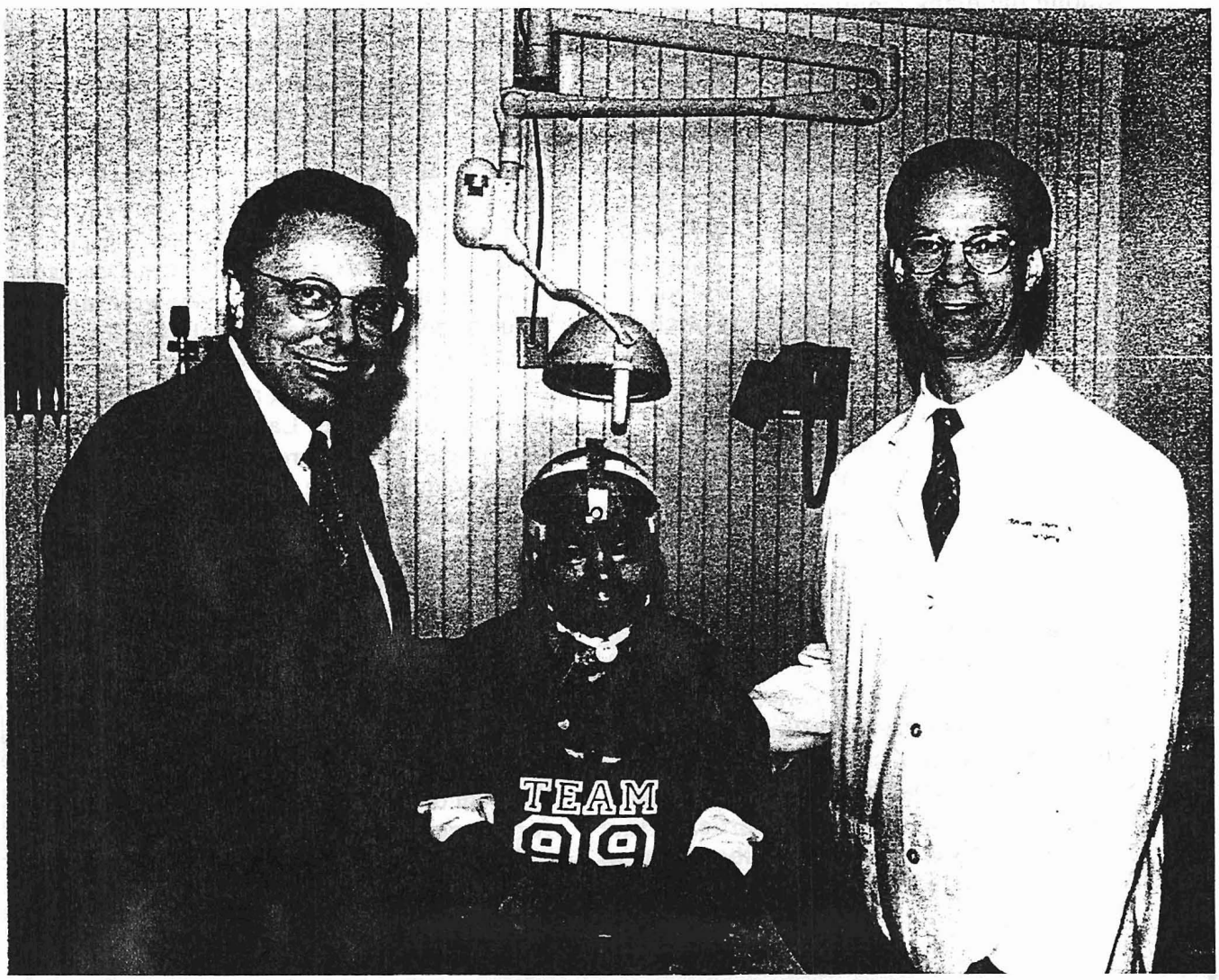
MEDICAL RESEARCH PROGRAMS of the SHRINERS HOSPITALS for CHILDREN

1999



enhanced and more complete understanding of how antibiotics can affect the patient, in addition to the bacteria, might ultimately allow the practitioner to make a more informed decision concerning the most appropriate selection of seemingly equivalent antibiotics, especially for serious infections in patients with underlying immune dysfunction.

Wound Healing/Coverage

Research is ongoing to find ways to reduce the requirement for donor skin autografts, a more rapid closure of massive burn wounds and the improvement of functional and cosmetic outcomes after burns. By culturing skin cells and their combination with implantable biopolymers into grafts that can form skin, the need for donor skin, the number of surgical procedures and the recovery time from major burn injury can be reduced. Cultured grafts when applied as sheets can also improve cosmetic outcomes. Engraftment continues to be consistently achieved with the use of the cultured skin substitute for our patients with more than 50% total body surface area burn. Dr. Steven T. Boyce's research is on the forefront in this area of composite skin grafting.

Cultured Skin Substitutes for Burns

Steven T. Boyce, Ph.D.
Director, Department of Tissue Engineering
Senior Scientist, Research Department
Cincinnati SHC

Among the many requirements for recovery from massive burn injuries is permanent replacement of burned skin to restore the protective barrier against infection and fluid loss. Cultured skin substitutes provide alternatives for rapid closure of burn wounds. However, the clinical benefits from cultured skin depend on performance that is similar to conventional skin grafts. The Skin Substitutes Laboratory at the Cincinnati SHC continues to study factors that contribute to improvement of clinical performance with cultured skin for rapid closure of severe burn injuries.

Preclinical studies identify and regulate factors that make the structure and function of cultured skin substitutes as close as possible to healthy skin. These factors include skin barrier, the organization of cells in the graft, the attachment of cells to the wound, skin color, and stimulation of blood flow in the skin. These factors are regulated in the laboratory by nutrient media, biopolymer substrates, and physical components of the incubation environment. Careful regulation of conditions in which skin substitutes are prepared allows regeneration of critical properties, such as skin barrier, before surgical application of skin substitutes to wounds. Although biochemical and molecular analysis of skin substitutes is fundamental to understand their anatomy and physiology, these techniques are not practical for routine assessment of structure and function.

Assessment of structure and function is essential to evaluate clinical performance of cultured skin substitutes for wound closure. Despite the importance of this issue, uniform standards for assessment of outcome after skin grafting continue to depend on the clinical examination of the caregiver. To reduce subjective factors in assessment of outcome, an important focus of the Skin Substitutes Laboratory is the use of instruments to measure the parameters of outcome on quantitative scales. By adaptation of instruments developed for dermatology, skin properties including hydration, pliability, color, shape and blood flow can be measured on absolute scales. Values for individual properties of outcome may be combined to take the place of a clinical examination. Validation of wound assessment with instruments will allow the establishment of standards that may be used by any clinic nationwide. Currently, the establishment of standards for composition and performance of engineered tissues, including cultured skin, has been undertaken by the American Society for Testing and Materials

with active support from the U. S. Food and Drug Administration. Research at the Cincinnati SHC on assessment of skin properties with instruments is a contribution to this national initiative.

Clinical studies completed to date show that wound closure with cultured skin substitutes results in similar properties of skin barrier and pliability as seen with conventional skin grafts. Preliminary studies also show that skin color is irregular after grafting of wounds with cultured skin. Restoration of normal skin color is also a focus of study in the Skin Substitutes Laboratory. Regulation of skin color has been accomplished in preclinical studies with cultured skin, and it is expected that matching of skin color in clinical treatment of burn wounds can be accomplished in the near future. Importantly, the main objective of the skin substitutes project has been demonstrated. Utilization of donor sites for wound closure with skin substitutes now exceeds conventional skin grafts by more than ten times. Effective wound closure and greater availability of cultured skin reduce requirements for donor skin for permanent closure of massive burns, and decreases the time of recovery. These medical advantages define the benefits of cultured skin substitutes for patients with extensive burn injuries. At the Cincinnati SHC, clinical use of cultured skin substitutes together with the comprehensive care of the burn team has contributed to the recovery of patients with greater than 90% total body surface area burns.

PROFILE

Dorothy M. Supp, Ph.D.
Research Fellow
Cincinnati SHC

Dorothy Supp, Ph.D. was born and raised in Yonkers, New York, just north of New York City. She acquired an early interest in science from her father who was a Pharmacologist at U.S. Vitamin (later Revlon Health Care). Her father would often take her into the lab with him on weekends when she was younger and also bring home slides for her to look at under her microscope. During summer and winter breaks from college, Dr. Supp worked as a toxicology intern at Revlon Health Care. This is where she first experienced the satisfaction involved in seeing a product move from research and testing in the laboratory to clinical use and effectiveness. At that point she knew she was destined for a career in medical research.

Dorothy M. Supp, Ph.D.

Dr. Supp graduated with a Bachelor of Science degree from Cornell University's College of Agriculture and Life Sciences in 1986, where she majored in Biology with a concentration in Genetics and Development. It was at Cornell that she met her husband, Andy, who later played a role in her joining the Scientific Staff at Shriners Hospitals for Children in Cincinnati. The two moved to Cincinnati in 1988 where Dorothy entered the Developmental Biology graduate program at the University of Cincinnati and The Children's Hospital Research Foundation. Andy went to work in the Laboratory of Dr. Steven Boyce at the Cincinnati SHC.

Dr. Supp received her Ph.D. in 1994, and con-