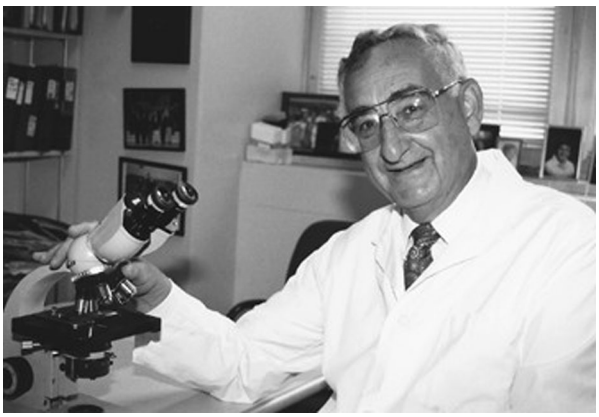
APS European Society for Paediatric Research Society for Pediatric Research

INSIGHTS

Alvin Zipursky (1930–2021): an unsurpassable mentor, counselor, and child health advocate

Victor Blanchette[1], Margaret Manley-Kucey[2], Robert Zipursky[3], Isaac Odame[1], Zulfiqar Bhutta[2], Johan Hitzler[4], Saroj Saigal[5], Vinod K. Bhutani[6] and Max J. Coppes[7,8]✉

Pediatric Research (2022) 92:902–904; https://doi.org/10.1038/s41390-021-01867-y



When Alvin Zipursky assumed the position of North American Editor-in-Chief of *Pediatric Research* in 1999, he was embarking on just one of an amazing array of diverse chapters that made up his extraordinary life. At the time, with characteristic enthusiasm, he wrote: "In the future, as we conclude the millennium and prepare to enter a new century, we shall try to have our Journal serve its readers by publishing high-quality manuscripts that reflect the rapidly expanding and exciting field of research into human development and the diseases and disorders that affect children. We believe that *Pediatric Research* is on a strong foundation with the potential to expand and broaden its mandate for the coming century."[1]

True to his word, over the 5 years that followed, Alvin (or "Zip" to many of his friends) did expand the mandate of *Pediatric Research*, and his experiences in so doing led to more than two additional decades of work that would positively impact the health and well-being of children around the world.

Alvin died on August 10, 2021; September 27 would have been his 91st birthday. His life was filled with service to others. He left a vast legacy that spans clinical care, research, knowledge translation, advocacy, and (international) collaboration. In addition, to those fortunate enough to know him—whether as patients, colleagues, mentees, or friends—he gave great warmth, deep respect, a sense of belonging, and unfaltering kindness.

Born in Winnipeg, Manitoba, Alvin graduated with an MD from the University of Manitoba and went on to do his internship in Winnipeg, followed by postgraduate training in pediatrics at Cincinnati's Children's Hospital and then a hematology fellowship at the University of Utah. He returned to Manitoba in 1957, taking up posts at the University of Manitoba, the Children's Hospital of Winnipeg, and the Canadian Red Cross Society Blood Transfusion Service. While in Winnipeg, Alvin's seminal research contributed to finding an effective approach for preventing Rhesus (Rh) hemolytic disease of the newborn that has saved thousands of lives in the decades that followed. In 1957, Kleihauer and Betke published a new acid-elution assay that bears their names till today to demonstrate the presence of fetal hemoglobin in erythrocytes of blood smears.[2] Alvin, employing the Kleihauer-Betke technique, documented the presence of fetal erythrocytes in the maternal circulation in a *Lancet* publication in 1959.[3] This seminal paper Alvin learned later triggered interest in Rh disease in Professor Cyril Clarke, whose group in the University of Liverpool, UK together with John Gorman's group at Columbia University and Bill Pollock's at Ortho Laboratories pioneered the use of anti-Rh gamma globulin in the prevention of Rh disease. As the Director of the Red Cross Transfusion Centre in Winnipeg, Alvin recruited women, who had a history of Rh disease in their children and had high titers of anti-Rh antibodies, to donate their plasma. In partnership with the Connaught Laboratory of the University of Toronto, this donor plasma pool was developed into vials of anti-Rh gamma globulin (named Rh Immune Globulin), the first such preparation in Canada. The Canadian Rh Immune Globulin was used in the successful Western Canadian clinical trial led by Jack Bowman and Bruce Chown. Alvin summarized the possibility to prevent Rh disease in a publication in 1968.[4]

In 1966, Alvin was recruited to Hamilton, Ontario to not only become the Chief of Pediatric Oncology, Department /Oncology but also the Founding Chairman of Pediatrics at McMaster University Medical School that pioneered problem-based learning

[1]Division of Hematology/Oncology, Department of Pediatrics, University of Toronto, Centre for Global Child Health, The Hospital for Sick Children, Toronto, ON, Canada. [2]Centre for Global Child Health, The Hospital for Sick Children, Toronto, ON, Canada. [3]Department of Psychiatry, University of Toronto, Toronto, ON, Canada. [4]Division of Hematology/Oncology and Developmental and Stem Cell Biology Program, Department of Pediatrics, University of Toronto, Sick Kids Research Institute, The Hospital for Sick Children, Toronto, ON, Canada. [5]Emeritus of Pediatrics, Faculty of Health Sciences, McMaster University, London, ON, Canada. [6]Emeritus of Pediatrics, Stanford School of Medicine, San Francisco, CA, USA. [7]Renown Children's Hospital, 1155 Mill Street, Reno, NV, USA. [8]Department of Pediatrics, University of Nevada, 1664 N Virginia Street, Reno, NV, USA. ✉email: mcoppes@renown.org

Received: 3 November 2021 Accepted: 8 November 2021
Published online: 3 December 2021

in medical education. He brought with him his passion for a patient- and family-centered, multidisciplinary care. During this period, his research focused on aspects of hematology in newborn infants and his scientific contributions in this area established neonatal hematology as a unique entity in its own right.

In 1981 Alvin was recruited to The Hospital for Sick Children (SickKids) in Toronto to become Head of a newly created Division that combined pediatric hematology and pediatric oncology. In this leadership role, he was also appointed Professor of Pediatrics at The University of Toronto. During the next 10 years, Alvin established multidisciplinary programs in stem cell transplantation, inherited bleeding disorders (focus on hemophilias), and hemoglobinopathies (sickle cell disease and the thalassemias). These programs continue to this day and are recognized internationally for their excellence in clinical care, education, research, and advocacy. During this very busy period of his life, Alvin's quest for new knowledge about diseases that affected children never waned. Together with Dr. Hans Hitzler, Alvin uncovered the pathogenesis of leukemia in newborn infants with Down syndrome and the need for an optimized management strategy for such children.[5] With his love for teaching, Alvin promoted the development of an international training program in the discipline of pediatric hematology/oncology at SickKids that today provides specialist training in this discipline to physicians from around the world. Many of these trainees have evolved as leaders in pediatric hematology/oncology programs in Canada and around the world. Throughout his professional career, Alvin led by example. He inspired hundreds of trainees and colleagues to be curious, critical, and compassionate. He also taught his trainees and professional colleagues to never give up when it comes to children, especially the most vulnerable.

When he retired from his clinical duties at SickKids, Alvin was approached by colleagues at the hospital to apply for the position of North American Editor-in-Chief of *Pediatric Research*. In partnership with his wife, Freda, Alvin subsequently drafted and submitted a successful application. Alvin formed wonderful relationships with the outgoing North American Editor-in-Chief, Dr. George Lister, and the two European Chief Editors with whom he worked: Professor Hugo Lagercrantz from the Karolinska Institute in Stockholm and Professor Jean-Christophe Mercier from the Hôpital Robert Debré in Paris. He loved to work collaboratively, to learn from others, and to share his own experiences and knowledge freely. During his tenure, Alvin oversaw an expansion of the scope of published papers in the Journal, moved *Pediatric Research* from a print-only to an electronic format, and worked with the publisher and the World Health Organization to make the journal freely available in low- and middle-income countries (LMICs).

Toward the end of his 5-year tenure as North American Editor-in-Chief, Alvin began noticing that very few of the papers published in *Pediatric Research* had any relevance to LMICs. He convened a special meeting at the 2003 Annual Pediatric Academic Societies' (PAS) meeting in Seattle to discuss this problem. Representatives of the American Pediatric Society, the Society for Pediatric Research, the Chinese Pediatric Society, the Japanese Pediatric Society, the International Pediatric Association, the United States Agency for Internal Development, and many others reached a consensus that this was a problem and requested Alvin to lead efforts that would be targeted to address global child health problems. These efforts rapidly led to the establishment of The Programme for Global Paediatric Research (PGPR), which Alvin led for a decade.

Based at SickKids, PGPR amassed a network of hundreds of researchers around the world and held symposia and workshops bringing global child health issues to major meetings (including the annual PAS meetings) of pediatric researchers. Alvin called this period in his life a "tipping point." He has said that his background in pediatrics and his international work for *Pediatric Research* moved him into global health work.

PGPR helped spawn subspecialist networks devoted to particular global child health issues: the Global Sickle Cell Disease Network, the Consortium for Universal Rh Disease Elimination, and —most recently—the Worldwide Initiative for Rh Disease Eradication. PGPR itself eventually evolved into the Coalition of Centres in Global Child Health and helped form what is now the SickKids Centre for Global Child Health, a global leader in research, capacity building, and knowledge translation programs.

Beyond his work, Alvin's life was devoted to his family. His wife of 52 years, Freda, provided encouragement and support throughout his career and created an environment at home that made it a welcome place for his students, colleagues and new recruits. Her love, warmth, and wisdom created a special milieu in which Alvin's career thrived. Freda died of amyotrophic lateral sclerosis (ALS) in 2005. Alvin worked with the ALS Clinic at Toronto's Sunnybrook Hospital, the largest of its kind in Canada, to establish the Freda Fund to provide support for patients living with ALS and to advance ALS research. Together, Alvin and Freda raised three sons: Larry, Bob, and Ben. Alvin wanted his sons to experience the same passion for their work that he had found. It was a great source of pride to him that each of his sons followed in his footsteps as professors and mentors: Larry in molecular biology, Bob in psychiatry, and Ben in law and philosophy. His inquisitiveness and love of learning were a great gift to all of his children and grandchildren.

At the core of all of Alvin's career achievements was his passion for the health and well-being of children and their families, and his abject refusal to heed unnecessary boundaries, borders, or barriers to progress. He did not just challenge them, he found ways to sweep past them as though they did not exist at all. In 2011, Alvin was awarded the Order of Canada, recognizing his outstanding distinguished service through lifelong contributions in Medicine and making the world a better place by his actions.

Photo credit: MCpl Dany Veillette, Rideau Hall. 2012 Office of the Secretary to the Governor General of Canada. Dr. Alvin Zipursky and David Johnston, Governor General of Canada.

He believed strongly in people and in the good inside everyone and he used his considerable skill as a collaborator and a communicator to build multidisciplinary teams to address challenges in pediatric health at local, national, and international levels. This was likely because he was such a good man himself, quick to laugh, to draw people together, and to bring out the best in everyone he met. His superb sense of humor was a disarming strength. A friend remembers commenting to Alvin on his 85th birthday that his birthday cake was crowded with too many

candles. Zip immediately replied with his trademark smile: "too small a cake!" He was a giant in the field of pediatric hematology/oncology and a shining example of a clinician-scientist. He exemplified the concept "from bench to bedside and back again" and he was a fervent believer that clinical observations could trigger important questions regarding diseases in children and could lead, through carefully conducted research, to solutions that would benefit children with diseases greatly. He is missed a great deal, but his was a life very well lived, with a legacy that will endure and a torch that will be carried on.

REFERENCES

1. Zipursky, A. & Lagercrantz, H. Pediatric Research at the threshold of the 21st century. *Pediatr. Res.* **45**, 1 (1999).
2. Kleihauer, E., Braun, H. & Betke, K. Demonstration of fetal hemoglobin in erythrocytes of a blood smear. *Klin. Wochenschr.* **35**, 637–638 (1957).
3. Zipursky, A., Hull, A., White, F. D. & Israels, L. G. Foetal erythrocytes in the maternal circulation. *Lancet* **1**, 451–452 (1959).
4. Zipursky, A., Pollock, J., Yeow, R., Israels, L. G. & Chown, B. The pathogenesis and prevention of Rh immunization in pregnancy. *Bibl. Haematol.* **29**, 280–283 (1968).
5. Hitzler, J. K., Cheung, J., Li, Y., Scherer, S. W. & Zipursky, A. GATA1 mutations in transient leukemia and acute megakaryoblastic leukemia of Down syndrome. *Blood* **101**, 4301–4304 (2003).

AUTHOR CONTRIBUTIONS

M.J.C.: Conceptualization/design, writing—review or editing of the manuscript; V.B.: conceptualization/design, investigation, supervision/oversight, data curation, writing—drafting the initial manuscript, writing—review or editing of the manuscript; M.M-K.: conceptualization/design, data curation, formal analysis, and writing—drafting the initial manuscript; R.Z.: data curation, resources, and writing—drafting the initial manuscript; I.O.: data curation, resources, and writing—drafting the initial manuscript; Z.B.: data curation, resources, and writing—review or editing of the manuscript; J.H.: data curation, resources, and writing—drafting the initial manuscript; S.S.: data curation, supervision/oversight, and writing—review or editing of the manuscript; and V.B.: data curation, supervision/oversight, and writing—review or editing of the manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

Correspondence and requests for materials should be addressed to Max J. Coppes.

Reprints and permission information is available at http://www.nature.com/reprints

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.