# High Dose Cytotoxic Chemotherapy with Peripheral Blood Stem Cell (PBPC) Transplantation - Malignancy and Beyond

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The current worldwide interest in the use of high dose chemotherapy (HDCT) followed by the reinfusion of stem cells is based upon certain appealing concepts. High dose cytotoxic treatment is based upon the principles of increasing both the dose intensity and dose density of chemotherapeutic agents in clinical settings[1]. Dose escalation is associated with significant bone marrow and non-bone marrow toxicity. The reinfusionofhemopoeitic stem cells following chemotherapy results in an abrogation or abbreviation of bone marrow suppression leaving the other systemic side effects as the only stricture to dose escalation of chemotherapeutic agents[2]. The peripheral blood has, however, largely replaced the bone marrow as a source for stem cell harvest in current clinical practice[3]. Moreover, now stem cell harvests in the allograft setting are also being largely carried out through peripheral blood apheresis. In the latter setting therefore, special concerns influence the use of growth factors to mobilize PBPC's in normal donors who are HLA matched with the recipient. Many of these concerns will take time to resolve[2,4]. The literature is replete with HDCT with PBPC being used in most malignant conditions that are known to be chemotherapy responsive and indeed even many, that are not. Novel methods continue to evolve worldwide in using this modality of therapy both creatively and for its maximum benefits. Interestingly, HDCT with PBPC itinfusion in the autograft setting is also being attempted for non-malignant disease. Some reports are now beginning to emerge about using this modality of therapy in some autoimmune disorders[5]. A first international meeting was held in Basel Switzerland to look at the issue of hematopoietic Stem cell therapy for autoinimune disease since many autoimmune diseases require cytotoxic chemotherapy for long term control and management[6].
There is much debate amongst physicians - those who believe in HDCT with PBPC and those who remain largely skeptical. Although, it may take many years to resolve the ultimate nagging issues, there is no doubt that HDCT with PBPC can no longer be ignored. No longer can HDCT with PBPC be considered an arcane method of therapy restricted only in circumstances of hematologic and oncologic settings. Physicians must be aware of the broad principles and more importantly the great difficulties associated with the use of HDCT and PBPC. Bone marrow stem cells circulate in the peripheral blood[7] but the numbers increase markedly following bone marrow recovery from cytotoxic chemotherapy[8,9]. These numbers can be augmented further by the addition of colony stimulating growth factors(CSFS) which further increases the yield of stem cells in this clinical setting. CSFS can also be used alone for this harvest purpose but in higher doses. Aithough, both GM-CSF and GCSF can be used as hematopoietic growth factors, the largest experience has been with the latter. Apheresis techniques are by now standard in modern blood banks and many machines are available to produce aproduct rich inthe putative stem cell. Prior therapies which affect bone marrow reserve significantly, also affect the richness of the stem cell product harvested. On a cininical level the minimum requirement to enhance marrow recovezy in the HDCT setting is approximately 1-2/$10^6$ CD 34 positive cells per kilogram of the patients body weight. Even though, the long term culture initiating cells are few in numbers, the CD 34 positive cell has proven to be an adequate and an easily measurable marker in clinical practice[1]. Clearly an excellent laboratory, antibiotic support and competent enumeration of these CD 34 positive cells is vital. The consequences of high dose chemotherapy are especially important and require intense supportive care. Effective management of these complications require a committed and a trained team

that works well together to enhance patient recovery. Good nursing care is vital in this regard. An excellent blood bank is needed and must have the capability of delivering platelet products on demand and the capacity to irradiate them. All of this requires trained manpower and money. Sadly in our country many of these issues still need to be improved just to deliver basic needs. Nevertheless, the dissemination of general knowledge about PBPC transplantation which the general public knows as bone marrow transplantation demands that despite the difficulties we must proceed forth carefully and cautiously. More exciting advances await us in this field. It is interesting that bone marrow canbe growninculture[10] just asbacteria may be inthe laboratory. This ex-vivo expansion of the hematopoietic stem cell would mean that in the future avery small amount of blood or bone marrow would be needed from the patient in order to have an adequate number of stem cells for henmtologic support. Moreover, infant cord blood[11] as a rich source of stem cells is also here and is being evaluated in study settings. None of us knows what all of this will eventually lead to but like itor not, we cannot ignore stem cell transplantation.

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