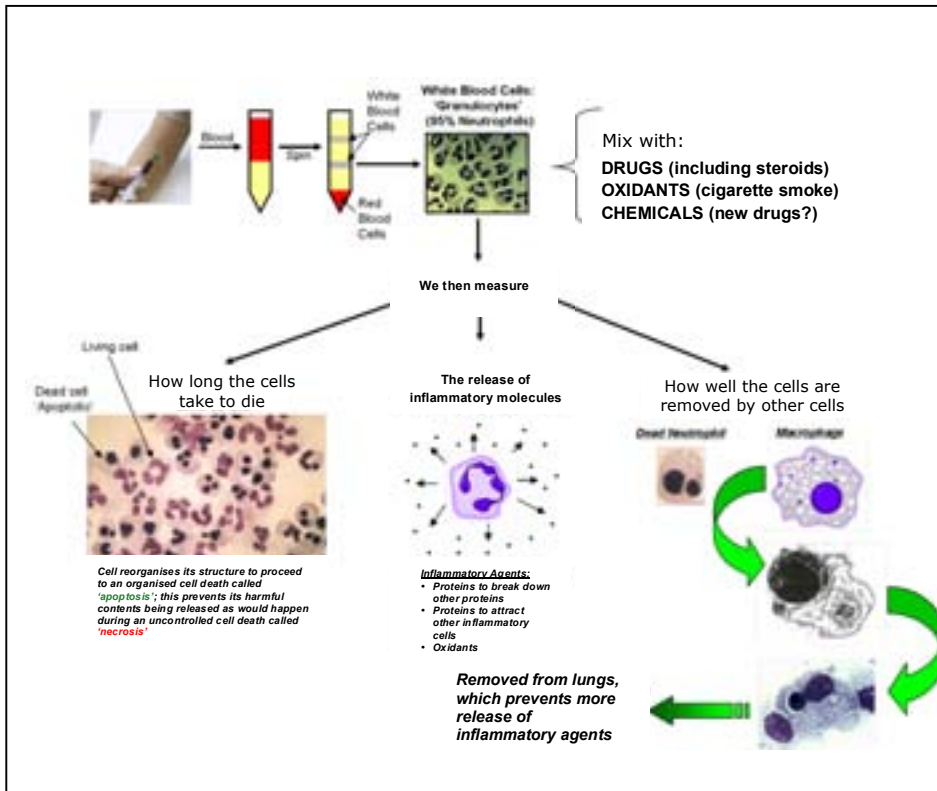


Controlling Inflammation

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Inflammation is normally a beneficial process, involving white blood cells which kill invading organisms, remove damaged tissue and start to repair affected tissues. An acute, strong episode of inflammation can, however, damage the body's organs, especially if they are already inflamed. People with severe asthma and chronic obstructive pulmonary disease (COPD) have chronically-inflamed lungs and, if they get an infection, they often also get acute episodes of inflammation (called exacerbations). These cause an excess of white blood cells (neutrophils) and can result in hospitalisation and death. COPD is the 5th leading cause of death worldwide and there are more than 90,000 COPD patients in Scotland alone.

Anti-inflammatory drugs like steroids are good at controlling inflammation, but they don't work well on neutrophils and are ineffective during exacerbations. We aim to find out why steroid-type drugs do not work well on neutrophils, so that new drugs might be developed which could reduce inflammation during exacerbations, thereby preventing hospitalisation and possible death.



Neutrophils can release many substances to kill foreign organisms and this is important during inflammation. However, many of these substances can also damage healthy parts of the body if the neutrophils are left at the inflammation site too long. So neutrophils are programmed to have a short life and die automatically soon after entering the organs. Initially, neutrophils die in a controlled manner (**apoptosis**), preventing the release of their toxic contents and allowing their removal by other cells. But if they are not removed, their dying becomes uncontrolled (**necrosis**) and they release their toxic substances, damaging healthy tissue and causing more inflammation.

Controlled death: Controlled inflammation
Uncontrolled death: Increased inflammation

Healthy neutrophil
Neutrophil changing its structure (preparing for controlled death)
Neutrophil becoming apoptotic
Apoptotic neutrophil
Neutrophil becoming necrotic
Necrotic neutrophil

Green colour shows a neutrophil forming the correct structure for apoptosis and safe removal
Red colour shows the controlled structure of correct apoptotic cell failing, leading to a necrotic cell

When we treat patients with steroids, they are usually very good at controlling inflammation, but not when the inflamed organ already has a lot of neutrophils. Steroids also cause neutrophils to live longer, so may be responsible for more damage to the inflamed organ, by allowing neutrophils to continue to produce and release more harmful substances than they would without the steroid treatment

Neutrophils just taken from blood
Neutrophils 20 hours after being taken from the blood
Neutrophils 20 hours after being taken from the blood but treated with a steroid

Confocal microscopy by Dr. Andrew Leitch

I am a Senior Research Fellow. I plan and run the experiments, analyse the data and present the results at internal, national and international meetings. I also teach students and fellow researchers and propose new research projects to understand better how diseases occur and how we can treat them.

Impact of oxidative stress and glucocorticoids on neutrophil function and macrophage clearance: Dr. John A. Marwick, Professor Adriano G. Rossi & Professor Christopher Haslett