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Fifth Ann Arbor Conference

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THE RED CELL
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PREFACE

The Fifth International Conference on Red Cell Metabolism and Function was held September 29 to October 2, 1980, at the Towsley Center for Continuing Medical Education on the campus of the University of Michigan in Ann Arbor. The main purpose of the conference continues to be interdisciplinary enrichment, that is the meeting provides an opportunity for investigators from diverse fields, but with common interests in the red blood cell, to meet and cross fertilize. The meeting was dedicated posthumously to Fred Oelshlegel, formerly of the University of Mississippi, in recognition of his contributions to red cell and malaria research.

One new feature of this conference was the Oelshlegel Research Award Competition. The Oelshlegel Research Award is a $500 cash prize, plus travel support for attendance at the meeting, given to that young investigator of assistant professor rank or below, who submits the best paper to the Conference. This competition resulted in the submission of 17 abstracts, almost all of them of high quality, from young investigators. These abstracts were reviewed by an *ad hoc* committee (Dr. Martin Steinberg, Dr. John Eaton, Dr. Alan Schechter, Dr. Kouichi Tanaka, and Dr. George Brewer). Six finalists were selected, all of whom submitted excellent papers which appeared on the program of the Conference. The final winner was Dr. Robert Hebbel of the University of Minnesota, with his paper on "Erythrocyte Adherence to Endothelium in Sickle Cell Anemia". All told, eleven papers on the Conference agenda came from the young investigators involved in this competition and all of these papers were of high quality. Since we plan the Oelshlegel Research Award to be a continuing facet of the Conference, we anticipate that this emphasis on young investigators will continue to be present in future conferences.

Partly because of the dedication of this meeting to Dr. Oelshlegel, a session on the interaction of malaria and the red cell were held. This session proved to be very stimulating and led to a great deal of interaction between malaria workers and workers dealing with other aspects of the red cell. For too long this interesting host/parasite interaction, which intersects in such fascinating ways with so many red cell fields, has been neglected by the vast majority of red cell workers. This session seems to have been a start in correcting this problem. Papers ranged from interaction of metabolism of the parasite with the host red cell, both in erythrocyte cultures and in whole organisms, to studies of the possible mechanism of chloraquine resistance in malaria. New techniques using continuous cultures of infected red cells appear to offer much for future studies in this area.

The red cell membrane continues to be an active and challenging area of research. Papers on basic aspects of membrane structure and function dealt with elegant models of the cytoskeleton, studies of calcium, calcium-ATPase and calmodulin, factors leading to instability of membranes, interaction of the red cell anion channels with other cellular components, and oxidative damage to the red cell membrane. Other related papers dealt with insulin receptors on the red cell membrane, and the mechanism of nuclear expulsion in mammalian erythrocyte cells. As in 1977, the main Conference was proceeded by a workshop on membranes. This workshop again proved to be very popular and added to the influx of membrane researchers to the meeting.

It is a tradition that red cell metabolism is an important focus of this meeting, and the Fifth Conference was no exception. One paper dealt with the interesting red cell enzyme abnormalities in Down syndrome (trisomy 21). A story is emerging that the superoxide dismutase locus, present in triple dose, is primarily responsible for Down syndrome abnormalities. According to a current hypothesis, the elevated levels of this enzyme leads to increased peroxide production and oxidant stress. Glutathione peroxidase, the genetic locus for which is on a different chromosome, is elevated as a compensation. Workers from France have shown a positive correlation between glutathione peroxidase levels in the red cell and the intelligence quotient of Down patients. This suggests that the greater

the glutathione peroxidase response, the more the protection against oxidant brain damage in this disease. While this story is still at the hypothesis stage, it fits with present knowledge. This fascinating hypothesis is particularly important because, if it turns out to have some validity, it immediately suggests modes of treatment to prevent some of the damage to the brain which occurs in this disease. Other interesting papers dealt with metabolic control including the role of enzyme phosphorylation and the influence of adrenalin on red cell metabolism, hemoglobin functional variation in high and low level DPG rat strains, environmental factors influencing metabolic adaptation of the red cell to altitude, mechanism of the reduction of methemoglobin, and fascinating studies on pyruvate kinase activity in canine postnatal anemia. An extremely interesting study related glutathione peroxidase abnormalities to the pathogenesis of malignant hyperthermia. Other papers related to red cell metabolism included the interactions of liver drug metabolizing systems with G6PD deficiency in producing variability in hemolysis from certain drugs, and the identification of possible substances from the fava bean which produces favism in G6PD deficiency.

Hemoglobin and the hemoglobinopathies continue to be a major area of investigation involving the red cell, and an area where, hopefully in the not too distant future, the information can be used to bring increased patient benefit. This time we initiated a Workshop on Advances in Red Cell Hemoglobin Analysis which preceded the main conference and ran simultaneously with the membrane workshop. This workshop was well attended and proved to be quite popular. Papers presented at the main Conference dealt with new techniques for studying hemoglobin, including prenatally, diesterase activity of hemoglobins, the role of beta-93 cysteine in hemoglobin, studies of gelation and crystallization of hemoglobins, and low output hemoglobin variants mimicking the phenotype of thalassemia. Other papers of a more applied nature dealt with zinc deficiency in sickle cell anemia, the potentially critical role of erythrocyte adherence to endothelium in sickle cell anemia, abnormal calcium transport of sickle cell anemia red cells, and a hypothesis on how membrane expansion/calmodulin inhibiting drugs may be useful in the therapy of the membrane lesion in sickle cell anemia. An interesting paper dealt with

globin synthesis in clonal erythrocyte cultures, and a paper was presented on the interrelationship between alpha-thalassemia and homozygous sickle cell disease.

A session was held on topics of interest in the blood storage area, and included papers on metabolic aspects of red cell preservation, and two papers on fluorochemicals and their use as blood substitutes in blood transfusion.

This volume contains the proceedings of this Fifth International Conference. It includes the formal papers and informal discussion sessions which took place after the papers. As with the previous conferences, it represents a good sample of the present state of the art and the status of current thinking in the various areas covered.

A conference such as this cannot take place without the work of many people. I am particularly grateful to Lucia Feitler Brewer, who was responsible for much of the non-scientific aspects of the conference's organization. Ms. Kim Olson also helped with organizational aspects of the meeting, and did a yeoman's job in supervising the typing of the discussion transcripts. She has also been invaluable in putting this volume together. Drs. Eric Schoomaker, John Eaton, Walter Kruckeberg and Samir Hanash were very helpful in many aspects of program development. Eric shouldered most of the responsibility for establishing the Oelshlegel Research Award, John and Walt were mostly responsible for organizing the Membrane Workshop, and Samir was primarily responsible for the Hemoglobin Workshop. A number of people associated with my laboratory contributed a great deal in helping with the conference. These included Conrad Knutsen, Joann Hamelin, Robert Dick, Ulana Bereza, Michael Stellini, William McBride, Nanette Wetterstroem, Jon Aster, Ikuko Mizukami, Jill Otto and Ken Meyers. Financial support for a conference such as this is absolutely essential, and we received generous grants from the Office of Naval Research, Arlington, Virginia; the U.S. Army Medical Research and Development Command, Fort Detrick, Frederick, Maryland; Gelman Instrument Co., Ann Arbor, Michigan; Al Meyers Foundation, Tecumseh, Michigan; Dow Chemical U.S.A., Midland, Michigan; The Upjohn Company, Kalamazoo, Michigan; Varian Instrument Division, Palo Alto, California, Warner-Lambert/ Parke Davis, Detroit, Michigan; Instrumentation Laboratories, Lexington, Massachusetts, American Instrument Co., Silver