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Haematologica 1998; 84:289-290 editorial, comments and views

Potential clinical implications of early diagnosis of chronic myeloid leukemia

Chronic myeloid leukemia (CML) probably originates from a single hematopoietic cell that acquires a proliferative advantage over the normal ones and is characterized by the *bcr/abl* fusion gene.[1] Normal *c-abl* function is critical for entry of human CD34+ hematopoietic cells into the S phase and for their differentiation to granulocyte-macrophage progenitors[2] and the fusion gene product ($p210^{bcr\text{-}abl}$) probably plays a crucial role in the pathogenesis of CML.[3]

It is well established that CML patients may have residual normal hematopoietic stem cells at clinical onset of their disease.[4,5] Frassoni *et al.*[6] have recently carried out studies to quantify Ph-negative (presumably normal) progenitors in CML patients at diagnosis and one year after diagnosis. For each patient, they examined bone marrow cells in the steady state and hematopoietic cells mobilized into the peripheral blood by chemotherapy plus granulocyte colony-stimulating factor (G-CSF). Taken together their findings indicate that normal hematopoietic progenitors are relatively well preserved in most newly diagnosed CML patients, but tend to decline rapidly with time. This observation has potential implications for treatment of CML using strategies that require autologous stem cell rescue. For the two thirds of patients with CML who are unable to benefit from either allogeneic stem cell transplantation (SCT) or interferon-α,[7-10] autografting may indeed represent a promising therapeutic option.[11-13] Since its outcome is probably improved when Philadelphia-negative hematopoietic progenitors are employed,[12] collections of circulating progenitors should be performed soon after diagnosis of CML.

In this issue, Cervantes *et al.*[14] show that a substantial proportion of CML patients are currently diagnosed early in the course of the disease. They conclude that the survival prolongation of CML patients shown by recent studies might simply be an effect of earlier diagnosis and longer follow-up. A further point that needs to be underlined is that CML patients at the very beginning of their disease may have just a few leukemic stem cells and a vast predominance of normal residual stem cells.[6] The question is how to manage these CML patients with a well preserved normal stem cell repertoire. Should we now seriously consider routine collection of peripheral stem cells in any newly diagnosed CML patient? This could be done through a basal leukapheresis, or through mobilization by G-CSF alone or by chemotherapy plus G-CSG. The collected stem cells might be used later in patients who are not eligible for allogeneic SCT and do not respond to interferon-α. These questions should be properly addressed in prospective clinical trials.

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Hereditary thrombophilia as a multigenic condition

In a recent review article in this journal, Dahlbäck *et al.* analyzed the importance of genetic factors in the pathogenesis of inherited thrombophilia with particular emphasis on those defects which affect the protein C system.[1] In this issue Vicente *et al.*[2] examine a new gene associated with thrombophilia, the prothrombin gene. Their systematic review shows that the prothrombin 20210G/A mutation, associated with elevated levels of factor II in plasma, significantly increases the risk of developing venous thrombosis.

The subject of molecular basis of hereditary thrombophilia is rapidly expanding, as shown also by the numerous contributions recently published in this journal.[3-9] Haematologica will be glad to consider for publication further papers on this topic.

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