

1. The role of cholesterol levels in mood disorders and suicide

D. De Berardis^{1,2}, C.M.V. Conti¹, N. Serroni², F.S. Moschetta², A. Carano³, R.M. Salerno¹, M. Cavuto⁴, B. Farina¹, M. Alessandrini¹, L. Janiri⁵, G. Pozzi⁵ M. Di Giannantonio¹

¹Department of Biomedical Sciences, Chair of Psychiatry, University G. d'Annunzio Chieti, Italy
²NHS, Department of Mental Health, Psychiatric Service of Diagnosis and Treatment, Hospital G. Mazzini Teramo; ³NHS, Department of Mental Health, ASUR Marche 8, Civitanova Marche;
⁴IASM, L'Aquila; ⁵Department of Psychiatry, Catholic University Medical School, Rome, Italy

The individuation of sensitive and specific biochemical markers, easily assessable on large samples of subjects and usefully employable as predictors of severe psychiatric disorders, such as mood disorders, could help clinicians to improve the diagnostic and therapeutic processes facilitating the long-term follow-up. In particular, serum cholesterol levels may potentially be optimal markers due to their relative easy sampling and low cost. The involvement of cholesterol in affective disorders such as Major Depression (MD), Seasonal Affective Disorder (SAD) and Bipolar Disorders (BD) is a debated issue in current research. However, current literature is controversial and, to date, it is still not possible to reach an agreement on its possible usefulness of cholesterol as a biological marker of affective disorders. Despite the controversial results on the relationships between cholesterol levels and affective disorders, the majority of literature seems to show a more consistent relationship between cholesterol levels and suicidal behaviour, with few studies that have found no relationships. The aim of this review is to elucidate current facts and views about the role of cholesterol levels in mood disorders as well as its involvement in suicidal behaviour. *J. Biol Regul Homeost Agents* 2009;23:133-140

2. IL-32: a newly-discovered proinflammatory cytokine

P. Felaco, M.L. Castellani¹, M.A. De Lutii², M. Felaco², F. Pandolfi³, V. Salini⁴, D. De Amicis⁴, J. Vecchiet⁵, S. Tetè⁶, C. Ciampoli⁶, F. Conti⁷, G. Cerulli⁸, A. Caraffa⁸, p. Antinolfi⁸, C. Cuccurullo⁹, A. Perrella¹⁰, T.C. Theoharides¹¹, P. Conti¹, E. Toniato¹, D. Kempuraj¹¹ and Y.B. Shaik¹²

Nephrology Division, Medical School, University of Chieti, Pescara, Chieti, Italy

¹Immunology Division, Medical School, University of Chieti-Pescara, Italy

²Division of Biology, University of Chieti, Italy

³Catholic University, Rome, Italy

⁴Department of Human Dynamic, University of Chieti-Pescara, Italy

⁵Clinical of Infectious Diseases, Medical School, University of Chieti-Pescara, Italy

⁶Dental School, University of Chieti-Pescara, Italy

⁷University of Chieti, Italy

⁸Orthopedics Division, University of Perugia, Italy

⁹Division of Medical Pathology, University of Chieti

¹⁰Department of Infectious Diseases, Cotugno Hospital, Naples, Italy

¹¹Department of Pharmacology and Experimental Therapeutics, Biochemistry and Internal Medicine Tufts University School of Medicine, Tufts-New England Medical Center, Boston, MA, USA

¹²Department of Medicine, Boston University School of Medicine, Boston, MA, USA

IL-32, a newly-discovered proinflammatory cytokine that activates the p38MAPK and NF-kappaB pathways, is an important player in innate and adaptive immune response. IL-32, a cytokine produced mainly by T, natural killer, and epithelial cells induces significant amounts of TNF α and MIP-2 and increases the production of both cytokines in a dose-dependent manner. IL-32 has been implicated in inflammatory disorders, mycobacterium tuberculosis infections, inflammatory bowel disease, and influenza A virus infection, as well as in some autoimmune diseases, such as rheumatoid arthritis, ulcerative colitis and Crohn's disease and in human stomach cancer, human lung cancer and breast cancer tissues. Moreover, it has been reported that IL-32 has pro-inflammatory effects on myeloid cells and causes the differentiation of osteoclast precursors into multinucleated cells expressing specific osteoclast markers. We recently found that human IL-32 has the capacity to provoke histamine release in human-derived cord blood mast cells (HDCBMC), but not in LAD 2 cells nor in rat peritoneal mast cells (RPMC), showing that IL-32 may be specie specific and act more in mature human mast cells (HDCBMC) than in transformed mast cells (LAD 2 cells). Certainly, IL-32 is another potent proinflammatory cytokine, however, the specific role of this newly-discovered protein in the network of cytokine biology remains to be determined. *J. Biol Regul Homeost Agents* 2009;23:141-147.

3. Effects on the glutathione pool of the insulin-induced hypoglycaemia test

J. Uberos, J.M. Fernández-García, A. Molina-Carballo and A. Muñoz-Hoyos

Department of Paediatrics, San Cecilio Hospital, Granada, Spain

The growth hormone (GH) stimulation test shows that hypoglycaemia can cause the generation of free radicals, or reactive oxygen species (ROS), together with the migration of amino acids, glutathione and various ions to the interior of fat or muscle cells. The aim of the present study is to evaluate the splitting of plasma glutathione into its two fractions, oxidized (GSSG) and reduced (GSH), after the induction of hypoglycaemia with insulin in the course of the GH stimulation test. We studied 41 short children (47% boys and 53% girls) at the Paediatric Department of the San Cecilio Hospital (Granada, Spain) to evaluate their size and growth. A GH stimulation test using insulin-induced hypoglycaemia was carried out, and GSSG and GSH values in plasma were determined. The glutathione level is associated with the level of glucose reached at 30 min after initiating the test. This provoked an initial reduction in the GSH/GSSG ratio, which fell to a minimum at 30 min after starting the test, although the values rose again at 60 min. The results obtained show that the insulin-induced GH stimulation test produces a decrease in plasma levels of the glutathione pool, that persists at least for 2 hours following the beginning of the test. *J. Biol Regul Homeost Agents* 2009;23:149-154.

4. CD81 expression on CD19+ peripheral blood lymphocytes is associated with chronic HCV disease and increased risk for HCV infection: a putative role for inflammatory cytokines

G. D'Agosto, E. Trento, L. Nosotti¹, v. Bordignon, m. Battista, G. Prignano, f. Pimpinelli, g. Biolcati², a. Macrì², g. Palamara³, L. Miglioresi⁴, a. Morrone¹, a. Di Carlo, p. Cordiali-fei and F. Ensoli

Department of Clinical Pathology and Microbiology, San Gallicano Dermatology Institute, Rome, Italy

¹Department of Preventive Medicine of Migrations, Tourism and Tropical Dermatology, San Gallicano Dermatology Institute, Rome

²Center for Porphyrias, San Gallicano Dermatology Institute, Rome

³Department of Sexually Transmitted Disease, San Gallicano Dermatology Institute, Rome;

⁴Liver Transplantation Unit, San Camillo-Forlanini Hospital, Rome, Italy

The level of CD81 cell surface expression, a cellular co-receptor for hepatitis C virus (HCV), is critical for productive HCV infection of host cells. In addition, the cross-linking of HCV-E2 protein to CD81 can alter the function of T and B lymphocytes as well as that of NK cells by interfering with the activation signalling pathway. The down-regulation of CD81 expression on peripheral blood lymphocytes (PBL) has been associated to effective therapy of HCV infection. The aim of the present study is to quantitatively assess the levels of CD81 expression in PBL from HCV-infected patients compared to subjects at high risk for HCV infection such as HIV-infected individuals or patients with *Porphyria Cutanea Tarda* (PCT). The expression of CD81 was quantified by flow-cytometry using Phycoerythrin-labelled standard beads. Determination of CD81 was performed on CD3+ and CD19+ lymphocytes from 34 healthy controls, 51 patients with HCV infection and different clinical outcomes [these included HCVRNA- negative subjects (8), patients with chronic active hepatitis (16), recipients of liver transplantation under immunosuppressive therapy (12), a subgroup with concomitant HIV infection (9) or concomitant PCT (6)]. In addition, 60 HIV-infected subjects and 4 patients with PCT were studied. The putative role of inflammatory cytokines in modulating CD81 was explored *in vitro* by assessing the effect of IL-6 or IFN- γ on cultured human hepatocytes. A significant increase of the CD81 expression was found on CD19+ lymphocytes in association with either HIV or HCV infection, as compared to the control group. Immunosuppressive therapy with FK506, subsequent to liver transplantation, restored CD81 expression at normal levels. Data gathered *in vitro* using the WRL 68 hepatocytic cell line confirmed that inflammatory cytokines can up-regulate CD81 expression in liver cell inclusion. Our data suggest that CD81 up-regulation can increase the risk of HCV infection, particularly in HIV-infected subjects. In addition, the results strongly suggest that the cytokines released by activated lymphocytes at sites of inflammation may play a part in up-regulating CD81 expression. *J. Biol Regul Homeost Agents* 2009;23:155-164.

5. Sublingual immunotherapy in polysensitized allergic patients with rhinitis and/or asthma: allergist choices and treatment efficacy

G. Ciprandi, g. Cadario ¹, m. Di Gioacchino ², s. Gangemi ³, m. Minelli ⁴, E. Ridolo ⁵, c. Valle ⁶, m. Verini⁷, r. Boccardo ⁸, c. Incorvaia ⁹, p. Puccinelli ¹⁰, S. Scurati ¹⁰ and f. Frati ¹⁰

Department of Internal Medicine, University Hospital San Martino, Genoa

¹Unit of Allergy and Clinical Immunology, San Giovanni Battista (Molinette) Hospital, Turin, Italy

²Department of Medicine and Sciences of Ageing, Immunology and Occupational Medicine, University G. d'Annunzio, Chieti, Italy

³Unit of Allergy and Clinical Immunology, Policlinico Hospital, Messina, Italy

⁴Department of General Medicine, Allergy, Campi Salentina Hospital, Lecce, Italy

⁵Department of Clinical Sciences, University Hospital, Parma, Italy

⁶Allergy Unit, San Paolo Hospital, Milan, Italy

⁷Unit of Allergy and Respiratory Pathophysiology, Pediatrics, Ospedale Clinicizzato, Chieti, Italy

⁸Clinica Pediatrica, University of Perugia, Perugia, Italy

⁹Allergy/Pulmonary rehabilitation, ICP, Milan, Italy

¹⁰Scientific Department, Stallergenes, Milan, Italy

Polysensitization is very common in allergic patients and was previously reported to be associated with more severe symptoms and impaired quality of life. Polysensitization is often considered as a contraindication for specific immunotherapy (SIT). This study is aimed at evaluating the allergist attitude for decision making in choosing SIT in a cohort of Italian polysensitized patients. Moreover, the 1-year effectiveness of the prescribed sublingual immunotherapy (SLIT) in this cohort was evaluated. The study was performed on 244 patients (109 males, 135 females, mean age 28.7 years, S.D. 12.0) with allergic rhinitis (assessed by ARIA criteria) and/or mild to moderate asthma (assessed by GINA criteria) treated with SLIT for 1 year. The kind and the number of prescribed allergen extracts, type of diagnosis, severity of symptoms, use of drugs, and adverse events were evaluated at baseline and after 1 year. A total of 230 patients were treated with SLIT: 165 with a single extract, and 65 with two different extracts (mix). SLIT treatment significantly improved disease staging, and reduced symptom severity and drug use. No systemic reaction was reported. In conclusion, these findings provide preliminary evidence that SIT is effective and safe in polysensitized patients after 1 year of treatment also using single extracts, and thus does not represent an obstacle for prescribing SIT. *J. Biol Regul Homeost Agents* 2009;23:165-171.

6. Recurrent infections in patients with nickel allergic hypersensitivity

E. Rosato, A. Giovannetti, C. Rossi, G. Menghi, S. Pisarri, F. Salsano

Sapienza University of Rome Department of Clinical Medicine, Clinical Immunology Unit, Rome, Italy

Nickel (Ni) is the most common contact allergen among the general population in the industrialized world. Ni has been shown to exhibit immunomodulatory, if not immunotoxic, effects in several experiments conducted on humans and on rodents. This study tests the incidence of different infectious diseases in 100 patients with Ni hypersensitivity and compares it to data from 100 healthy volunteers. One hundred subjects with Ni hypersensitivity were enrolled. A group of 100 matched healthy volunteers with negative European standard patch test were enrolled as healthy controls. In patients with Ni hypersensitivity a higher incidence of recurrent herpes labialis (RHL), urinary tract infections (RUTI), genital candidiasis, and upper respiratory tract infections (RURTI) was detected. Fifteen patients with nickel allergic hypersensitivity (NAH) followed a Ni-poor diet. After a one-year diet a net reduction of incidence of RHL was found. Indeed, the number of episodes of RHL per year decreased from 6 ± 2.75 to 2.4 ± 1.2 . Conversely, among the matched control group with NAH following a normal daily dietary nickel intake the RHL number did not show any statistically significant changes (6.1 ± 1.7 vs 6 ± 1.5). In conclusion, our study demonstrates a higher incidence of recurrent infections among patients with NAH. A low-Ni diet reduces the number of RHL episodes per year. *J. Biol Regul Homeost Agents* 2009;23:173-180

7. Nasal-sinus polyposis: clinical-cytological grading and prognostic index of relapse

M. Gelardi, R. Fiorella, M.L. Fiorella, C. Russo, P. Soleti¹, G. Ciprandi²

Department of Ophthalmology and Otolaryngology, Otolaryngology II, University School of Medicine, Bari, Italy

¹Department of Statistic Sciences, Faculty of Economics, University of Bari, Italy

²Department of Internal Medicine, University of Genoa, Genoa, Italy

This longitudinal and prospective study aimed at investigating the influence of some parameters, including nasal cytology and clinical findings (such as asthma, atopy, acetylsalicylic acid (ASA)

sensitivity, ASA associated with asthma), as risk factor of post-surgical relapse of nasal-sinus polyps. One hundred sixty-one consecutive patients (92 males and 69 females, mean age 47 years), affected by bilateral nasal polyposis and who had undergone surgical nasal polypectomy (endoscopic FESS), were examined post-surgically at least every 6 months for a period of 10 years. Endoscopic exam and nasal cytology exam were carried out on all patients and their case histories were carefully examined. The association eosinophilic-mast cell cellularity and the contemporary presence of asthma + ASA sensitivity showed the highest level of relapse (OR 4.5). In conclusion, cytological data in association with certain clinical parameters can predict a “high risk” prognosis of relapse. *J. Biol Regul Homeost Agents* 2009;23:181-188.

8. Anti-inflammatory properties of the plant *Verbascum mallophorum*

L. Speranza ¹, S. Franceschelli ², M. Pesce ², I. Menghini ³, A. Patruno ³, I. Vinciguerra ², M.A. De Lutiis², M. Felaco², P. Felaco ⁴ and A. Grilli ^{2,5}

¹Department of Biomorphology, Department of Biomedical Sciences, University G. d’Annunzio, Chieti

²Department of Human Dynamics, Department of Biomedical Sciences, University G. d’Annunzio, Chieti

³Department of Drug Sciences, Department of Biomedical Sciences, University G. d’Annunzio, Chieti

⁴Division of Nephrology, University G. d’Annunzio, Chieti;

⁵Online University Leonardo Da Vinci, Torrevicchia Teatina, Chieti, Italy

Verbascum mallophorum is part of a large family of Scrophulariaceae consisting of more than 360 species. *Verbascum mallophorum* contains diverse polysaccharides, iridoid glycosides, flavonoids, saponins, volatile oils and phenylentanoids. *Verbascum* has been used in popular medicine for treating wounds, chilblains, respiratory ailments, acne and arthritic disturbances. Inducible nitric oxide synthase (iNOS) represents one of the three isoforms that produce nitric oxide using L-arginine as a substrate in response to an increase in superoxide anion activated by NF- κ B. It is implicated in different pathophysiological events and its expression increases greatly during an inflammatory process due to oxidative stress. In our study we reproduced an inflammatory state by treating THP-1 cells (human myelomonocytic leukaemia) with pro-inflammatory stimuli, such as LPS and IFN- γ , obtaining an up-regulation both in the expression and in the activity of iNOS. The aim of our work is to investigate the possible anti-inflammatory action of verbascoside extract from *Verbascum mallophorum* using a concentration of 100 μ M. Our results show a significant decrease in the expression and activity of iNOS and extracellular O₂ when cells were treated with verbascoside. Based on these results we hypothesize that verbascoside extract from *Verbascum mallophorum* has anti-inflammatory properties since it reduces the production of superoxide radicals and consequently reduces the activity of iNOS. *J. Biol Regul Homeost Agents* 2009;23:189-195.

9. Pemphigus vulgaris with circulating anti-desmoglein 3 and anti-BP180 antibodies: a case report and brief review of cases with coexistence of pemphigus vulgaris and bullous pemphigoid

N. Cassano, V. Mastrandrea, M. Tampoia ¹, R. Filotico ², M. Vestita, G.A. Vena

2nd Dermatology Clinic, Department of Internal Medicine, Immunology and Infectious Diseases, University of Bari, Italy

¹Unit of Clinical Pathology, University of Bari;

²Unit of Dermatology, A. Perrino Hospital, Brindisi, Italy

Pemphigus vulgaris (PV) and bullous pemphigoid (BP) are two autoimmune blistering diseases involving the skin and the mucous membranes characterized by circulating autoantibodies directed against desmosomal cadherins or antigens expressed in the basement membrane zone, respectively. The simultaneous presence of clinical and/or immunopathological features of PV and BP in the same patient has been reported in very few cases in the literature to date. Most of these cases had exclusive cutaneous involvement, while a minority showed concomitant oral lesions. We describe the case of a 59-year-old female patient with a 10-year history of refractory PV lesions limited to mucous membranes (conjunctiva, oral cavity and genital mucosa), which were controlled by the addition of mycophenolate sodium to oral prednisone. Immunofluorescence studies revealed findings consistent with PV, whereas enzyme-linked immunosorbent assay revealed circulating anti-BP180 antibodies in association with anti-desmoglein 3 antibodies. The significance and relevance of this finding are briefly discussed, in light of the literature data. *J. Biol Regul Homeost Agents* 2009;23:197-201.

10. Neuroimmune biology of physical exercise

V. Verratti

Department of Basic and Applied Medical Sciences, G. d'Annunzio University, Chieti, Italy

Physical inactivity plays a negative role in several aspects of health status. A sedentary lifestyle represents a predisposing base for the development of obesity, type 2 diabetes, cardiovascular disease, osteoporosis, depression and cancer. On the other hand, an active life is distinguished by physical exercise and the beneficial effects it brings to health, reducing the risk of contracting these diseases. The general state of exercise-related psycho-physical health is regulated by a variety of mechanisms that affect the highly integrated and synergistic responses of the central nervous system and efficiency of the overall immune system. There is positive evidence concerning the influence of neuro-immune systems on the status of health, during moderate and regular physical exercise. *J. Biol Regul Homeost Agents* 2009;23:203-206.