Abstracts of the 23rd Sysmex Hematology Seminar

The Sysmex Hematology Seminar, sponsored by the Scientific Division of Sysmex Corporation, was held annually and focuses on academic or scientific themes.

This year the main theme of the seminar was "Hematology." Four lectures were given on various hematology topics by well-known doctors in each field in Japan. The lecture titles were "Thrombosis and Hemostasis," "White Blood Cells and Lymphocytes," "Red Blood Cells" and "Cell and Gene Therapy for Malignant Diseases."

This Sysmex Seminar, which was the 23rd in the series was seen in two other cities via satellite from Kobe city which was the main venue on June 3rd. So, many people were able to participate in this event.

We gratefully acknowledge all participants, speakers, chairpersons and all others concerned for their participation in these seminars.

We hope we are achieving our aim, which is to support the progress of medical science by means of the Sysmex Hematology Seminar.

The following are the summaries of each seminar.

Miyuki Uehara
Scientific Division of Sysmex Corporation

Date : Kobe June 3, 2000
Tokyo June 24, 2000

Lecturers : **Yasuo IKEDA, MD**
Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan
: **Kazuhiko NAKAHARA, MD**
Department of Clinical Laboratory Medicine, Tokyo University Graduate School of Medicine, Tokyo, Japan
: **Hideaki MIZOGUCHI, MD**
Department of Hematology, Tokyo Women's Medical University, Tokyo, Japan
: **Shigetaka ASANO, MD**
The Advanced Clinical Research Center and The Research Hospital, The Institute of Medical Science, The University of Tokyo, Tokyo, Japan

Chairman : **Hidehiko SAITO, MD**
First Department of Medicine, Nagoya University School of Medicine, Aichi, Japan

Thrombosis and Hemostasis
Molecular Mechanisms of Thrombus Formation

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There are two types of thrombus formation, one is hemostatic plug to protect the body from excessive bleeding and the other is pathological thrombus that occludes blood vessels leading to serious organ dysfunctions. The mechanisms of hemostatic plug formation have been the main topics for years by analysing the pathophysiology of inherited bleeding disoder. They are now fairly well understood at the molecular level. On the other hand, based upon the recent progress in cell biology vascular biology and rheology, important roles of platelets, coagulation and vascular factors different from those in case of hemostatic thrombus have been demonstrated in pathological thrombus formation. The knowledge of them is greatly contributing to the new development of anti-thrombotic therapy for myocardial and cerebral infarction. We hope that you will deepen understanding of various clinical disease states by comprehension of the molecular mechanism of thrombosis shown in this report.

White Blood Cells and Lymphocytes
Their Discovery to Clinical Applications

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Only about 100 and several years have passed since Virchow discovered leukocytes and Ehrlich developed morphological classification of white blood cells. On the other hand, when we review the advancement of modern medicine and medical care, we can only marvel that the 20th century is such a unique age of scientific development invaluable for human being. During this period of only a hundred years, marked advancement has been achieved in medical science including establishment of morphology of white blood cells, elucidation of its physiological functions, and investigation of white blood cell-related diseases and their pathology. Recent progress in diagnosis and treatment of hematopoietic tumors among others is striking. It has been driven by the development in mechanical engineering, immunology, and genetic, which appears one of typical cases where basic medicine is effectively and successfully applied in clinical medicine. In the 20th century, human beings have made numerous discoveries, which have given many benefits to the public. What is waiting for us in the 21st century? Now that we are in the face of the 21st century, it may be useful to review the development in the 20th century to get ready for the coming century.

Red Blood Cells
Pathogenesis and Treatments of Intractable Diseases

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Progress in the research of erythroid diseases during the 20th century will be summarized, focusing on the pathogenesis and treatment of intractable diseases such as aplastic anemia, pure red cell anemia and refractory anemia.

Aplastic anemia was first reported by Ehrlich in 1888, and is characterized by pancytopenia and a fatty marrow. Recently, more than 50% of moderate and severe cases of aplastic anemia have been cured by immunosuppresive treatments using antithymocyte globulin and/or cyclosporin. Moreover, in responding cases, cytotoxic T cells are found to suppress the hematopoietic stem cells. These results indicate that most cases of aplastic anemia occur through immune mechanisms. Moreover, allogeneic stem cell transplantation from HLA-identical siblings improves the survival rate of patients with severe cases from 30% to 80%. Aplastic anemia also occurs with paroxysmal nocturnal hemoglobinuria (PNH). The causative gene of PNH was discovered by T. Kinoshita, and is called the PIG-A gene. It is interesting to note that 10 to 30% of patients with aplastic anemia showed an obvious increase in PNH clones.

Pure red cell anemia is characterized by severe anemia and erythroid hypoplasia in the marrow. Idiopathic cases are characterized by the suppression of erythroid stem cells by $CD8^+$ lymphocytes,and most cases can be treated successfully with cycloesporin. In cases accompanied by large granular lymphocyte leukemia, $CD8^+$ leukemic lymphocytes also suppress the erythroid stem cells. However, most cases respond well to 50 to 100 mg of cyclophosphamide given orally every day, which results in a decrease in the leukocyte count to around 2,000. The relationship between idiopathic cases and cases accompanied by large granular lymphocyte leukemia is one of the themes to be discussed.

Refractory anemia is considered to be a preleukemic state. However, it was reported recently that 30 to 80% of cases responded well to immunosuppressive agents such as steroid hormones, ATG and/or cyclosporin. Moreover, it was found that PNH clones increased in some cases of refractory anemia, and these cases with increases in PNH clones responded better than those without increases in PNH clones. Similar observations were noted also in cases of aplastic anemia. From these findings, the relationship between aplastic anemia and refractory anemia is now a popular topic of discussion.

Cell and Gene Therapy for Malignant Diseases

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The research of the cell/gene therapy in which many advanced technologies including gene insertion into transplantable cells are applied has become important. In the clinical research turned to the development of these new treatment strategies, special consideration is necessary to secure not only the efficacy but also the safety. The establishment of the watch system similar to that of the United States is urgently needed for its proper development.