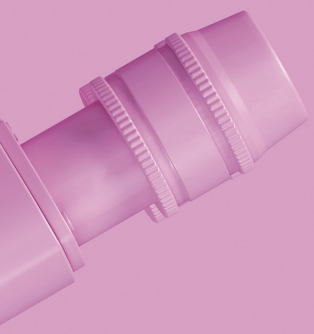
" Blood films are still an integral diagnostic tool, which should be used alongside the patient's clinical history and blood count results"



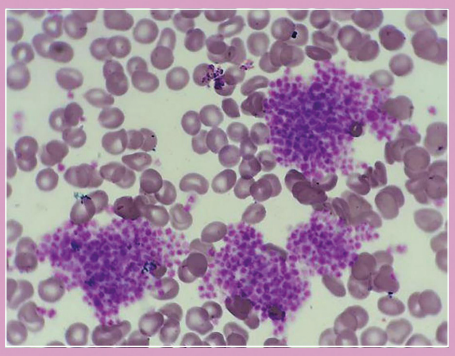
IS MORPHOLOGY DEAD?

Anas Nasir, a Specialist Biomedical Scientist in haematology and blood transfusion, puts the future of blood films under the microscope.

Advancements in technology and other techniques are often conflated with morphology being made redundant. Analysing and reporting blood films is difficult, labour intensive and requires extensive training and experience. Morphological examination may highlight issues with automated analysers and also show things that are currently not detectable by the machines. This article will discuss, with a few examples, why it may be a little early to pronounce the death of blood films.

Platelet clumping

Platelets are integral components of haemostasis, clot formation and they help to stop bleeding. It is, therefore, imperative that accurate platelet counts are provided, as patients have different targets that would determine their need for a transfusion. In a small percentage of patients, platelets clump together due to the commonly used anticoagulant ethylenediaminetetraacetic acid (EDTA) in full blood count samples, resulting in a falsely reduced platelet count or pseudothrombocytopaenia.



This agglutination of platelets is an *in vitro* phenomenon caused by IgG/IgM autoantibodies directed against platelet surface glycoproteins. EDTA exposes epitopes by inducing a conformational change in GPIIb/IIIa and subsequently causes the agglutination to occur. Alternative anticoagulants, such as sodium citrate or heparin, can be used to overcome this issue. Platelet clumping is significant as patients may be subjected to unnecessary platelet transfusions if falsely low counts are reported.

Platelet satellitism

First described by Field and Macleod in 1963 as an *in vitro* phenomenon seen in peripheral blood films, platelet satellitism

is a rare occurrence seen only in blood taken containing EDTA and is absent in other anticoagulants. It is thought that IgG antibodies are formed in the presence of EDTA and directed against the GPII/IIIa complex on the membranes of platelets and the Fc gamma receptor on neutrophils. Coated platelets form a rosette cluster around segmented neutrophils. Platelet satellitism has clinical implications as well as it may result in spurious thrombocytopaenia or pseudothrombocytopaenia, which would require further investigations and interventions. Though satellitism is usually associated with neutrophils, there have also been reported cases of adherence of platelets to lymphocytes and even basophils.

Micro-organisms

The presence of micro-organisms in the peripheral blood can interfere with automated platelet counts, giving a falsely elevated result. Blood film analysis shows certain bacteria to be approximately similar in size and shape to platelets, explaining the error in the automated count. Apart from the bacterial infection, a genuine thrombocytopaenia may indicate other underlying complications such as DIC, for example, which may require further attention.

Red cells simulating platelets

Red-cell fragments (schistocytes) if seen on a blood film require urgent attention, but may also interfere with the platelet count. In patients that have suffered burns, or those with red-cell fragmentation syndromes, fragments may give a falsely elevated platelet count. This can be of clinical significance as in the latter group of patients, an accurate platelet count is essential in the diagnosis and monitoring of thrombotic thrombocytopenic purpura. Burns patients contain microspherocytes and microdiscocytes in their blood that may also be counted as platelets by the analysers.

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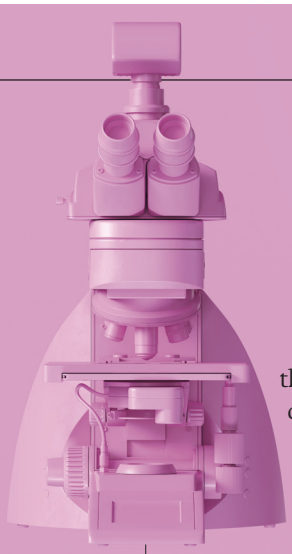
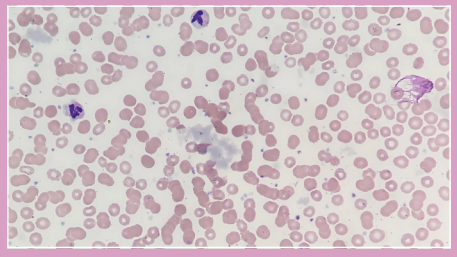


White-cell fragments

White-cell fragments, though rarely recognised, are quite common and seen in AML and ALL and occasionally lymphoma and hairy cell leukaemia. In a study published in the *Journal of Clinical Pathology*, blood films from 169 patients diagnosed with AML or ALL were reviewed. A 500 particle count was performed and the automated platelet count was compared to what was seen microscopically. More than 5% of "pseudoplatelets" as a proportion of platelets plus pseudoplatelets was regarded as significant and recorded. Pseudoplatelets were seen on the blood films of 25% (43) of the patients. In total, 30% (32/107) of those with AML and 18% (11/62) of patients with ALL had these pseudoplatelets. Retrospective analysis showed that 11 of the 43 patients with pseudoplatelets were thought to be at risk of a major bleeding event. Their automated counts ranged from 10 to 75 x10^9/L but once corrected these dropped to 2-15x10^9/L. Morphologically, these white-cell fragments are comparable to agranular platelets, but with a deeply stained cytoplasm in accordance with the cytoplasm of malignant cells.

Cryoglobulins

Type I cryoglobulins are normally associated with B-cell lymphomas and myeloma, whereas types II and III are associated with infective and inflammatory disorders. Cryoglobulins may falsely increase haemoglobin, platelet count or rarely, white blood cell count, depending on the analyser. Blood film analysis shows precipitates scattered throughout the film, occasionally attached to the red blood cells. The cryoglobulin precipitates sometimes alter the red cell morphology in such a manner that keratocytes may be seen.



Conclusion

Blood films give information that automated analysers are unable to detect or cannot do so properly. These include schistocytes, spherocytes and other poikilocytes, inclusions within red cells or white cells, leukaemic cells or other dysplastic cells. A blood film is usually made in three scenarios: when requested by the clinician, reflex test after a flag or numerical abnormality on the instrument, or just before validation of a full blood count result by the biomedical scientist. Clinically, films may be requested for a vast array of reasons, including unexplained anaemia or jaundice, lymphadenopathy, sickle cell-like symptoms (chest or abdominal pain), pain in bones or joints (may indicate acute leukaemia, sickle cell disease or myeloma) or suspicion of bacterial or parasitic diseases. In the laboratory, the indications for making a blood film are different though just as varied and include an unexplained anaemia or sudden unexplained change in counts, macrocytosis or microcytosis, instrument flags (blast cells, variant lymphocytes), and factitious results for red cell indices. In the laboratory, minimal clinical details are often provided and for unknown patients, it is important to provide a thorough analysis of the features seen on the blood film. The blood film may be the primary diagnostic tool for certain conditions, such as myelodysplastic syndromes, leukaemia and lymphomas. It can facilitate prompt diagnosis and indicate which further tests should be performed. Blood films are still an integral diagnostic tool, which should be used alongside the patient's clinical history and blood count results. BMS