

Clotting matters – the ebb and flow of blood

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Blood clot formation is a normal physiological process in the body that is designed to protect an individual from blood loss should injury to the blood vessels occur. Once the site of injury has been healed, the clot should then be broken down to again allow the normal flow of blood in healthy blood vessels. In a healthy individual there exists therefore a balance between blood clot formation and breakdown. What happens if this balance is disturbed? If clot breakdown supersedes clot formation, this will lead to bleeding tendencies and if it's the other way around, blood clots will form and remain in the blood vessels, resulting in possible occlusion of such a vessel with tissue death downstream of the clot. These events are better known as a heart attack, occlusive stroke, lung embolism or deep venous thrombosis e.g. in the leg. Collectively these events are classified as end point events of diseases of the heart and blood vessels, called cardiovascular disease (CVD).

Blood clots consist of blood cells such as platelets and red and white blood cells trapped in a network of rod-shaped fibres. These fibres are formed when the soluble protein, fibrinogen, is activated by the coagulation cascade into fibrin molecules which then interact with each other to form long insoluble fibres that seal the site of vessel wall injury in order for the damaged tissue to be healed. The structure of these fibrin fibres can vary and can influence the mechanical properties of the clot i.e. whether it is brittle with a higher risk of breaking into smaller pieces that can occlude small vessels downstream (embolism) or whether it is more elastic or pliable. It can also influence the speed with which the clot is broken down (lysed) and therefore determine whether a formed clot will persist and possibly become occlusive or whether the body will break it down to restore normal blood flow.

Fibrin network structure is currently acknowledged as a risk factor for CVD. Compared to CVD patients, healthy individuals have a more porous network structure with thick fibres that are easily lysable. CVD patients on the other hand are known to have tight, rigid fibrin clots composed of thinner fibres with a less porous structure which are more difficult to lyse. The structure of fibrin networks can be

influenced by several factors such as concentration of certain proteins in the blood, genetics and also lifestyle factors

The question Prof Pieters aims to answer with her research is which lifestyle factors can influence fibrin network structure in order to prevent thrombotic complications of CVD. Her research has recently also expanded to include other coagulation and lytic proteins to get a better understanding of the overall effect of lifestyle modification on blood clot formation and breakdown.

Prof Pieters believes that a healthy lifestyle including the correct diet, physical activity and weight management can modulate blood clot formation and breakdown. This has been proven employing both clinical experimental studies, as well as population-based epidemiological studies. Abnormal blood coagulation profiles are already observed in obese children, contributing to increased CVD risk at an early age. This phenomenon is of particular concern in the African population who is currently undergoing a process of urbanisation where families and individuals move from rural areas to urban areas where they adopt a more Westernised lifestyle with access to an abundance of food sources, including fast foods and a decline in physical activity levels. In the South African context it is however, also important to note, that not only over-nutrition (i.e. obesity), but also under-nutrition can result in an abnormal blood clotting profile. Children, who experienced prolonged periods of under-nutrition, have stunted growth and these stunted children also display abnormal blood clotting profiles.

A prothrombotic blood clotting profile is not only associated with unhealthy lifestyle factors, but an improvement in lifestyle has been shown to improve the blood clotting profile. Increased intake of specific dietary factors for example, vitamin C has been shown to improve fibrin clot structure. Improvement in clotting factors and fibrin network structure has also been demonstrated with weight loss. Additionally attainment of blood glucose control by Type 2 diabetes patients also resulted in an improvement in fibrin network structure.

Prof Pieters furthermore strongly supports the idea that ethnic specific data should be obtained in terms of modulators of blood clot formation and breakdown. While

this topic has been extensively studied in Caucasian populations, virtually no information is available for Africans. Although the basic physiology is similar, ethnic differences do exist and data obtained from studies investigating European individuals cannot simply be extrapolated to the African population. In addition, there has been a recent explosion in the prevalence of CVD in Africans, which was previously considered to occur less frequently in African populations. This increase in CVD, together with known ethnic differences, necessitate the need to investigate factors that influence blood clot formation and breakdown in Africans, in order to develop tailor made health care and disease prevention strategies.

Lastly, the genetic make-up of an individual can also not be ignored as it has the potential to influence the response of the blood clotting and breakdown processes to lifestyle modification. There is clear evidence from the literature that a specific genetic profile can significantly influence the biochemical response to external stimuli such as diet, physical activity, obesity, etc. The African population is considered to be more genetic diverse than populations from European descent, providing another reason why African specific data need to be collected.

Thrombotic complication is a major determinant of CVD event outcome. It can make the difference between life and death and is, to a large extent, modifiable by our lifestyle. Both over- and under-nutrition are associated with abnormal blood clotting and breakdown, making it a relevant topic in the South African setting where both conditions are highly prevalent. Increasing our understanding of the relationship between lifestyle and disease has direct practical implication in health policy and disease prevention strategies.