Report

Modern Trends in Human Leukemia V
Wilsede, June 20–24, 1982

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Everybody concerned with the management of leukemia appreciates that Rolf Neth, supported by many not named helpers and by the Dr. Mildred Scheel Stiftung, brought together scientists from all over the world in the National Park Lüneburger Heide (FRG) for three days. It was the 5th time that "Modern Trends in Human Leukemia" have been extensively discussed in Wilsede. More than 100 scientific presentations have been offered in lectures and poster sessions. The most important data will be summarized in this meeting report.

Cell Biology and Clinical Aspects

J.W. Singer (Seattle), using human long term marrow cultures in patients after allogeneic marrow transplantation and in a patient with CML, all heterozygous for G6PD, demonstrated the common origin of adherent stromal layer cells and hematopoietic cells, both being transplantable. It was shown in double-layer, solid agar culture that removal of MBG6+, OKT 3+, OKT 8+, Okt 4 lymphocytes results in the loss of differentiation of GM-CFC while proliferation is unaffected (G.E. Francis, London). Details on the alterations in normal and leukemic progenitor cells after incubation with different biological regulators, e.g. G-CSF and GM-CSF, were reported by A.W. Burgess and D. Metcalf (Victoria). In the myelomonocytic leukemic cell line of the mouse, WEHI-3 B, exposure to differentiating factor (DF) significantly reduces clonogenicity (leukemic stem cell self regeneration). The suppressed cells are not killed but exhibit an irreversible premature differentiation. DF can be separated from GM-CSF and identified as G-CSF (N.A. Nicola, Victoria). After stimulation differences in the proteins synthesized are observed between leukemic and normal progenitor cells (A.W. Burgess).

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M.A.S. Moore (New York) presented results of a phase I trial of the use of endotoxin in twelve patients with AML or myeloid blast crisis of CML. After application of 1 µg endotoxin a decrease of blast cells and an increase in mature cells is seen. Tolerance does not develop up to 30 µg endotoxin. The human post-endotoxin serum contains CSF, and leukemia inhibitory activity. The effects of retinoic acid (RA) and dihydrocholecalciferol (Vit. D₃) were tested in vitro. Whereas RA inhibits the growth but does not inhibit the differentiation of the promyelocytic cell line HL-60 vitamin D₃ mediates both, the inhibition of growth and the induction of differentiation in HL-60 and WEHI-3 B cells. Normal mouse and human marrow CFU-C are enhanced by Vit. D₃. No synergism of RA and Vit. D₃ has been found.

The combination of RA and of differentiation inducing factors produced by mitogen stimulated mononuclear blood cells and some malignant T-lymphocyte lines, e.g. HUT 102, induce maturation in HL-60 and in the monoclast like cell line U 937 (I. Olsson, Lund). Substances elevating the level of intracellular c-AMP are synergistic to RA.

R. Mertelsmann (New York) reported that in patients with acute lymphoblastic leukemia (ALL) the production of interleukin 2 (IL 2 = TCGF = T-cell growth factor) is greatly enhanced and seems to play a role in the clonal growth of ALL cells in culture. In immunodeficiency syndromes, i.e. in patients with Nezeloff's syndrome, Kaposi's sarcoma, and in half of the patients with common variable immunodeficiency, in chemotherapy-induced immunosuppression and in advanced Hodgkin's disease, IL 2 is able to normalize or nearly normalize T-cell proliferation in vitro. First in vivo results showed a similar effect.

H. Stein (Kiel) and V. Diehl (Hannover) presented studies on primary biopsies of patients with Hodgkin's disease as well as Hodgkin-derived cell lines. The Hodgkin-derived cell lines most closely resemble early myeloid-monocytoid progenitor cells. With the use of the monoclonal antibody Ki 1, directed against a Hodgkin and Sternberg-Reed cell antigen, an until now unidentified small cell population can be detected which is located between, around or within cortical follicles in normal and hyperplastic lymphoid tissue.

New trends in the use of bone marrow transplantation (BMT) in leukemia were reviewed by E.D. Thomas (Seattle). BMT is indicated in first remission of acute non-lymphoblastic leukemia (ANLL) or second remission of ALL. If there are signs of relapse, one should transplant immediately since these patients do better than those being transplanted after the second remission has been induced. BMT in the chronic phase of chronic myelocytic leukemia now seems to be the treatment of choice in young patients if a suitable donor is available. Although the presence of a suitable donor (HLA-identical, MLC-negative relative) is still a major limitation, the use of totally unrelated, phenotype-identical donors will become feasible in the future. Five out of ten patients with ANLL in 1st remission, receiving the transplant from a mismatched donor (1 haplotype identical) are alive after 6 months to 4 years. As to survival, patients with ANLL in remission who were conditioned with fractionated total body irradiation (TBI) do better than those receiving single dose TBI. The present results of another still ongoing study comparing methotrexate and Cyclosporin A for prevention of graft-versus-host disease (GVHD) do not indicate a difference between the two drugs. As to the antileukemic effect of the graft, low grade GVHD could be used as an antileukemic process, as can be buffy coat cells in patients with