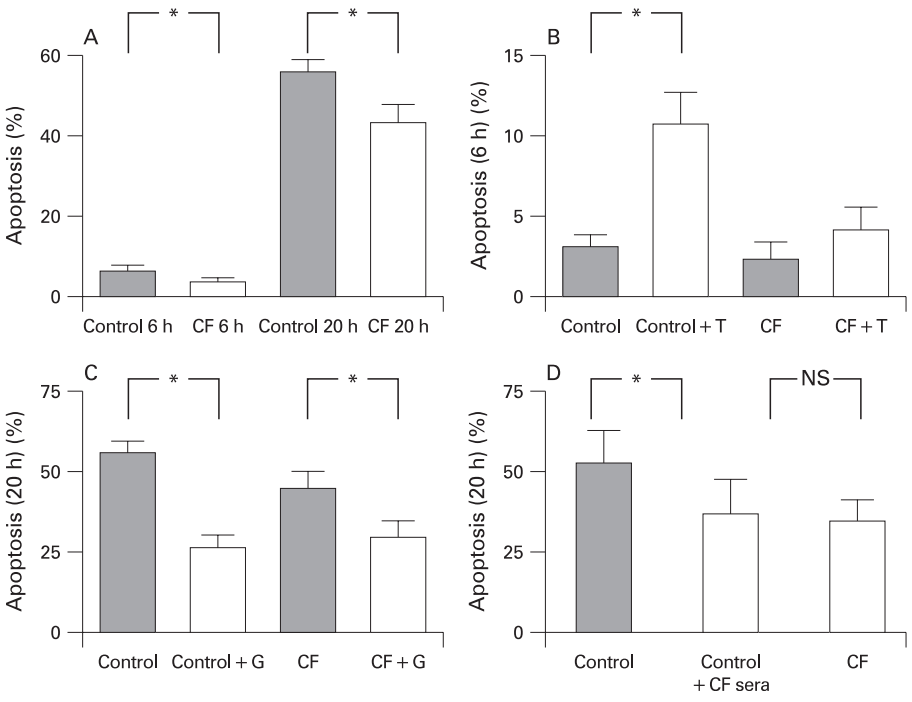

Figure 1 Human peripheral blood neutrophils from patients with cystic fibrosis (CF) and matched control subjects were incubated for 6 or 20 h in DMEM containing 10% autologous serum (unless otherwise stated) and then assessed for apoptosis using morphological criteria. (A) Delay in constitutive apoptosis in CF neutrophils at 6 and 20 h (*$p<0.05$, $n = 12$). (B) Loss of the early proapoptotic effect of tumour necrosis factor α (T) at 6 h (*$p<0.05$, $n = 5$). (C) Preserved prosurvival effect of granulocyte macrophage-colony stimulating factor (G) in CF neutrophils (*$p<0.05$, $n = 11$). (D) Ability of sera from patients with CF to delay apoptosis in normal neutrophils (*$p<0.05$, $n = 4$). Parallel assessment of apoptosis using annexin-V– fluorescein isothiocyanate binding and propidium iodide staining[3] resulted in essentially identical data (note shown). Data are expressed as mean (SEM) of (n) separate experiments, each conducted in triplicate and analysed using non-parametric (Mann–Whitney) calculations of significance.

the cytokine preparation.[4] Moreover, the delay in constitutive apoptosis in CF neutrophils was inhibited by LY294002 (10 μM), a phosphoinositide 3-kinase (PI3 kinase) inhibitor (% apoptosis 20 h: control 54 (2), control+LY294002 61 (5), CF 33 (7), CF+LY294002 50 (9), n = 3).

These findings add to the body of data suggesting broader defects in innate immune responses in CF. Factors present in CF serum appear to inhibit both constitutive and TNFα induced apoptosis, which would be predicted to impair the physiological removal of these cells at inflamed sites. A potential role for CRP is supported by reports that monomeric CRP, which is generated in inflamed tissues, can inhibit neutrophil apoptosis via a mechanism involving activation of FcγRIII (CD16) and PI3 kinase.[5] Together, these results suggest that CF neutrophils have an impaired capacity to undergo apoptosis, even prior to migration to the lung.

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Funding: Funded by the CF Trust UK (DJM), Wellcome Trust (AMC), Asthma-UK (ASC, NF), Papworth Hospital and BLF (KCC).

Competing interests: None.

Ethics approval: Ethics approval was obtained.

Thorax 2008;**63**:660–661. doi:10.1136/thx.2008.096834

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NOTICE

New drugs and targets for asthma and COPD

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