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The proinflammatory cytokine TNF-α modifies the resorptive behaviour of newly generated osteoclasts in vitro from patients with acute Charcot osteoarthropathy NL Petrova[1], PK Petrov[2], , C Shanahan[3], ME Edmonds[1] [1]Diabetic Foot Clinic, King's College Hospital, Department of Materials, Imperial College, and [3]Cardiovascular Department, James Black Centre, King's College London, UK

Aims: To investigate the role of TNF-α as a modulator of osteoclastic activity *in vitro* in patients with acute Charcot osteoarthropathy. **Material and methods:** Peripheral blood mononuclear cells were isolated from 9 patients with acute Charcot osteoarthropathy, 7 diabetic patients and 6 healthy subjects and cultured *in vitro* on bovine disks for 21 days in the presence of (1) macrophage-colony stimulating factor (M-CSF) and receptor activator of nuclear factor κß ligand (RANKL) and (2) M-CSF, RANKL and neutralising antibody to TNF-α (na-TNF-α). Bovine discs in duplicates were stained with toluidine blue. The surface profile of each disc was measured by a Dektak 150 Surface Profiler. A stylus with a radius of 2.5 μm was dragged across the surface in hills and valleys mode with vertical measurement range of 65.5 μm. Five separate scans (scan length 1000 μm and scan duration of 60 sec) were carried out for each bovine disc. On average, 60 pits per condition/ per subject were analyzed and the median area of disc erosion was calculated in μm^2 using Origin Pro 8.6 software. **Results:** The newly generated osteoclasts in patients with acute Charcot osteoarthropathy exhibited increased resorbing activity in cultures with M-CSF and RANKL compared with diabetic and healthy controls. The median area of disc erosion was significantly greater in Charcot compared with diabetic patients (9.1 μm^2 (6.3) versus 4.3 μm^2 (3.3), median (interquartile range); p= 0.022) and also greater in Charcot patients compared with healthy subjects (9.1 μm^2 (6.3) versus 3.3 μm^2 (2.4), p=0.002). The addition of na-TNF-α to cultures with M-CSF and RANKL led to a marked decrease in the median area of disc erosion only in patients with Charcot osteoarthropathy (from 9.1 μm^2 (6.3) to 4.1 μm^2 (5.5) , p=0.05 but not in patients with diabetes (from 4.3 μm^2 (3.3) to 2.9 μm^2 (3.3), p=0.456) nor in healthy subjects (from 3.3 μm^2 (2.4) to 3.5 μm^2 (1.8), p=0.818). **Conclusion:** In acute Charcot osteoarthropathy, the proinflammatory cytokine TNF-α modifies the resorptive behaviour of newly generated osteoclasts *in vitro*. The active mode of their resorption cycle is maintained and this results in large and deep areas of bone excavations.