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## Physiological Basis for a Rational Therapy of Bone Marrow Diseases.

The reproduction, differentiation and realease of blood cells from bone marrow seem to be governed by metabolic products, by water displacement from cellular to intercellular compartment, by neuro-hormonal agents, by poietin formation and activation. Urea and uric acid increase the bone marrow density distribution, and probably accelerate maturation of granulocytes. Bone marrow extracellular normal hyperosmolar fluid seems to play a role in mitogenesis and differentiation of bone marrow cells. Some leukemic patients suffer nocturnal diuresis due to a probable biorhythmic deficiency of dispensable adiuretin, during a leukemia relapse. Cell water content probably reduces during maturation as a consequence of organic phosphate compounds accumulation, of intracellular pH depression, of ATP, GTP, and other nucleotides polymerization in dense bodies, under the influence of hormones and neural transmitters, like nor-adrenalin, 5-OH-tryptamin, dopamin and 5-OH-dopamin.

Melatonin (MLT), however, seems to play a dominant role, insamuch as:

a) habenular nuclei stimulation induces thrombocitosis; b) i.v., injected MLT induces blood platelet rise in thrombocytopenic patients; and c) systematic oral or parenteral administration of MLT induces a seemingly healing state from acute or chronic lumphocytic leukemia. MSH and ACTH, or shorter corresponding polypeptide chains, seem to play as much an important role for a normal bone marrow function as MLT.

The aforesaid factors validly contribute to effectuate the formation and activation of erythro-thrombo-, and leukopoietins. The relative trouble reveals through a decrease of red blood cells and platelet blood count, as well as with a rise of eosinophil cell blood count.