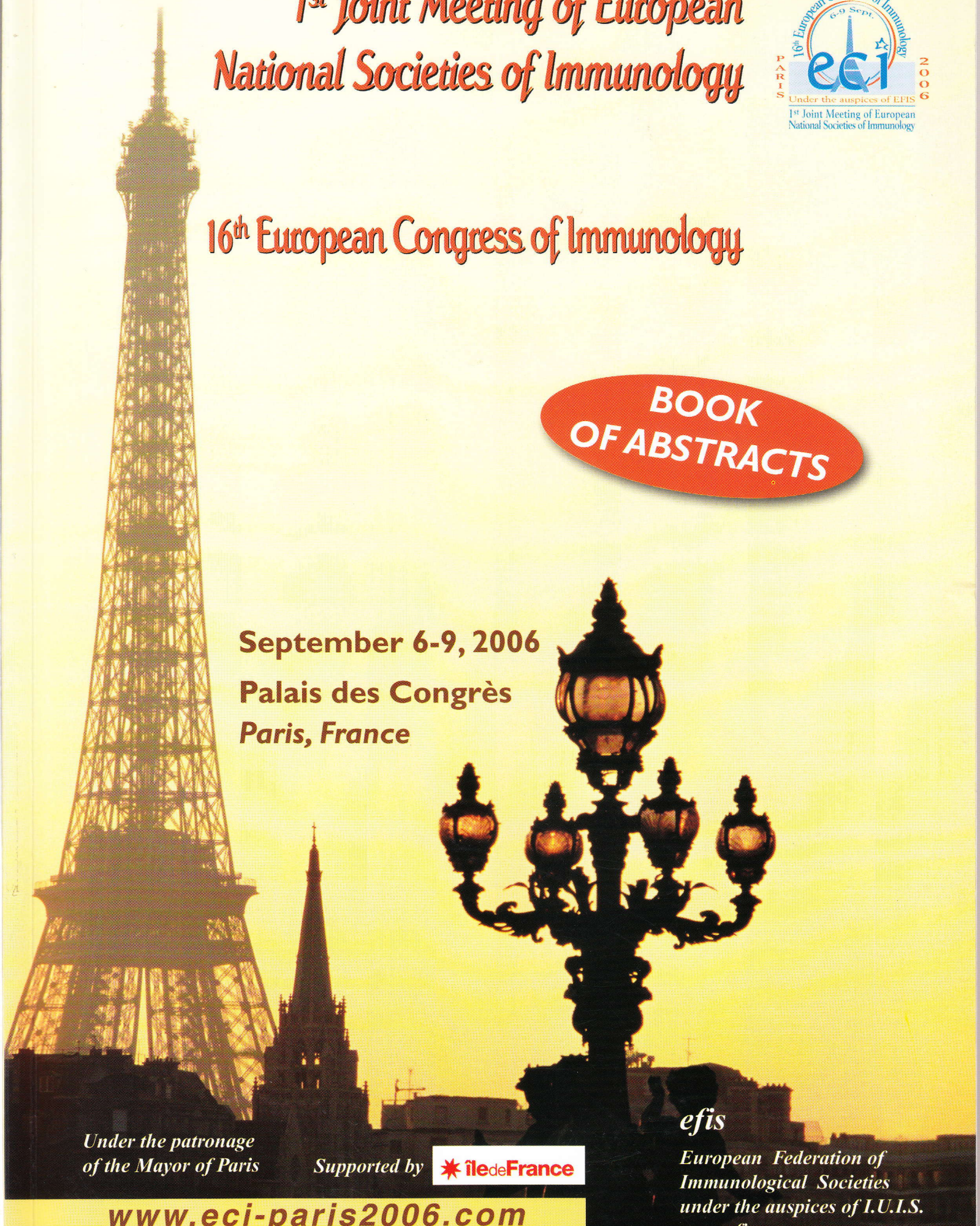
1st Joint Meeting of European National Societies of Immunology

16th European Congress of Immunology
6-9 Sept.
PARIS
eci
2006
Under the auspices of EFIS
1st Joint Meeting of European National Societies of Immunology

16th European Congress of Immunology

BOOK OF ABSTRACTS



September 6-9, 2006

Palais des Congrès

Paris, France

Under the patronage of the Mayor of Paris

Supported by îledeFrance

www.eci-paris2006.com

efis

European Federation of Immunological Societies under the auspices of I.U.I.S.

Committees

Steering committee

Catherine SAUTÈS-FRIDMAN, President
Nuala MOONEY, General Secretary
Reinhold E. SCHMIDT, EFIS
Alain BERNARD, SFI
Marco A. CASSATELLA, SIICA
Miguel LOPEZ-BOTET, SEI
Seppo MERI, SSI
Hans-Hartmut PETER, DGfI
Judith WILLETTS, BSI

Local organising committee (SFI)

Catherine SAUTÈS-FRIDMAN, President
Nathalie BONNEFOY-BERARD, GI Secretary
Nathalie AUPHAN-ANEZIN
Ghislaine BERNARD
Anne HOSMALIN
Jean KANELLOPOULOS
Patrice MARCHE
Bach-Nga PHAM

Finance committee

Antoine TOUBERT, France, SFI - President
Reinhold E. SCHMIDT, Germany, EFIS
Francisco LOZANO, Spain, SEI
Werner SOLBACH, Germany, DGfI
Silvano SOZZANI, Italy, SIICA
Judith WILLETTS, U.K., BSI
Olli VAINIO, Finland, SSI

Scientific programme committee

Alain BERNARD, France, SFI - President
Hans-Hartmut PETER, Germany, DGfI
Eddy LIEW, UK, EFIS
Stefan H.E. KAUFMANN, Germany, EFIS
Nathalie BONNEFOY-BERARD, France, SFI
Mario Paolo COLOMBO, Italy, SIICA
Angel CORBI, Spain, SEI
Manuel FRESNO, Spain, SEI
Wolf H. FRIDMAN, France, SFI
Beatrix GRUBECK-LOEBENSTEIN, Austria, OGAI
Gunter HAMMERLING, Germany, DGfI
Sirpa JALKANEN, Finland, SSI
Hans G. LJUNGGREN, Sweden, SSI
Bernard MALISSEN, France, SFI
Seppo MERI, Finland, SSI
PierLuigi MERONI, Italy, SIICA
Ricardo PUJOL-BORELL, Spain, SEI
Fiona POWRIE, U.K., BSI
Christopher RUDD, U.K., BSI
GianPietro SEMENZATO, Italy, SIICA
René VAN LIER, the Netherlands, NVVI
Neil A. WILLIAMS, U.K., BSI

Promotion committee

Nathalie AUPHAN-ANEZIN, France, SFI - President
Stefan H.E. KAUFMANN, Germany, EFIS
Anna ERDEI, Hungary, EFIS
Luciano ADORINI, Italy, SIICA
Ghislaine BERNARD, France, SFI
Jean KANELLOPOULOS, France, SFI
Elli NARVI, Finland, SSI
Anders ÖRN, Sweden, SSI
Bach-Nga PHAM, France, SFI
Augusto SILVA, Spain, SEI
Judith WILLETTS, U.K., BSI

CYTOPLASMATIC EXPRESSION OF CD152 AND CD28 IN PERIPHERAL BLOOD LYMPHOCYTES FROM CHILDREN WITH HASHIMOTO DISEASE (HD)

E GORSKA[1], K POPKO[1], A KUCHARSKA[2], U DEMKOW[1], M WASIK[1]
(1) 1. LABORATORY DIAGNOSTICS AND CLINICAL IMMUNOLOGY OF DEVELOPMENTAL AGE. MEDICAL UNIVERSITY OF WARSAW, WARSAW, POLAND. (2) 2. PEDIATRICS, DEPARTMENT OF ENDOCRINOLOGY. MEDICAL UNIVERSITY OF WARSAW, WARSAW, POLAND.

Cytotoxic T lymphocyte-associated protein 4 (CTLA-4) is one of the most important factors responsible for regulation of T lymphocytes activation. It is known to act as a receptor for B7 ligands present on antigen –presenting cells. Stimulation of this receptor results in blockade of T cell activation. CD152 receptor is upregulated on T cells after initial activation. This upregulation, along with high affinity for the B7 ligands competes with the activation receptor CD28 resulting in reduced stimulation. CD28-CTLA-4/B7 ligand pairs play an important role as a costimulatory system for T-cells. It is well known that in autoimmune diseases eg. HD, regulation of lymphocyte activation does not work properly. One of the reasons is low expression of regulatory factors on the surface of lymphocytes.
The aim of this study was to evaluate cytoplasmatic expression of CD152 and CD28 in 22 children with HD and 7 healthy children.
Cytoplasmatic expression of CD152 and CD28 was assessed using flow cytometry (Epix XL Coulter) after previous cell membrane permeabilization (IntraPrep Coulter) in whole peripheral blood lymphocytes and isolated lymphocytes. Measurement was carried out at zero time and after 48h of cell culture with and without PHA stimulation.
Our results showed that CD152 expression on CD4+ lymphocytes was significantly lower in healthy children (1,65%) than in children with HD (2,1%) ($p<0.05$). Inversely cytoplasmatic expression of CD28 on CD8+ cells was higher in control group (11,4%) than in children with HD (6,88%) ($p<0.01$). After 48h of unstimulated cell culture decreased expression of CD28 on CD4+ lymphocytes in HC was found. Expression of CD152 antigen on CD8+ lymphocytes was significantly higher in control group (3,67%) than in HD population (0,9%) ($p<001$). No significant differences between study and control group after 48h of culture with PHA stimulation were found.
These results indicate that T lymphocytes from children with HD have higher cytoplasmatic expression of CD152 antigen and lower CD28 expression. It suggests possibility of impaired antigene's structure and its disturbed transport to the membrane surface in selected autoimmune diseases.

PRESENCE OF AUTOIMMUNE THYROID DISEASE IN THE PATIENTS WITH RHEUAMATOID ARTHRITIS

I KOSTIC[1], S ZIVANCEVIC SIMONOVIC[1], M BUKILICA[2], R PETROVIC[2] - (1) Institute of Pathophysiology, School of Medicine, University of Kragujevac, Kragujevac, Serbia and Montenegro. (2) Institute of Rheumatology, Belgrade, Serbia and Montenegro.

The objective of this study was to evaluate the prevalence of autoimmune thyroid disease (ATD) in the patients with rheumatoid arthritis (RA). Thyroid function and anti-thyroid autoantibodies concentrations in the sera of 24 RA patients and 34 control subjects (healthy blood volunteers) were analysed. Serum levels of free thyroxine (FT4), thyroid stimulating hormone (TSH), as well as autoantibodies specific for thyroperoxidase (anti-TPO Abs) and thyroglobulin (anti-Tg Abs) have been determined using *CIS biointernational* kits. Subjects were considered to have subclinical and clinical thyroid dysfunction (hypothyroidism or hyperthyroidism) according to the measured FT4 and TSH concentrations. Five RA patients (20.83%) had thyroid dysfunction which was significantly more than one subject in the control group ($p<0.05$). Four RA patients (16,67%) had hypothyroidism, two of them had anti-TPO Abs, one had anti-Tg Abs and one had the both Abs. Only one RA patient (4,17%) was subclinically hyperthyroid without anti-thyroid antibodies. Subclinically hypothyroid RA patients were younger than clinically hypothyroid RA patients (55.3 vs 62 years). Two healthy controls (5.88%) tested anti-TPO Abs positive and had normal thyroid function, whereas one subclinically hypothyroid control subject (2.94%) had anti-Tg Abs.
This was the first study in which the prevalence of ATD in our patients with RA is estimated. A significantly higher frequency of thyroid dysfunction and a higher rate of anti-thyroid antibodies in the RA patients group compared with the controls was found.

THE ROLE OF AUTOANTIBODIES DETECTION IN POLYGLANDULAR AUTOIMMUNE SYNDROME TYPE II

M CHICIUDEAN[1], P IONESCU[2] - (1) EAACI, Stokolm, Sweden. (2) Roumain Society of Laboratory Medicine, Bucharest, Romania.

Polyglandular autoimmune syndrome type II (PGA II) is a constellation of multiple endocrine gland insufficiencies that includes primary adrenal insufficiency, autoimmune thyroid disease (Graves' disease or autoimmune hypothyroidism) and type I diabetes mellitus.
A variety of autoantibodies are found in PGA II : autoantibodies directed against thyroid antigens such as thyroid peroxidase, thyroglobulin, thyroid-stimulating-hormone receptor; against glutamic acid decarboxylase and aslet cells for type I diabetes mellitus; autoantibodies to 21-hydroxylase, 17-hydroxylase; against parietal cell and anti-antrinsec factor in search of pernicious anemia; antibodies against antitissue transglutaminase for celiac disease.
The production of organ-specific autoantibodies occurs early in the pathogenesis of the syndrome, during of a subclinical phase and they persist thoughout the clinical history.
So, the detection of autoantibodies is useful in verifing the autoimmune etiology of the disease, in indentifing the patients who may later complete the syndrome and in sceening asymptomatic family members.

AUTOIMMUNE REGULATOR PROTEIN (AIRE) IS PHOSPHORYLATED AT THR68 AND SER156 BY DNA-DEPENDENT PROTEIN KINASE

I LIIV[1], T ORG[1], M SAARE[1], A REBANE[1], M BOTTOMLEY[2], L VALMU[3], N KALKKINEN[3], P PETERSON[1] - (1) Molecular Pathology,Tartu University, Tartu, Estonia. (2) Inst.di Ricerhe di Biologia Molocolare P. Angeletty, Pomezia, Italy. (3) University of Helsinki, Helsinki, Finland.

The AutoImmune REgulator protein (AIRE) is the key mediator of the central tolerance regulating transcription of peripheral-tissue antigens in the thymic medullary epithelial cells. In humans, mutations in AIRE gene cause the autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED). As AIRE has characteristic localisation to nuclear bodies in vivo and in vitro, our aim was to investigate AIRE interaction with other nuclear proteins. We found interaction of AIRE with heterotrimeric protein complex containing Ku70, Ku80 and DNA-PK (DNA-Dependent Protein Kinase) by pulldown and immunoprecipitation assay. We also found that AIRE is phosphorylated by DNA-PK and identified two phosphorylated amino acids, Thr68 and Ser156. Transfection of the mutated Thr68Ala and Ser156Ala AIRE constructs demonstrated aberrant AIRE cellular localization in immunofluorescence assays. The AIRE phosphorylation site mutated constructs were further tested in transactivation assay with CBP (CBREB-binding protein) showing lower transcriptional activation of epithelial specific gene promoters when compared to wild type AIRE. In conclusion, we demonstrate that the postranslational modifications are important for AIRE function.

MHC-II EXPRESSION ON THYROID CELLS-PROTECTION AGAINST AUTOAGGRESSION

S LIALIKAU[1], S LUPACHIK[1], W BASINSKIJ[1], V FILAS[2], J BREBOROWICZ[2], M SOBIESKA[2], W SAMBORSKI[2] - (1) Medical University, Grodno, Belarus. (2) University of Medical Sciences, Poznań, Poland.

The comparative analysis of cells phenotype in thyroid gland (TG) of patients with euthyroid nodular goitre (ENG) and those with Hasimoto's disease (HD) was performed. TGs of patients operated because of ENG (5 cases, 1st group) and of HD (5 cases, 2nd group) were investigated. Sections for histological research were prepared acc. to standard procedure and stained with haematoxylin-eosin. Section for immunocytochemical examination were incubated with either monoclonal antibodies against CD74, CD3, CD8, CD20 and CD79α. Results of microscopy were estimated semi quantitatively.
Lymphoid infiltration with various degree of expressiveness was revealed in all samples of 1st group. CD3+cells were uniformly allocated within and outside lymphoid infiltrations. Single CD8+cells were found both in infiltrations and in TG parenchyma. CD20+cells were mainly located in infiltrations and in lymphoid follicles. CD796+cells were present on periphery of infiltrations and lymphoid follicles, and also inside thyroid follicles. CD74 expression was found on periphery of infiltrations, in the light centres of lymphoid follicles and outside of nodular formations on thyroid cells in thyroid follicles. Immunocytochemical findings in samples of 2nd group were almost identical as in patients with ENG, only expression of all markers was higher especially CD8, CD79α and CD74 in TG parenchyma).
The results showed B-lymphocyte infiltration in TGs of patients with ENG, but though the cells have access to antigen it does not result in increased production of autoantibodies. Thus a mechanism suppressing development of the autoimmune answer must be present in thyroid tissue. Probably this mechanism bases on the expression of MHC-II, but not co stimulatory molecules on thyroid cells. The presentation of an antigen on non-professional antigen presentation cells without co-stimulating signals promotes and supports maintenance of immunologic tolerance of potentially auto reactive -cells, via mechanism of inhibition of effective synthesis of auto antibodies, no switching of antibodies isotype, reduced cytotoxic activity of killers and phagocytes. Thus: maybe expression of MHC-II protects TG against auto aggression in patients with ENG. In HD cases thyroid cells expressing MHC-II play a role of antigen presenting cells and may activate T lymphocytes.

THYROTROPIN RECEPTOR ANTIBODIES IN TUNISIAN PATIENTS WITH GRAVES' DISEASE

A MANKAI[1], M CHADLI-CHAIEB[2], F SAAD[2], D TOUMI[1], L GHEDIRA-BESBES[1], M OUERTANI[3], H SFAR[4], M LIMEM[5], M BEN ABDESSALEM[5], L CHAIEB[2], M JEDDI[1], I GHEDIRA[1] - (1) Department of Immunology, Research Unit (03/UR/07-02), Faculty of Pharmacy, Monastir, Tunisia. (2) Endocrinology department, Farhat Hached Hospital, Sousse, Tunisia. (3) Endocrinology department, Ibn El Jazzar Hospital, Kairouan, Tunisia. (4) Endocrinology department, Tahar Sfar Hospital, Mahdia, Tunisia. (5) Department of Immunology, Farhat Hached Hospital, Sousse, Tunisia.

Objective To determine the frequency and the levels of anti-TSH receptor antibodies (TRAb), in Tunisian patients with Graves'disease (GD) and to compare the validity of TRAb to that of thyroperoxydase antibodies (TPO Ab) and thyroglobulin antibodies (TG Ab).
Patients and methods ELISA was used to measure the levels of TRAb, TPO Ab and TG Ab in sera of 190 patients with GD. Patients were divided into four groups: those with untreated active GD (groupe A, n = 71), those receiving treatment with antithyroid drugs (group B, n = 85), those in relapse (group C, n = 15) and those in remission (group D, n = 19), sera of 100 healthy blood donors served as controls.
Results TRAb were negative in all healthy blood donors. At diagnosis, TRAb had high sensitivity (95.77%). The positive rate of TRAb was lower in group B than in group A (70.58% and 95.77 respectively, p = 0.0001). The levels of TRAb were significantly higher in group A than in group B (mean level: 30.13 IU/l and 14.22 IU/l respectively, p =0.006). Moreover, 27 patients of 71 (38%) in group A had TRAb levels higher than 20 IU/l (10-fold normal range) compared to 16 out of 85 (19%) in group B (p = 0.012). Mean TRAb levels in group D were lower than TRAb values in group C (4.2 IU/l compared to 27.2IU/l), but the difference was not statistically significant (p=0.13). The sensitivity of TRAb for the diagnosis of GD (95.77%) was significantly higher than that of TPO Ab (73%) and TG Ab (42%) (p = 0.0005 and $p<10^{-7}$ respectively). In group B, the frequency of TG Ab (37.6%) was significantly lower than that of TRAb (70.58%) and TPO Ab (68%) (p = $3.2.10^{-5}$ and p = 0.0001 respectively).
Conclusions TRAb, but neither TPO Ab nor TG Ab, are valuable in the diagnosis and management of patients with GD.