Title

Androgens inhibit phagocytosis by macrophages via the androgen receptor.

Names

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Key words

Macrophage, Inflammation, Androgens, Testosterone, Phagocytosis, Chronic wounds.

Abstract

The cost to healthcare services for the treatment of chronic wounds in the elderly exceeds $9 billion per annum. Chronic wounds are frequently colonised by opportunistic nosocomial pathogens such as *Staphylococcus aureus*. Endogenous androgens are known to contribute to delayed healing whilst in contrast, estrogen accelerates healing. Healing in the elderly is impaired, particularly in elderly males due to the concomitant decline in estrogen levels yet largely unchanged levels of circulating androgens. This study investigated the effect of the two main endogenous androgens, testosterone (T) and dihydrotestosterone (DHT), on the clearance of methicillin-resistant *S. aureus* (MRSA) by macrophages derived from U937 monocytes. Concentrations of T and DHT were chosen to model adult physiological ranges of androgen levels ($1x10^{-9}$M, $1x10^{-8}$M, $1x10^{-7}$M) and supraphysiological levels following exogenous supplementation ($1x10^{-6}$M). The involvement of androgen receptor (AR) activation in bacterial clearance was confirmed using AR antagonists.

Concentrations of T and DHT typical of adults or supraphysiological levels significantly ($P<0.05$; $n=30$) inhibited phagocytosis of MRSA in a concentration-dependent manner compared to untreated controls. Confocal and scanning electron microscopy confirmed androgens decrease the co-localisation of fluorescent GFP-*S. aureus* with macrophages and inhibit bacterial internalisation. AR antagonism reversed the effect of T and DHT, significantly ($P<0.05$) enhancing phagocytosis.

These findings suggest androgens inhibit the resolution of wound bacteria. Novel dressings that induce local blockade of the AR may be an effective treatment option to promote the bacterial clearance of colonised wounds, particularly in elderly males.