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## DO LOW BONE MINERAL DENSITY AND LOWER FRACTURE RISK IN MEN WITH METABOLIC SYNDROME HAVE DIFFERENT DETERMINANTS? - THE MINOS STUDY

P. Szulc<sup>1,\*</sup>, A. Varennes<sup>2</sup>, R. Chapurlat<sup>1</sup>, J. Goudable<sup>2</sup>, P.D. Delmas<sup>1</sup>

<sup>1</sup>INSERM 831 Unit, Hôpital Edouard Herriot, University of Lyon, Lyon, France, <sup>2</sup>Central Biochemical Laboratory, Hôpital Edouard Herriot, University of Lyon, Lyon, France  
E-mail address: pawel.szulc@inserm.fr (P. Szulc).

Data on the association of the metabolic syndrome (MetS) with bone mineral density (BMD) and fracture risk in men are scanty and inconsistent. We studied association between MetS and bone status in 762 men aged 50 to 85 followed up for 10 years. After adjustment for age, body mass index (BMI), height, physical activity, smoking, alcohol intake and serum levels of 25-hydroxyvitamin D and 17 $\beta$ -estradiol, men with MetS had lower BMD at the hip, whole body and distal forearm (2.2-3.2 %, 0.24-0.27 SD,  $p < 0.05-0.005$ ). This difference was related to abdominal obesity (assessed by waist circumference, waist-hip ratio or fat mass of the trunk), but not other components of MetS. Men with MetS had lower bone mineral content (3.1-4.5 %, 0.22-0.29 SD,  $p < 0.05-0.001$ ), whereas differences in bone size were not consistent. Men with MetS had lower incidence of osteoporotic vertebral and peripheral fractures (12 vs 69 men, 6.7 vs 12.0 %,  $p < 0.05$ ). After adjustment for confounding variables, MetS was associated with lower incidence of fracture (OR=0.33, 95%CI: 0.15-0.76,  $p < 0.01$ ). Among the components of MetS, hypertriglyceridaemia was associated most strongly with the lower risk of fracture (OR=0.25, 95%CI: 0.10-0.62,  $p < 0.005$ ). Lower fracture risk in men with MetS cannot be explained by differences in bone size, rate of bone turnover rate and bone loss, history of falls or prior fracture.

In conclusion, in older men, MetS is characterised by lower BMD which is related to the abdominal obesity and by lower risk of fracture which is related to hypertriglyceridaemia.

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## DETERIORATION OF THE TRABECULAR MICROARCHITECTURE IN MODERATE MEN SMOKERS - THE STRAMBO STUDY

P. Szulc\*, E. Debieesse, S. Boutroy, R. Chapurlat

INSERM 831 Unit, University of Lyon, Lyon, France  
E-mail address: pawel.szulc@inserm.fr (P. Szulc).

Smoking increases the risk of osteoporotic fracture which is only partly explained by lower areal bone mineral density (aBMD), especially in men. In order to elucidate microarchitectural changes underlying this effect, we studied bone microarchitecture at the distal radius and distal tibia assessed by high resolution peripheral quantitative computed tomography (Xtreme CT, Scanco Medical, Bassersdorf, CH) in 766 men aged 60 to 85 years. Forty-six men were moderate current smokers (median — 8 cigarettes per day). After adjustment for age, weight, height, physical activity at work, leisure physical activity and alcohol intake, they had aBMD similar to men who never smoked. However, their trabecular volumetric BMD (vBMD) was decreased (tibia: 10.4 %, 0.47 SD,  $p < 0.005$  vs never-smokers) which was associated with lower trabecular number ( $p < 0.05$ ). By contrast, they had no deficit in the cortical bone (bone mineral content, vBMD, cortical thickness) in comparison with the former smokers and men who never smoked. After additional adjustment for aBMD, current smokers still had lower trabecular vBMD (5.8 to 8.7 %, 0.33 to 0.39 SD,  $p < 0.01-0.002$ ), lower trabecular number (4.5 %, 0.25 and 0.31 SD,  $p < 0.05$ ) and more heterogenous distribution of trabeculae ( $p < 0.02-0.001$ ). In similar multivariate models, there was no difference in BMD between the current smokers who smoked more than 8 cigarettes per day (median) and those who smoked less. By contrast, current smokers who smoked more had more severe deterioration of bone microarchitecture at distal radius and tibia than current smokers who smoked less.

In summary, older men being moderate smokers had lower trabecular vBMD and poor trabecular microarchitecture which was not detected by aBMD measured by DXA. These data contribute to a better understanding of the smoking-induced increase in bone fragility in men.

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## IMMUNOMAX FOR THE THERAPY OF DISORDERS OF THE UROGENITAL TRACT: A NOVEL IMMUNOSTIMULATORY THERAPY TO OBTAIN RELIEF IN BACTERIAL INFECTIONS, PROSTATITIS AND IN PROSTATE CARCINOMA

Ravshan Ataulakhanov<sup>1</sup>, Hartwig Bauer<sup>2</sup>, Rupert Holms<sup>3</sup>, Wolfgang G. Bessler<sup>4,\*</sup>

<sup>1</sup>Institute of Immunology, Moscow, Russia, <sup>2</sup>Urologie, München, <sup>3</sup>Medezrin Limited, London, UK, <sup>4</sup>Institute for Molecular Medicine and Cell Research, University Clinic, Freiburg, Germany  
E-mail address: alsanafreiburg@yahoo.com (W.G. Bessler).

Immunomax, an acidic peptidoglycan of a molecular mass 1000—4000 kDa, constitutes a novel immunostimulant obtained from potato sprouts. In animal experiments, the substance stimulates NO production in murine bone marrow derived macrophages and activates murine splenocytes comparable to bacterial lipopeptides. In human patients, urethritis and prostatitis are widespread diseases caused by different bacterial species like Chlamydia, Ureaplasma, Mycoplasma, E.coli, and Staphylococcus. Typical treatment is based on antibacterial drugs, but chronic urethritis and prostatitis are often resistant to treatment. Immunomax is effective in treatment of these chronic diseases if combined with the conventional protocols of treatment, and treatment results in a sustained recovery with no recurrence of the infection in most patients. Immunomax therapy also shows a therapeutic benefit in prostatitis type IIIa patients. In preliminary studies, patients responded well to the treatment with significant reductions of leukocytes in the exprostate urine, and in increase of life quality as determined by the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI). In case reports on prostate carcinoma, patients responded well to the treatment with a reduction of PSA. Thus, the novel immunostimulant Immunomax acts as a potent macrophage activator in animal studies and is, in human patients, a novel useful therapeutic agent for the therapy of disorders of the urogenital tract.

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## TIME FOR INTERNATIONAL ACTION ON TREATING TESTOSTERONE DEFICIENCY SYNDROME

Malcolm Carruthers

Centre for Men's Health, 20/20 Harley Street, London W1G 9PH UK  
E-mail address: m.carruthers@btconnect.com.

**Objectives:** Testosterone deficiency is having an increasing impact on men's health because of global aging, increasing obesity, diabetes and environmental factors and an explanation is needed why so few androgen deficient men are being treated.

**Methods:** Demographic data for men over the age of 50 from different regions of the world have been compared with the number of men in that age group estimated from sales figures to be receiving testosterone treatment.

**Results:** Based on the 20% of men over 50 in the general population who are expected to have testosterone deficiency symptoms, on average only 0.69% these men in most European countries were receiving treatment. The proportion was higher in the UK (1.00%) and Germany (1.89%), but lower in France (0.49%), Italy (0.51%) and Russia (0.54%). Australia had higher figures (1.64%), in spite of tight state control measures on androgen use. The USA has the highest treatment rate (7.96%) and this is increasing rapidly.

Based on symptoms plus low total and free testosterone levels, androgen deficiency would be diagnosed in at least 5% of men over 50, and percentage treatment rates therefore four times higher. However, even on that basis, only in the USA do these exceed 10%.

**Conclusions:** International action is urgently needed to raise awareness in the medical profession in the various countries of these unacceptably low levels of testosterone treatment. Improvement in this requires education and motivation of doctors and those regulating the healthcare systems.

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