# The Biophysics of Organ Cryopreservation

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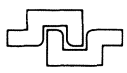

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# The Biophysics of Organ Cryopreservation

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**PREFACE**

This book is the Proceedings of a NATO Advanced Research Workshop held in Atlanta, Georgia, USA, 12-14 April 1987.

Following the discovery of the cryoprotective properties of glycerol by Polge, Smith and Parkes in 1948 (1), continuing research has made it possible to cryopreserve erythrocytes, leucocytes, bone marrow cells, spermatozoa, embryos and skin, to mention only those systems of greatest clinical relevance. The extension of these methods to whole organs has so far eluded us; yet, the cryopreservation of whole organs would be of inestimable value. The purpose of the workshop and of this book is to explore, in a multi-disciplinary setting, the reasons for this impasse and possible avenues for progress: experts from the fields of physical chemistry, biophysics, physiology, mechanical engineering and electrical engineering joined forces with medical cryobiologists.

The chapters in this book are designed to be read in sequence. The first section sets the scene for the role of organ storage techniques in transplantation and for cryopreservation in organ storage. Part two deals with the physical and physiological basis of attempts to cryopreserve organs using techniques extrapolated from the highly successful cell preservation technqiues. First we consider the problems of adding cryoprotectants to, and removing them from organs, and discuss the nature and organisation of intracellular water. Much of this general area is reasonably well understood, although it must be admitted that existing knowledge is not always well used by experimenters. The study of heat transfer in biological systems has received less attention in the past, although it, too, is amenable to quite precise analysis. The mode of formation of ice when organs are frozen and the mechanism by which it inflicts damage are dealt with in some detail, and it is concluded that extracellular, and particularly intravascular ice, is the crucial problem in the techniques that are currently proposed for organ cryopreservation. Progress requires a more extensive knowledge of the freezing process in aqueous systems, their modification in tissues and organs, and means for reducing the total mass of ice formed during the cryopreservation process.

The third section deals with these more fundamental matters: the processes of nucleation, ice crystal growth, vitrification (glass-formation) and liquefaction in aqueous systems subjected to extremely low temperatures are all examined. The emphasis is on non-equilibrium states, where the quantity of ice formed is substantially reduced, and we explore means that might be used to achieve such an end. The application of vitrification to biological systems is reviewed in some detail and the hazards of devitrification and recrystallization (the formation and growth of ice during warming) are explored: the utility of rapid heating in avoiding these catastrophies is emphasized.

How might one obtain controlled and, if necessary, rapid heating in bulky biological samples? Part four of the book deals with the favoured approach - electromagnetic heating. The measurement of dielectric properties of relevant materials, the use of phantoms for studying energy absorption from electromagnetic fields, the selection of the most favorable frequency for irradiation and the design and control of specific power sources and applicators are all described.

The final section deals with an area of major difficulty in organ preservation research; how can we obtain the maximum information from each expensive whole organ experiment without interferring with the intrinsic nature of the organ in so doing? The non-invasive technique of nuclear magnetic resonance (NMR) and radioactive tracer methods have already proved useful in studies of organ storage at temperatures above 0°C, and promise to be even more valuable in cryopreservation research. The potential of proton and phosphorous NMR and of positron emission tomography (PET) is discussed in this book.

The central problem remains unsolved in the sense that we still cannot cryopreserve a mammalian organ in a state that will satisfy a transplant surgeon. But we do understand the nature of the problems much more clearly now, and can propose how they might be tackled. It is our hope that this book will contribute to further research in this field and perhaps point the way to final "success", in the transplant surgeon's sense.

David E. Pegg
Armand M. Karow Jr.

**Reference**

(1) C. Polge, A.U. Smith and A.S. Parkes, Revival of spermatozoa after vitrification and dehydration at low temperatures, Nature 164:666 (1949).

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