FIBRINOLYTIC ACTIVITY (FA) OF NORMAL HUMAN PERIPHERAL BLOOD MONONUCLEAR CELLS (MC). E. Grau and L.A. Moroz. Royal Victoria Hospital and McGill University, Montreal, Quebec, Canada.

FA of blood encompasses a large cellular phase in addition to a fluid (plasma) phase. Polymorphonuclear neutrophils (PMN) have been implicated in this cellular activity, and MC have demonstrated fibrinolytic potential. Using a solid phase radiolysis assay, we have examined FA of normal blood and plasma, and of purified PMN and MC alone, and with purified plasminogen (PLG), mini-plasminogen (mPLG) produced by PMN elastase digestion, or autologous plasma. PMN alone (0.5 x 10^6/ml) had striking activity (292 ± 25 SEM f/min fibrin lysed/h), (n=10 normal subjects) while MC alone (0.5 x 10^6/ml) had mean FA of 32 ± 4 ng/h, all of which could be accounted for by contaminating PMN in the MC preparations (36 ± 8 ng/h). In comparison, mean whole blood FA was 72 ± 4 ng/h, and plasma FA was 22 ± 4 ng/h. When MC (0.5 x 10^6/ml) were assayed with PLG (2-40 ng/ml) or autologous plasma for 1 h, no significant FA was generated, indicating that neither intrin­sic nor PLG-dependent (plasminogen activating) FA activity of MC contribute significantly to the FA of whole blood as measured by routine 1 h assay, where 70% of measured FA involves the cellular phase. However, with longer assay times (0-24 h), there was time-dependent appearance of FA when MC were mixed with PLG or with autologous plasma. This FA was dependent upon interaction between MC and PLG, since no FA was generated by supernatants of MC preincubated alone, while FA was readily detected in the medium when MC and PLG were mixed. Comparing effects of PLG and mPLG, FA of MC (0.5 x 10^6/ml) with PLG (40 ng/ml) was 447 ± 8 ng/h, while FA with mPLG (40 ng/ml), an approximate 3-fold polar excess was 156 ± 5 ng/h, indicating a possible role for the N-terminal portion of the PLG molecule (containing kringle domains 1-4 absent in mPLG) in interaction of MC and PLG, or of MC-derived and PLG. FA of MC (0.5 x 10^6/ml) in autologous plasma (85 ± 3 ng/h/ml) was markedly reduced, while dose-dependent inhibition of PLG (1 ng/3 h/ml) washed blood by addition of tranexamic acid (10 mM/ml) (5 ± 1 ng/h/ml). Thus, normal peripheral blood monocytes, like MC, may contribute, albeit minimally, to FA in whole blood. FA of blood may encompass a large cellular phase in addition to a fluid (plasma) phase. shed plasminogen activator (PA) activity. MC activity of MC contribute significantly to the FA of whole blood as measured by routine 1 h assay, where 70% of measured FA involves the cellular phase. However, with longer assay times (0-24 h), there was time-dependent appearance of FA when MC were mixed with PLG or with autologous plasma. This FA was dependent upon interaction between MC and PLG, since no FA was generated by supernatants of MC preincubated alone, while FA was readily detected in the medium when MC and PLG were mixed. Comparing effects of PLG and mPLG, FA of MC (0.5 x 10^6/ml) with PLG (40 ng/ml) was 447 ± 8 ng/h, while FA with mPLG (40 ng/ml), an approximate 3-fold polar excess was 156 ± 5 ng/h, indicating a possible role for the N-terminal portion of the PLG molecule (containing kringle domains 1-4 absent in mPLG) in interaction of MC and PLG, or of MC-derived and PLG. FA of MC (0.5 x 10^6/ml) in autologous plasma (85 ± 3 ng/h/ml) was markedly reduced, while dose-dependent inhibition of PLG (1 ng/3 h/ml) washed blood by addition of tranexamic acid (10 mM/ml) (5 ± 1 ng/h/ml). Thus, normal peripheral blood monocytes, like MC, may contribute, albeit minimally, to FA in whole blood. FA of blood may encompass a large cellular phase in addition to a fluid (plasma) phase.