

**P014** DHEA regulates neutrophil function and apoptosis directly via PKC and NF- $\kappa$ B signalling pathways  
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Dehydroepiandrosterone (DHEA) is an adrenal steroid with immune enhancing and anti-glucocorticoid effects. As humans age serum DHEA declines whilst immune suppressing corticosteroids remain constant, resulting in a relative glucocorticoid excess in old age. As immune status declines during ageing, it is possible that loss of DHEA is a contributing factor. We have shown that neutrophil function declines with age, contributing to increased susceptibility of the elderly to bacterial infections. In this study we have investigated the effects of DHEA on neutrophil function. Neutrophils from healthy human donors were incubated with DHEA (1 nM – 1000 nM) and four aspects of neutrophil function were assessed. DHEA did not affect neutrophil phagocytic ability but did significantly improve superoxide generation (two-fold) and chemotaxis (three fold). We also found that 100 nM DHEA decreased apoptosis from 60% to 25% ( $p < 0.05$ ) and that this effect was dependent upon activation of protein kinase C- $\beta$  and NF- $\kappa$ B. Our data suggest that DHEA acts directly upon neutrophils via regulation of PKC and PKB signalling pathways and that loss of DHEA with age will impact upon immune status.