INTERNATIONAL EXPERT PANEL

LUCY LETBY CASE

SUMMARY REPORT | FEBRUARY 3, 2025

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INTRODUCTION

In August 2023, Lucy Letby was convicted of the murder of seven babies and attempted murder of seven other babies at the Countess of Chester Hospital Neonatal Unit. In April 2024, she appealed her conviction but her appeal was rejected. Dr Shoo Lee testified at her appeal and was concerned that there were problems with the medical evidence used in her trial and appeal. As Lucy had exhausted all avenues of appeal, Dr Lee proposed to Lucy's solicitors that he would convene an International Expert Panel to examine all the medical evidence in detail, and to produce an impartial, evidence-based report about the causes of death or injury of all the cases involved in the trial. The report would be released regardless of whether the findings were favorable or unfavorable to Lucy. Lucy and her solicitors agreed.

INTERNATIONAL EXPERT PANEL

The International Expert Panel is an independent panel of some the most experienced and distinguished neonatologists and pediatric specialists in the world.

ACKNOWLEDGEMENT OF FAMILIES

Members of the International Expert Panel would like to acknowledge the families of affected infants and to share our sympathies and condolences. We understand their stress and anguish, and our work is not meant to cause more distress. Rather, it is to meant to give comfort and assurance in knowing the truth about what really happened. We know that the families want to know the truth, and that is why the panel is doing this work. To tell the truth.

OBJECTIVE

The objective of the International Expert Panel is to provide an impartial, evidence-based report about the causes of death or injury among patients in the Lucy Letby case, based on the medical evidence. There would be no determination about innocence or guilt of the defendant.

INSTRUCTIONS

Dr Shoo Lee has been instructed to convene an International Expert Panel to examine the medical evidence. The panel is independent and worked under the agreement with Lucy and her solicitors that all findings will be released even if they did not favor the defendant. The

defendant and her lawyers provided the panel with access to medical records and witness statements used in the trial. The panel self-determined how to examine the medical evidence, interpret the findings and produce a report.

As Chair, Dr Shoo Lee issued the following instructions to the International Expert Panel:

1. Review the medical records and determine the cause of death or injury
2. Review and comment on the expert witness statements and opinions
3. Issue an independent report about the causes of death or injury

METHODS

Each case was examined by 2 experts independently, who then submitted their reports to the Chair. If their findings were in agreement, their conclusions were accepted as final. If their findings differed, a third member of the panel was asked to review the case and a consensus opinion was developed. Summaries of each case were then developed by the Chair, approved by the panelists who examined the case, and shared with the entire panel. Strict confidentiality was observed.

MEMBERSHIP

Dr Shoo Lee invited members of the panel to participate on a voluntary basis and to work pro bono. Members of the panel did not receive any benefits, in cash or in-kind, for their work.

The panel comprises fourteen very experienced and well-known experts from highly prestigious institutions in 6 countries around the world, including Canada, United States of America, Japan, Germany, Sweden and the United Kingdom. They include ten neonatologists, one pediatric surgeon, one pediatric infectious disease specialist, one senior neonatal intensive care nurse, and one other pediatric specialist.

With the exception of the Chair and member from the UK, the other members of the panel knew about the existence of the case but otherwise had little knowledge about it.

Members of the panel are:

1. Shoo K. Lee, OC, DHC, PhD, FRCPC, MBBS (Chair)
   Professor Emeritus, University of Toronto, Canada
   Honorary Physician, Mount Sinai Hospital
   President, Canadian Neonatal Foundation

2. Eric Eichenwald, MD, FAAP
   Professor of Pediatrics, Perelman School of Medicine at University of Pennsylvania, USA
   Chief of the Division of Neonatology at Children's Hospital of Philadelphia
   Holder of the Thomas Frederick McNair Scott Endowed Chair.

3. Helmut Hummler, MD
   Senior Medical Director, European Foundation for Care of Newborn Infants, Germany

4. Tetsuya Isayama, MD, MSc, PhD
   Head of Division of Neonatology, National Center for Child Health and Development, Tokyo, Japan
   Japan Director, Asian Neonatal Network

5. Joanne Langley, MD. MSc, FRCPC. FSHEA, FIDSA, FPIDS
   Head of Division of Pediatric Infectious Diseases, Dalhousie University, Canada
   Professor, Departments of Pediatrics and Community Health & Epidemiology, Faculty of Medicine, Dalhousie University
   Holder of the Canadian Institutes of Health Research – GlaxoSmithKline Chair in Pediatric Vaccinology, Dalhousie University
   Active Staff, Pediatric Infectious Diseases, IWK Health Centre

6. Neena Modi, MB ChB; MD; FRCP; FRCPCH; FFPM; FMedSci
   Professor of Neonatal Medicine & Vice-Dean (International), Imperial College London
   Honorary Consultant, Chelsea and Westminster NHS Foundation Trust
   President, European Association of Perinatal Medicine

7. Sandra Moore, RN
   Staff Nurse, NICU, Southlake Regional Health Center, Newmarket, Canada
   Sullivan Medicolegal Experts, Richmond Hill, Ontario

8. Mikael Norman, MD, PhD
   Professor/Senior Physician, Department of Clinical Science, Intervention and Technology, Karolinska Institutet, Sweden
   Chairman, Swedish Neonatal Quality Register
   Founder, International Society of Evidence-Based Neonatology (EBNEO)

9. Bruno Piedboeuf, MD, FRCPC
   Professuer Titulaire en Pediatrie, Universitaire Laval, Canada
   Coordonnateur des Services Cliniques du RUIS de l'Universite Laval

Directeur des Affaires Universitaires, Ministere de la Sante et des Services Sociaux du Quebec

10. Prakeshkumar Shah, MSc, MBBS, MD, DCH, MRCP, FRCPC
    Professor of Pediatrics, University of Toronto, Canada
    Head, Department of Pediatrics & Maternal-Infant Care Research Center, Mount Sinai Hospital
    Senior Clinician Scientist, Lunenfeld-Tannenbaum Research Institute
    Director, International Network for Evaluation of Outcomes for Neonates (iNEO)
    Director, Canadian Preterm Birth Network
    Scientific Advisor & Past Director, Canadian Neonatal Network

11. Nalini Singhal, MBBS, FRCPC
    Professor Emeritus, University of Calgary, Canada
    Co-Editor of WHO/AAP Helping Babies Survive Programs

12. Erik Skarsgard, MD, MSc, FRCSC, FACS, FAAP
    Professor, Division of Pediatric Surgery, University of British Columbia, Canada
    Director, Canadian Pediatric Surgery Network

13. Ann R. Stark, MD, FAAP
    Professor in Residence of Pediatrics, Harvard Medical School, USA
    Director of Faculty Development, Department of Neonatology, Beth Israel Deaconess Medical Center.

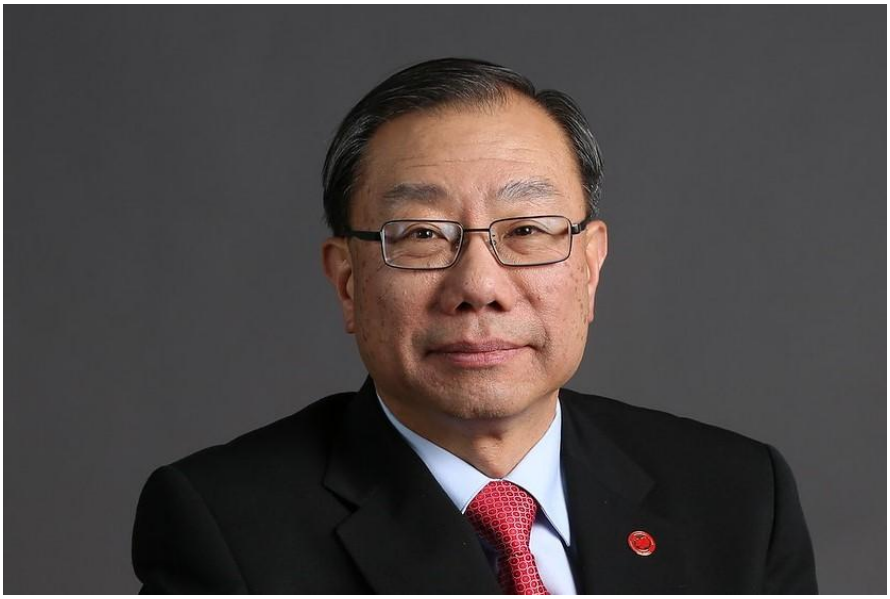
One member of the panel has chosen to remain anonymous for the time being.

The panel also relied on the reports of external experts in engineering, Professor Geoff Chase and Helen Shannon, for information about insulin and c-peptide testing (Annex). These experts were instructed by those representing Lucy Letby.

Biographies of members of the panel are on the following pages.

BIOGRAPHIES

Professor Emeritus Shoo K. Lee, OC, DHC, PhD, FRCPC, MBBS (Chair)



Dr. Shoo Lee is a neonatologist and health economist. He is Professor Emeritus at the University of Toronto, Honorary Physician at Mount Sinai Hospital, and President of the Canadian Neonatal Foundation. He was formerly Pediatrician-in-Chief at Mount Sinai Hospital, Head of the Division of Neonatology at the University of Toronto and the Hospital for Sick Children, Head of the Department of Newborn and Developmental Pediatrics at Sunnybrook Hospital, Canada Research Chair (Tier 1) and Scientific Director of the Institute of Human Development, Child and Youth Health at the Canadian Institutes of Health Research.

Dr. Lee received his medical degree from the University of Singapore, completed his paediatric training at the Dr Charles A. Janeway Child Health Centre in Canada and neonatal fellowship training at Boston's Children's Hospital, and is a Fellow of the Royal College of Physicians of Canada. He received his PhD in Health Policy (Economics) from Harvard University, and the Doctorate Honoris Causa in Medicine from Laval University.

His research focuses on health policy and healthcare quality improvement. He founded the Canadian Neonatal Network and transformed Canada's neonatal outcomes into one of the best among OECD countries. He created Family Integrated Care to empower parents as NICU care providers, and established training, research and quality improvement programs in Latin America, Africa and Asia. He has published more than 400 scientific papers in peer reviewed journals and received many awards, including the Aventis Pasteur Research Award and the Distinguished Neonatologist Award from the Canadian Pediatric Society, the Knowledge Translation Award from the Canadian Institutes of Health Research, the Douglas K. Richardson Award for Lifetime Achievement in Perinatal Research from the US Society for Pediatric Research, the Premier Member Award from EPIC Latino, and the Magnolia Gold Award from the Shanghai Government. He is an Officer of the Order of Canada, the highest award given to a Canadian.

Professor Eric Eichenwald, MD, FAAP

Dr. Eichenwald graduated from Harvard Medical School in 1984. He received his training in pediatrics at Boston Children's Hospital, and his training in Neonatal-Perinatal Medicine in the Joint Program in Neonatology, based at Boston Children's, Brigham and Women's and the Beth Israel Hospitals in the United States. He joined the faculty at Harvard Medical School in 1990 and was a staff neonatologist at the Brigham and Women's and Boston Children's Hospitals. He remained on the faculty at Harvard Medical School until 2006, when he was named the Medical Director of the Newborn Center at Texas Children's Hospital and Associate Professor of Pediatrics at Baylor College of Medicine in Houston, Texas. Dr. Eichenwald later joined the faculty of the University of Texas and Children's Memorial Hermann Hospital in 2010, where he was the David R. Park Professor of Pediatric Medicine, Chair of the Department of Pediatrics, Division Director of Neonatal/Perinatal Medicine and Physician-in-Chief at Children's Memorial Herman Hospital.

In 2016, Dr. Eichenwald relocated to the Children's Hospital of Philadelphia, where he is Chief of the Division of Neonatology, and the Thomas Frederick McNair Scott Endowed Chair, Professor of Pediatrics at the Perelman School of Medicine, University of Pennsylvania. He is currently the Alternate PI for the University of Pennsylvania NIH Neonatal Research Network site, and co-PI for an RO1 grant entitled "Intermittent Hypoxia and Caffeine in Infants Born Preterm (iCAF Study)".

Dr. Eichenwald is a member of the Society for Pediatric Research, the American Pediatric Society, and served on the Board of Directors of the American Board of Pediatrics until 2024. He is the current Chair of the American Academy of Pediatrics Committee for Fetus and Newborn and is an Associate Editor of the Archives of Diseases in Children – Fetal and Neonatal Edition.

Professor Helmut Hummler, MD

Dr. Hummler graduated in 1986 from the medical school of the University of Tübingen, Germany. After his residency in Pediatrics in Germany he received his training in Neonatology from 1992 to 1995 by Eduardo Bancalari, M.D. at the Division of Neonatology, Department of Pediatrics, Jackson Memorial Medical Center, University of Miami, Florida, U.S.A. After returning to Germany Dr. Hummler joined the staff of the Division of Neonatology und Pediatric Critical Care, Children's Hospital, University of Ulm, Germany in 1996, where he became Division Chief in 2005. He received his M.B.A. and became Professor of Pediatrics in 2006 and Vice-Chairman of the Dept. of Pediatrics in 2008. He joined the faculty at Sidra Medicine, Doha, Qatar to become Chief of the Division of Neonatology in 2017 and was appointed as Professor of Pediatrics at Weill Cornell Medicine – Qatar in 2018. His team introduced family-centered care the new standard in Sidra Medicine, Doha, Qatar. In 2021 he joined the Dept. of Neonatology, Tübingen University, Germany, and became Chief of the Division of Neonatology and Pediatric Critical Care, Marburg, Germany in 2023. In September 2024 he became the Senior Medical Director of the European foundation for the care of newborn infants (EFCNI). His research interests are related to neonatal lung injury, mechanical ventilation, permissive hypercapnia and to the effects of hypoxemic episodes in VLBWI. He was involved in the development of an automated device for closed-loop FiO2 control. His group was actively participating in many international clinical trials, and he has published more than 150 original articles in peer-reviewed journals and editorials and book chapters. In recent years his activities were focused on research activities related to quality of care as well. In a close collaboration with other stakeholders from obstetrics he led a multidisciplinary team to reduce the rate of IVH and to improve neurodevelopmental outcome substantially. He received the Scientific Award of the German Society of Neonatology and Pediatric Intensive Care and received several awards as a Top Physician in Neonatology in Germany. In 2018 he received the Chief Executive Recognition Award (CEO Sidra Medicine, Doha, Qatar). He has been/is a member of many national and international scientific committees and a frequent peer reviewer for many scientific journals. He is a fellow of the American Academy of Pediatrics and a member of the Society of Pediatric Research and the European Society of Pediatric Research. Dr. Hummler served as an invited speaker at more than 150 national and international meetings and postgraduate courses. Dr. Hummler is a strong advocate of family-centered care, based on "core principles such as dignity and respect for parents/families, information exchange, family participation in care, and cooperation on all levels needed". Furthermore, in his opinion participation in "Quality related clinical research should be a uniform standard in NICUs thriving for excellence".

Dr Tetsuya Isayama, MD, MSc, PhD

Dr. Tetsuya Isayama is a neonatologist and clinical epidemiologist. He is the Head of the Division of Neonatology, National Center for Child Health and Development (NCCHD), Tokyo, Japan. He is an emeritus task force member of the Neonatal Life Support (NLS) of the International Liaison Committee of Resuscitation (ILCOR), the Director of the Asian Neonatal Network Collaboration (AsianNeo), and board member of several neonatology related Japanese academic societies.

He completed neonatology fellowship training at Osaka Women's and Children's Hospital, Osaka, Japan, and then completed the neonatology fellowship of the University of Toronto, Canada. He obtained his PhD in Clinical Epidemiology and Biostatistics at McMaster University, Canada.

He is a recognized expert in the clinical management of extremely preterm infants. His research interests are in neonatal and perinatal epidemiology, international comparative studies on clinical practices and outcomes of preterm infants, neonatal respiratory management & bronchopulmonary dysplasia, circulatory management & patent ductus arteriosus, and systematic reviews & clinical practice guidelines. He has authored more than 100 publications in peer review journals including JAMA, JAMA Pediatrics, Pediatrics, and Circulation.

Joanne M. Langley MD. MSc, FRCPC. FSHEA*, FIDSA*, FPIDS*

Dr. Langley is a pediatric infectious disease physician and vaccine researcher at the Canadian Center for Vaccinology and Professor of Pediatrics and Community Health and Epidemiology at Dalhousie University. She is Head of the Division of Pediatric Infectious Diseases, IWK Health. She is an active investigator in the CIHR-funded Canadian Immunization Research Network (CIRN) and is the co-lead of its Clinical Trials Network.

Dr. Langley's research focuses on the epidemiology, prevention and control of respiratory viruses (particularly influenza and respiratory syncytial virus) and other vaccine-preventable infections. Dr. Langley formerly was Medical Director of Infection Prevention and Control services at IWK Health. Her research also focuses on vaccine policy and evidence-based immunization decision making. During the COVID-19 pandemic she served as co-chair of Canada's COVID-19 Task Force, and as a member of the COVID-19 Expert Panel for the Chief Science Advisor of Canada. She is currently co-chair of the Council of Expert Advisors to the Government of Canada's Ministries of Innovation, Science and Economic Development and of Health, for the development of the Biomanufacturing and Life Sciences Strategy. She is a former member of the Canadian Task Force on Preventive Health Care and served as vice and chair of Canada's National Advisory Committee on Immunization.

https://medicine.dal.ca/departments/department-sites/pediatrics/our-people/our-faculty/joanne-langley.html

**Fellow, Society of Hospital Epidemiology of America; Fellow, Infectious Disease Society of America; Fellow, Pediatric Infectious Disease Society*

Neena Modi MB ChB; MD; FRCP; FRCPCH; FFPM; FMedSci

Professor of Neonatal Medicine, Imperial College London

Neena is a distinguished clinician scientist and Fellow of the Academy of Medical Sciences. She qualified from the University of Edinburgh and has worked in tertiary neonatal intensive care for over three decades. She heads a multiprofessional neonatal research group and has authored over 400 original research papers, chapters in textbooks, and other publications. She has held a number of professional leadership roles and is the current president of the European Association of Perinatal Medicine, and a past-president of the British Medical Association, and Royal College of Paediatrics and Child Health.

In 2022 she received the US Critical-Path Institute, Pioneer Award for *"contributions to health data research"* and Medical Women International Association award "*to a woman physician who has made outstanding contributions to the cause of women in medicine",* and in 2023, the Joint European Neonatal Societies *"outstanding neonatologist"* award.

Neena is a longstanding advocate for fairness, equity, and evidence-informed decisions. Her involvement on the panel is as an individual, and not representative of any organisation or institution.

Professor Mikael Norman, MD, PhD

Mikael Norman was born 1957 in Stockholm, Sweden. He graduated as M.D. at Karolinska Institutet (KI) in 1982 and finalized his Ph.D. in 1992. In 1995, he was appointed Consultant and in 1998, he became associate professor in pediatrics. In 2001-2004 Mikael Norman worked as senior researcher at the Swedish Research Council. He received a chair as professor in pediatrics & neonatal medicine at KI in 2008. Between 1995 and 2015, he worked - besides being a clinician and researcher - in different administrative positions (head of department) at Karolinska university hospital. Mikael Norman has supervised 26 PhD-students and lists over 270 scientific papers with more than 18,000 citations. He is the editor of 3 Swedish textbooks in pediatrics and neonatology. At present, he works as professor at KI and director for the Swedish Neonatal Quality Register.

Research interests:
- Cardiovascular system in newborn infants and children, structure and function in health and disease
- Developmental origins of health and disease
- Preterm birth: risk factors, interventions and short and long-term outcome
- Perinatal epidemiology
- Patient safety and quality of care

Academic awards:
Swedish Society of Medicine: Regnell´s prize 2010 and 2014 for best scientific manuscripts (all categories), and Hugo Lagercrantz Award 2024 for distinguished international research.

Professor Bruno Piedboeuf, MD, FRCPC

Bruno Piedboeuf, MD, has done his medical school, his pediatric residency and neonatology fellowship at the University of Montreal. After completing an additional three years in Molecular Biology at the University of Rochester, he has joined, in 1993, the Pediatric Department at Université Laval and the CHU de Québec as a clinician researcher where he practiced neonatology for 30 years. From 2003 to 2012, he was the Chair of the Pediatric Department at Université Laval and the pediatric chief at the CHU de Québec, and from 2012 to 2017, he was the executive vice-dean of the Faculty of medicine of Université Laval. Since 2009, he is the president of the Table sectorielle mère enfant of the province of Quebec. In 2018, he was appointed Director of the University affairs for the Quebec Ministère de la Santé et des Services sociaux. His direction his responsible for the planification of the medical resources for the province.

He has maintained research activities over the years, and he is currently director of the Reproductive, maternal and child health research division of the CHU de Québec-Université Laval Research Centre and because of his involvement in different administrative functions in the educational and health-care system, his interest in using evidence based medicine to improve the organization of the health care system growth and has directed his interests in research. He is the new president of the board of governance of the Canadian Neonatal Network.Network in the shared aims of improving the organization of health care for pregnant women and newborns while supporting a new generation of health care researchers.

Professor Prakeshkumar Shah, MSc, MBBS, MD, DCH, MRCP, FRCPC

Dr Prakesh Shah is the Pediatrician-in-Chief at Mount Sinai Hospital, Toronto and Professor in the Department of Pediatrics and Institute of Health Policy, Management and Evaluation at the University of Toronto, Canada. He is the Director of the Canadian Preterm Birth Network (CPTBN) and an International Network for Evaluation of Outcomes of Neonates (iNeo) whereby he oversees a project of benchmarking outcomes of very preterm neonates in 13 countries with population-level neonatal networks with an overarching aim of improving quality of care across 240 NICUs. His areas of interest include Patient and Disease oriented research in Neonatal-Perinatal Medicine, Health Services and Epidemiological Research in Maternal-Newborn care, Knowledge Synthesis and Quality improvement. He has evaluated and produced policy documents on interventions and programs for preterm birth for provincial and national agencies. He is engaged in policy and advocacy work with his role in executive committees and advisory board membership as local, provincial, national, and international levels. He has led the Canadian Neonatal Network as Associate Director between 2010-12 and then was Director from 2012-2024.

Professor Emeritus Nalini Singhal, MBBS, FRCPC

Dr Singhal trained at the All India Institute of Medical Sciences in Delhi in India and did her residency and fellowship in Canada. Her clinical work has been with sick newborn babies both in level 2 and 3 units.

Administratively she developed and implemented resuscitation by respiratory therapists, served on the ILCOR committee for over 10 years, was Chair of the Canadian Neonatal Resuscitation Program committee and was the Regional Division Head of Neonatology in Calgary overseeing both the Level 2 and 3 units.

Her research interests are Resuscitation of the newborn, delayed cord clamping and implementation of newborn programs in resource limited areas and quality improvement.

Educationally she has helped develop simple training programs for stabilization of the sick newborn and contributed to the Newborn Resuscitation Program.

In Canada, she has been part of the group for EPIQ (Evidence-based Practice for Improving Quality) that has helped decrease newborn mortality and morbidity across the country.

For the past 25 years she has been involved in Global Child Health. Her work has involved contributing to development of 'Helping Babies Breathe,' a program for education in low resource settings, Essential Care for Every Baby and Essential Care of Small Baby.

She works as a volunteer with the World Health Organization in developing and implementing newborn programs.

She was part of the team implementing Maternal Newborn and Child program in Tanzania, and Kangaroo Mother Care in Ethiopia. She was the principal investigator of SIM 4Life (A simulation program for Uganda, Tanzania and Nigeria).

Her focus is on implementation of programs that lead to knowledge translation and quality care.

Professor Erik D. Skarsgard MD, MSc, FRCSC, FACS, FAAP

Dr. Skarsgard is the Surgeon in Chief at BC Children's Hospital and professor of surgery at the University of British Columbia, Vancouver, Canada. He is a graduate of the UBC School of Medicine and received training in pediatric surgery at Toronto's Hospital for Sick Children and fetal surgery at the University of California San Francisco. He served on the pediatric surgical faculty at Lucile Packard Children's Hospital at Stanford from 1994-2001, and since 2001 has been at BC Children's Hospital in Vancouver.

Dr. Skarsgard is past-chair of the Advisory Board for the Institute of Human Development, Child and Youth Health (IHDCYH) at Canadian Institutes of Health Research (CIHR), Past-President of the Canadian Association of Pediatric Surgeons and past Governor of the American Pediatric Surgical Association and Advisory Council member for pediatric surgery for the American College of Surgeons. He is the founding Principal Investigator of the Canadian Pediatric Surgery Network (CAPSNet), which targets best practices for the treatment of surgical birth defects. He has published over 170 peer-reviewed articles, 8 textbook chapters and one textbook, and serves on the Editorial boards for the Journal of Pediatric Surgery and World Journal of Pediatric Surgery.

He has appeared as an invited witness to the Standing Committee on Health in the Canadian House of Commons to address children's surgical wait times on behalf of the Pediatric Surgical Chiefs of Canada.

Professor Ann R. Stark, MD, FAAP

Dr. Ann Stark graduated from Mount Holyoke College in 1967 and from Harvard Medical School in 1971, trained in pediatrics at St Louis Children's Hospital and Children's Hospital of Philadelphia, then returned to Boston to complete her fellowship at the new Joint Program in Neonatology, based at Boston Children's, Brigham and Women's, and Beth Israel Hospital. Upon completion of fellowship in 1977, she joined the Harvard Medical School faculty, and practiced in the NICU at Boston Children's, and became Director of the NICU, as well as Clinical Director of the Joint Program in Neonatology. In 2004, she was recruited by Dr. Ralph Feigin to Texas Children's Hospital and Baylor College of Medicine, where she became Director of the Neonatal-Perinatal Medicine Fellowship Program and Head of the Section of Neonatology. After Dr. Feigin's untimely death, she moved to Vanderbilt in 2011, where she directed the Neonatology Fellowship Program and oversaw the Fellowship Programs in the Department of Pediatrics. In 2018, Dr. Stark returned to Boston to join the Department of Neonatology at Beth Israel Deaconess Medical Center (BIDMC) where she is currently Director of Faculty Development and Professor in Residence in Pediatrics at Harvard Medical School in the Department of Neonatology at BIDMC. Working with colleagues, Dr. Stark developed the American Academy of Pediatrics NICU Verification Program and led the development of Standards of Neonatal Care, published in Pediatrics in 2023. Her research interests have focused primarily on respiratory physiology and care. She has held leadership positions including serving as Chair of the AAP Neonatal Perinatal Section, the AAP Committee on Fetus and Newborn, and Chair of the American Board of Pediatrics Sub-board on Neonatal Perinatal Medicine, of which she was also the medical editor.

Distinguished Professor Geoff Chase, FRSNZ, DistFEngNZ

Professor Geoff Chase received his B.S. from CWRU in 1986, with M.S. and PhD from Stanford University (1991, 1996). He spent 6 years working for General Motors and 5 years in Silicon Valley, including Xerox PARC, ReSound, Hughes Space and Communications, and Infineon Technologies, before joining the University of Canterbury, where he is its inaugural Distinguished Professor.

His research focuses on the intersection of engineering and clinical medicine, primarily in intensive care, metabolic disease, and cardio-pulmonary diseases, based on close clinical collaborations and clinical engineering overlap to achieve best outcomes.

These efforts have led to a range of model-based systems to improve care and outcomes, and reduce costs, which are in clinical trials or standard of care use in both adult and neonatal intensive care units (ICU, NICU). Dr. Chase has published over 1800 journal and conference papers and 20 US and European patents. He founded 3 startup companies, and is a Fellow of the Royal Society of NZ (FRSNZ) and Distinguished Fellow of Engineering NZ (DistFEngNZ) among others.

CASE SUMMARIES

BABY 1 SUMMARY

Baby 1 was a 31+2/7 week, 1.66 kg birth weight, twin 2, male infant, who was delivered by emergency caesarean section for maternal hypertension. Mother had anti-phospholipid syndrome and gestational cholestasis (not charted in medical records). At birth, Baby 1 required resuscitation but stabilized. The next day, at 1600 hours, the intravenous (IV) peripheral line tissued and IV fluids were stopped. An umbilical venous catheter was inserted but replaced for malposition. A long peripheral line was inserted at about 1900 hours. Fluids were reinfused at about 2000 hours. Soon after, he suddenly became pale, poorly perfused, apnoeic and desaturated. He was intubated, resuscitated, and received 7 doses of adrenaline but no blood gases were done during the 30 minutes of resuscitation. His heart rate dropped and small ECG complexes were noted. Skin discoloration, with blotchy patches of brighter pink on a bluey grey background was observed. The infant did not respond and treatment was withdrawn.

CONVICTION

It was alleged that Baby 1 died from injection of air into the intravenous line, causing air embolism resulting in collapse, patchy discolorations of the skin and death.

PANEL OPINION

In Dec 2024, Zhou and Lee (Am J Perinatol 2024 Dec 27. doi: 10.1055/a-2508-2733) published new research showing that patchy skin discoloration has never been reported in infants with venous air embolism, including IV air injection. When air is injected into the veins, air bubbles must first traverse the lungs where they are filtered out by a vast bed of small blood vessels. In infants, there is a hole in the heart (foramen ovale) that normally closes shortly after birth, so it is possible for air bubbles to escape through the hole into the arterial system but Zhou and Lee reported no patchy skin discolorations in infants with IV injection of air. Patchy skin discolorations are caused by dilation and contraction of small blood vessels in the skin in response to hypoxia, which can occur in many conditions.

Mother had anti-phospholipid syndrome, which is a condition in which the immune system mistakenly creates antibodies that attack tissues in the body. These antibodies can trigger blood clots to form in arteries and veins. During pregnancy, antibodies can pass through the placenta to the neonate and lead to thromboembolism, particularly if there is concurrent infection. Post mortem of Baby 1 showed a recent non-occluding thrombus in the liver, which means there was a recent thrombotic event. On the day of collapse, Baby 1 had 2 central catheters that were left without infusion for up to 4 hours, which predispose to thrombosis when there is no infusion. Shortly after infusion was started in the most central line, Baby 1 collapsed. A thrombus from the catheter tip likely migrated to an artery supplying the brain stem, causing sudden collapse and inability to resuscitate the infant. It is also possible that Baby 1 had placental fetal vascular malperfusion, in which the fetal villi in the placenta present small thrombi that can travel to and occlude small blood vessels in major organs like the heart, brain and liver. If a small thrombus lands in the artery supplying a critical structure like the brain stem, it can cause sudden death and they are very hard to find on post mortem. Collapse associated with fetal vascular malperfusion can occur 1-2 days after birth.

CONCLUSIONS

1. Baby 1 died from thrombosis.
2. There was no evidence of air embolism.

BABY 4 SUMMARY

Baby 4 was a 37+1/7 week, 3.13 kg birth weight, female infant, who was delivered by emergency Caesarean section for failed induction of labour after prolonged premature rupture of membranes. The Apgars were 8 at 1 min, 9 at 5 min. At 12 minutes, she became pale and floppy and needed respiratory support with bag and mask. She was admitted to the neonatal unit 3½ hours later; she was cold, blue, dusky, and had respiratory distress, polycythemia and infection (high white cell and neutrophil counts). The first blood gas taken 4 hours after birth showed high CO2 and respiratory acidosis. Continuous positive airway pressure (CPAP) was started nearly 4 hours after birth. She was electively intubated after 3 attempts and ventilated. Chest x'ray showed pneumonia. The following day, she developed fever, deteriorating blood gases, and increasing metabolic acidosis. The next day, she was mottled, and had dark brown and black tracking lesions across the trunk, and two evolving purpuric looking patches on the abdomen. She had prolonged coagulation times, raised CRP, and repeated episodes of apnoea and desaturation, until final collapse and death.

CONVICTION

It was alleged that Baby 4 was a stable infant, who died from injection of air into the intravenous line, causing air embolism resulting in collapse, patchy discolorations of the skin and death.

PANEL OPINION

In Dec 2024, Zhou and Lee (Am J Perinatol 2024 Dec 27. doi: 10.1055/a-2508-2733) published new research showing that patchy skin discolorations have never been reported in infants with venous air embolism, including IV air injection. When air is injected into the veins, air bubbles must first traverse the lungs where they are filtered out by a vast bed of small blood vessels. In infants, there is a hole in the heart (foramen ovale) that normally closes shortly after birth, so it is possible for air bubbles to escape through the hole into the arterial system but Zhou and Lee reported no patchy skin discolorations in infants with IV injection of air. The mother should have been given antenatal antibiotics for prolonged premature rupture of membranes in a preterm infant. NICU admission, blood gas and CPAP were delayed for 3-4 hours, and Chest x'ray was delayed for 6 hours, which subjected the infant to unnecessary acidosis, high CO2 and delay of antibiotic treatment. The infant continued to deteriorate after admission and showed signs of worsening infection, with fever, intolerance of CPAP removal, deteriorating blood gases, increasing metabolic acidosis, raised CRP and repeated episodes of apnoea and desaturation. She developed prolonged coagulation times, which indicate the infection was going out of control and causing early disseminated intravascular coagulation (DIC). DIC causes coagulation in the blood vessels, coagulation defect and bleeding. Coagulation defects do not occur with air embolism. The patchy skin discolorations were caused by DIC causing clotting in the small blood vessels of the skin which compromised blood flow, which together with hypoxia, triggered dilation and contraction of small blood vessels in the skin, resulting in patches of skin discoloration, purpuric patches and tracking lesions.

CONCLUSIONS

1. Baby 4 died of systemic sepsis, pneumonia and disseminated intravascular coagulation.
2. The mother should have received intrapartum antibiotics.
3. There was delay in recognizing respiratory distress after birth and starting antibiotics, and treatment
4. There was no evidence of air embolism.

BABY 6 SUMMARY

Baby 6 was a 29+5/7 week, 1.434 kg birth weight, twin 2, borderline intrauterine growth restriction (IUGR), male infant who was born by emergency Caesarean section for absent end diastolic flow. He had mild respiratory distress syndrome and hyperglycemia requiring insulin treatment. On 5/8/15 at 0130 hours, he developed sepsis and hypoglycemia, and was treated with antibiotics and intravenous (IV) glucose infusion. Over the next 17 hours, his blood glucose remained low (range 0.8 to 2.4) despite repeat boluses of 10% dextrose. At 1000 hours, his long IV line was noticed to have tissued; with extensive swelling and induration of the right groin, thigh and leg. IV fluids were stopped from 1000 to 1200 hours while a new long line was inserted. At 1200 hours, the IV bag was changed. At 1900 hours, the dextrose infusion was increased to 15% and the hypoglycemia resolved.

CONVICTION

It was alleged that Baby 6 was given exogenous insulin through the infusion bag because there was a prolonged period of hypoglycemia, his blood glucose inexplicably rose from 1.3 to 2.4 when his dextrose infusion stopped from 1000 to 1200 hours, his blood sugar rose after his infusion bag was changed at 1900 hours, and he had high insulin but low c-peptide levels which indicates exogenous insulin was used.

PANEL OPINION

The hypoglycemia started with sepsis and was prolonged because the IV infiltrated for several hours. When hypoglycaemia persisted despite 10% dextrose infusion, a higher glucose infusion should have been given earlier. Repeat boluses of 10% dextrose worsen hypoglycemia because they cause surges of blood sugar, which trigger surges of insulin secretion, resulting in a yo-yo pattern of sharp rises and falls in insulin and blood sugar. When the dextrose infusion was stopped from 1000 to 1200 hours, the blood sugar did not rise from 1.3 to 2.4 as alleged, because the blood sugar was 1.4 at 1146 hours. The 2.4 level was measured after 1200 hours, when the IV was restarted. Since infusion bags were prepared in the pharmacy, stored in the unit, and changed at 1200 hours, multiple infusion bags would have to be contaminated if there was insulin poisoning. The blood sugar rose after 1900 hours, not because the infusion bag was changed, but because the dextrose was increased to 15%. Chase and Shannon (see Annex) reported that preterm infants have different insulin and c-peptide normative standards than adults. Exogenous insulin is unlikely to be the cause of hypoglycemia because the C-peptide was not low for preterm infants (20-45 percentile), potassium levels were normal (insulin decreases potassium), glucose levels should be lower if exogenous insulin was used, the Insulin / C-Peptide (I/C) ratio was within the expected range for preterm infants, insulin autoimmune antibodies (IAA) which are common in preterm infants bind to insulin and increase measured insulin levels, and the immunoassay test is unreliable because interference factors like sepsis and antibiotics can give false positive insulin readings.

CONCLUSIONS

1. Baby 6 had prolonged hypoglycemia because of sepsis, prematurity, borderline intrauterine growth restriction, lack of intravenous glucose when the long line infiltrated for a prolonged period of several hours, and poor medical management of hypoglycemia.
2. Baby 6's insulin level and I/C ratio do not prove that exogenous insulin was used, and are within the norm for preterm infants. Preterm infants and especially those with illness and drug treatments like antibiotics have different normative standards compared to healthy adults and older children.

BABY 7 SUMMARY

Baby 7 was a 23+6/7 week, 535 gm birth weight, female infant, who was born in the toilet at Arrowe Park Hospital after premature rupture of membranes with suspected chorioamnionitis. She was resuscitated at birth, and treated for severe membrane hyaline disease, bilateral pulmonary interstitial emphysema, hyperglycaemia, anaemia, and thrombocytopenia. She had patent ductus arteriosus and mild bilateral dilatation of the cerebral ventricles. She was transferred to Countess of Chester Hospital (CoCH) at 34+ weeks on Optiflow and had gastroesophageal reflux. At 38+ weeks, she had sudden projectile vomiting, large watery stools and desaturation, followed by apnoea 2 hours later. The abdomen was described as purple and distended. She was bagged and intubated with #3 endotracheal tube. Blood stained fluid was noted coming up the trachea. She was ventilated, sedated and given antibiotics. Chest x'ray showed patchy consolidation consistent with chronic lung disease. Her CRP and white cell counts were unremarkable. She stabilized and was transferred to Arrowe Park Hospital, where she was ventilated for 6 days and given antibiotics for CRP rising to 218. Blood, urine, cerebrospinal fluid and respiratory cultures were negative. She returned to CoCH and was discharged home.

CONVICTION

It was alleged that Baby 7 was deliberately overfed and had air injected into her stomach through the nasogastric tube, causing the vomiting and clinical deterioration.

PANEL OPINION

Baby 7 had infection on the night she vomited because she clinically deteriorated with desaturation and apnoea, and had CRP rising to 218 over the next days, which are all signs of infection. It is not uncommon for the CRP to climb after onset of clinical signs when there is infection. She had vomiting and large watery stools, which are common in enterovirus infection and would explain why the blood, urine, cerebrospinal fluid, and respiratory cultures were negative for bacteria while the CRP was high at Arrowe Park Hospital. Large watery stools are not consistent with overfeeding. Abdominal distension and discoloration over the abdomen are common when infants are ill with ileus and they usually disappear when the infant recovers. The abdominal x'rays showing gaseous distension of the intestines were all taken after bag and mask ventilation, and are consistent with air introduced by bagging and ileus in a sick infant. The blood stained fluid coming up the trachea are most likely due to trauma during intubation. Chest x'ray post intubation did not show any continuous consolidation suggestive of pneumonia or pulmonary haemorrhage. She received 7 days of antibiotics and recovered after 7 days, which is consistent with enterovirus infection since it is usually a self-limiting disease.

CONCLUSIONS

1. Baby 7 had vomiting and clinical deterioration due to infection, possibly enterovirus
2. There is no evidence to support air injection into the stomach or overfeeding.

BABY 9 SUMMARY

Baby 9 was a 27 week, 970 gm birth weight, female infant, with intrauterine growth restriction (IUGR), who was born after premature rupture of membranes at Liverpool Women's Hospital. She was treated for mild respiratory distress syndrome (RDS) with respiratory support and antibiotics for sepsis beginning on day 1 of life, and with intravenous and enteral feeds by oral tubing. She developed bradycardias, respiratory distress and an elevated white count, leading to her first of 5 transfers to 4 hospitals on day 12 of life. She developed chronic lung disease (CLD), abdominal distension and recurrent episodes of apnoea, desaturation and bradycardia requiring resuscitation and ventilation. She had viscous, gelatinous secretions from her airway and mouth that were associated with frequent blockages of her endotracheal tube (ETT), and "sticky stools". A registrar stated that "It's not unusual for babies on breathing support to get secretions but it was a bit unusual for them to be so stubborn at being removed." Testing for cystic fibrosis was sent. She had an episode of lung collapse. At 2½ months, she had an episode of severe apnoea, bradycardia, desaturation and heart block and deceased.

CONVICTION

It was alleged that air was 'injected' into Baby 9's stomach via a naso-gastric tube, leading to recurrent episodes of abdominal distension, "splinting" of the diaphragm, and respiratory arrest. On 13/10/15, it was alleged that the apnoea alarm was deliberately turned off, resulting in delay in response to a collapse. On 15/10/15, it was alleged that air was injected into her intravenous tubing, causing air embolism and death.

PANEL OPINION

Baby 9 was a very preterm, IUGR infant with respiratory distress syndrome and chronic lung disease. *Stenotrophomonas maltophilia*, was detected in surveillance cultures from her ETT. *S. maltophilia* is a multi-resistant opportunistic pathogen that can colonize the airway in "biofilms" that are resistant to antibiotics and generally impossible to clear in patients with chronic lung disease. The thick secretions can block ETTs and interfere with ventilation in the small airways of these vulnerable infants, which together with other factors like chronic lung disease, lead to recurrent episodes of apnoea, desaturation, bradycardia, respiratory failure, and collapse. *S maltophilia* colonisation would have further compromised her ventilatory capacity. The initial abdominal distension was likely due to sepsis causing ileus or to lactose intolerance, as there was a family history and stools were positive for reducing substances. The repeated abdominal x-rays showing intestinal gaseous distension were all taken after resuscitation, and air was likely introduced by bagging. A nurse explained that the reason the apnoea alarm did not sound was because "The apnoea alarm goes off if there is a 20 second period of no breaths, but because she was gasping and it was less than 20 seconds, it hadn't gone off." There is no evidence that air embolism was involved. Baby 1 was not treated for *S. maltophilia.*

CONCLUSIONS

1. Baby 9 died of respiratory complications caused by respiratory distress syndrome and chronic lung disease, complicated by *S. maltophilia* colonization.
2. The doctors failed to respond to surveillance warnings about *S. maltophilia*, did not recognize the diagnosis, and did not treat her with the appropriate antibiotics. This was a likely preventable death.
3. There is no evidence of air causing splinting of the diaphragm or of air embolism.
4. There is evidence that the apnoea alarm was not turned off.

BABY 11 SUMMARY

Baby 11 was a 25 week, 692 gm female infant who was born by footling breech. At birth, she was dusky, floppy, and had low heart rate (60/minute) and no spontaneous respiration. She was resuscitated with bagging and intubated after 3 attempts with a size 2 endotracheal tube (ETT). Blood stained secretions were noted. She was mechanically ventilated and a large air leak of 94% was noted. Her blood gases showed respiratory and metabolic acidosis. One and half hours later, she desaturated. A consultant bagged her with Neopuff but there was no chest movement. The capnography test was negative for carbon dioxide. He reintubated Baby 11 with a size 2.5 ETT, re-established chest movement, and stabilised the infant. Chest x'ray was consistent with respiratory distress syndrome or pneumonia. There were 2 further episodes of desaturation requiring resuscitation. Baby 11 was transferred to Alder Hey Hospital.

CONVICTION

The consultant alleged that Baby 11's first episode of clinical deterioration was caused by deliberate dislodgment of her endotracheal tube, since bagging failed to move the chest and carbon dioxide was not detected by capnography. He alleged that the incubator alarms were deliberately turned off to prevent prompt rescue response because he did not hear the alarms when he entered the room.

PANEL OPINION

Baby 11 required a size 2.5 ETT. Instead, she was traumatically intubated with a size 2 ETT, with a resulting 94% air leak. As a result, ventilation was ineffective because 94% of the air was leaking out and only 6% was entering the lung. Effective gas exchange could not occur and mechanical ventilation could not generate sufficient pressure to keep the small air spaces in the lung open. This led to gradual collapse of the small air spaces in the lung and deteriorating gas exchange. When the tipping point was reached, the infant decompensated, desaturated and collapsed. Bagging to reopen the collapsed small air spaces in the lung requires relatively high pressures. With a 94% air leak, bagging with the Neopuff, which has a safety feature to limit air pressures, did not generate sufficient pressure to move the chest. Capnography did not work because the device measures build-up of carbon dioxide in the endotracheal tube during expiration, but with 94% air leak, the carbon dioxide could not build-up sufficiently to trigger measurement. There is no evidence to support dislodgement of the endotracheal tube. The consultant stated that he did not hear the alarms, but a nurse (not LL) stated that "When I returned to the unit, I immediately became aware of the alarms sounding from Baby 11's incubator."

CONCLUSIONS

1. There is no evidence to support a dislodged endotracheal tube.
2. The clinical deterioration was caused by use of an undersized endotracheal tube.
3. The initial intubation was traumatic and poorly supervised.
4. The consultant did not understand the basics of resuscitation, air leak, mechanical ventilation, and how equipment that were commonly used in the unit work, e.g. Neopuff and capnograph.
5. There is evidence that the incubator alarms were not turned off.

BABY 15 SUMMARY

Baby 15 was a second triplet born at 33+2/7 weeks gestation, by in-labour Caesarean section at the Countess of Chester Hospital, a District General Hospital. He weighed 2.02kg. He had mild respiratory distress requiring continuous positive airway pressure (CPAP) and oxygen. The triplets were extracted at Caesarean section very quickly, a minute apart. Baby 15's haemoglobin on the day of birth (day 1) was 168g/l. The next day (day 2), he was changed to Optiflow and started on small amounts of feeds. At 36h he was noted to have a rising heart and respiratory rate, temperature instability and mild abdominal distension. He did not pass meconium until 32 hours of age; meconium is usually passed within the first 24 hours. The next morning (day 3), his abdomen was more distended, with visible loops of bowel, and he was uncomfortable after a feed. By afternoon, he vomited undigested milk, and had high blood lactate (5.4), carbon dioxide (7.09), bilirubin (156) and acidosis (pH 7.2). He was given fluids and antibiotics. At 1440h he developed a profound desaturation and low heart rate (80-90/min) and looked mottled. His abdomen was very distended. He was intubated and ventilated with high pressures (28/5). A small purpuric discolouration was transiently seen on his right chest during the resuscitation. At 1551h he desaturated again and was reintubated, receiving cardiac massage, adrenaline (8 doses), bicarbonate (3 doses), and saline infusions. His ventilation pressures were increased to 32/6 in 100% O2. Dopamine was started and needle aspiration of the abdomen was performed. An intraosseous line was inserted because of poor circulation. At 17.43h blood gas showed marked acidosis (pH 7.014; BE -17) and a haemoglobin level that had halved (Hb 86g/l); no heart rate was heard. At 17.47h resuscitation was stopped after consultation with parents. Post mortem showed a ruptured subcapsular haematoma of the liver.

CONVICTION

It was initially alleged that Baby 15 received inflicted blunt trauma to the abdomen, causing purpuric discolouration and a ruptured subcapsular haematoma of the liver; and that air was injected into the nasogastric tube to cause gaseous distension of the intestines. Later, the accusation was changed to deliberate injection of air into his circulation.

PANEL OPINION

Baby 15 collapsed because the subcapsular haematoma ruptured causing acute major haemorrhage into the peritoneal cavity sufficient to cause a near halving of the haemoglobin level. Subcapsular liver haematoma is the result of "traction" or "shear" forces applied to the thin, fragile liver capsule through the hepatic ligaments. In Baby 15, this was highly likely the result of the extremely rapid delivery, which is a well-recognised cause of birth injury. Bleeding into a subcapsular haematoma is characteristically initially slow because it is contained by the pressure of the enveloping liver capsule; in these early stages the clinical signs are insidious and difficult to recognise. High pressure ventilation decreased venous return to the heart and contributed to liver congestion. The slow, deterioration is then characteristically followed by acute collapse when the capsule ruptures, releasing free blood into the peritoneal cavity. The significance of the rising heart rate and falling pH before the terminal collapse were not recognised. The blind abdominal insertion of a needle during resuscitation may have penetrated the right lobe of the liver, causing further injury, noted by the pathologist as parenchymal haematoma and laceration. Blunt direct trauma to the right abdomen or chest is implausible because it is very difficult to generate the kind of forces required to produce the observed injuries in a liver protected by the lower chest wall. The gaseous distension of the intestinal tract was likely due to air swallowing and insufflation during non-invasive respiratory support. The suggestion of injection of air into the circulation is conjecture.

CONCLUSION

Baby 15 died from a subcapsular liver haematoma caused by traumatic delivery, resulting in haemorrhage into the peritoneal cavity, and profound shock. This was not recognised ante-mortem.

SUMMARY OF FINDINGS

COUNTESS OF CHESTER HOSPITAL FINDINGS

To summarize, we found numerous problems in medical care related to the 17 cases, including:

1. Medical histories were incomplete
2. Failure to consider the obstetric history
3. Disregard for surveillance warnings about infectious bacterial colonization
4. Misdiagnosis of diseases
5. Caring for patients that were beyond their designated level of care
6. Unsafe delays in diagnosis and treatment of acutely ill patients
7. Poor skills at resuscitation and intubation
8. Poor supervision of junior doctors in procedures like intubation
9. Poor skills in basic medical procedures like insertion of chest tubes
10. Lack of understanding about respiratory physiology and basics of mechanical ventilation
11. Poor management of common neonatal conditions like hypoglycemia
12. Lack of knowledge about commonly used equipment in the NICU, e.g. Neopuff, capnograph
13. Failure to protect at risk patients (e.g. haemophilia) from trauma during intubation
14. Lack of teamwork and trust between the health professions

GENERAL FINDINGS

Statements given by witnesses point to serious resource and infrastructure deficiencies that impact on general patient care at the Countess of Chester Hospital. Specific concerns expressed in witness statements include:

1. Inadequate numbers of appropriately trained personnel
2. Lack of training for assigned nursing roles
3. Inadequate staffing
4. Work overload
5. Poor plumbing and drainage, resulting in need for intensive cleaning; this was a potential factor in *Stenotrophomonas maltophilia* colonization and infection
6. Poor environmental temperature control in facility
7. Difficulty in finding a doctor when need arose
8. Congestion at medication cabinet and preparation trolley
9. Lack of appropriate facilities for sterile preparation, e.g. IV drugs prepared in corridor
10. Some high risk infants who should have been born and cared for at higher level institutions were born and cared for in Countess of Chester Hospital because of a shortage of beds at higher level facilities where they should have been admitted
11. There were delays in transfer of sick infants to higher level facilities when the need arose

CONCLUSIONS

CONCLUSIONS

1. There was no medical evidence to support malfeasance causing death or injury in any of the 17 cases in the trial
2. Death or injury of affected infants were due to natural causes or errors in medical care
3. There were problems related to the medical care of patients at the Countess of Chester Hospital neonatal unit
4. There were problems related to teamwork and inter-disciplinary collaboration at the Countess of Chester Hospital neonatal unit

ANNEX

Press Release Summary

Analysis of Babies 6 and 12: A full Bioengineering and Clinical Analysis of evidence in the insulin cases

The authors fully empathise with the stress and anxiety the parents of these, and all, infants in these cases are facing. Thus, this analysis does not ascribe innocence or guilt but presents a full clinical and bioengineering analysis of the evidence presented at court based on the full body of knowledge available regarding insulin delivery and action in preterm infants, rather than simplified first order analyses.

The following summary analysing the evidence against Lucy Letby for Babies 6 and 12 ("the insulin cases") focuses on a detailed analysis of the evidence presented, as well as the full medical records made available. Thus, this release presents only the briefest high-level overview of a full ~100 page report with 250+ supporting references from peer-reviewed science publications to support the points below, many of which were published since the trial.

1. Independent data shows exogenous insulin as the cause is very unlikely:

- **C-Peptide levels** were not suppressed and were typical for this cohort.
- **Potassium (K) levels** were not suppressed and typical for this cohort. Insulin reduces potassium levels.
- Extremely high levels of exogenous insulin might be expected to lead to **far lower glucose than observed** based on a wide range of studies where smaller doses led to far lower glucose levels
- The **high glucose infusion rates required with minimal response** continued after hypoglycemia for both babies, where such **unresponsive hypoglycemia is not uncommon**
- The babies showed **no symptoms of severe insulin poisoning**, such as seizures or heart arrythmia.

→ All these points indicate insulin levels and dose suggested by the assays was in error, too high, or not present.

2. The interpretation of data presented in court is inconsistent with exogenous insulin:

- **Neonatal hypoglycemia is not uncommon**, affecting up to 40% or more of some NICU cohorts
- **Failure to respond to dextrose boluses is also not uncommon** in ~50% hypoglycemic infants
- In the exogenous insulin hypothesis, **far more Insulin would have been required than postulated** because it "sticks" to infusion lines and other things. This phenomenon is well-known.
- **Insulin / C-Peptide (I/C) ratios > 0.2 (0.2 is presented as normal) are not uncommon** in preterm infants, as seen in independent datasets and studies.
- **Insulin autoimmune antibodies (IAA) and other are relatively common and bind to insulin increasing measured insulin levels** several times over, leading to false-positive insulin poisoning.

→ All these points indicate insulin levels and dose suggested by the assays were misinterpreted or not given.

3. The immunoassay test is not reliable:

- The immunoassay insulin tests are **not of forensic quality**
- Standards and guidelines state **unexpected insulin results should be checked with gold standard methods**.
- Standards and guidelines state **unexpected insulin results should lead to checking antibody levels**.
- **Several external factors** in either mother and/or baby **could account for apparent elevated insulin levels, due to assay interference** and/or antibody binding, all of which are increasingly well-known.

→ These points indicate the measurements themselves can be unreliable and were not confirmed / checked.

The authors are willing to discuss any points above in detail in conjunction with the lead barrister Mark McDonald, and subject to UK law which may prohibit discussion at certain times.

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Vascular Air Embolism in Neonates: A Literature Review

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Abstract

Neonatal vascular air embolism is a rare but often fatal condition. The literature comprises mostly case reports and a few dated systematic reviews. Our objective was to review all case reports of neonatal vascular air embolism to date and provide up-to-date information about patient characteristics, clinical presentations, outcomes, pathogenesis, diagnosis, prevention, treatment, and prognosis. We searched the literature for case reports of neonatal vascular air embolism, using MEDLINE, CINAHL, and EMBASE, and the keywords "neonates" and "vascular air embolism." Results were summarized. There were 117 cases of neonatal vascular air embolism, with a mean gestational age of 30.4 weeks (range: 23–40), mean birth weight of 1,422 g (range 830–3,844), and median age of occurrence of 2 days (range: 1–540) after birth. The majority were preterm (75.2%), male (62.7%), on assisted respiratory support (90.5%), and had air leak syndrome (52.9%). The most common clinical presentation was sudden acute clinical deterioration, sometimes accompanied by crying, cardiac rhythm abnormalities, skin discoloration, and a decrease in end-tidal carbon dioxide concentration. Incidence of mortality and adverse neurological sequelae among survivors was 73.9 and 16.6%, respectively, overall, but significantly ($p < 0.05$) higher among preterm infants (81.8 and 31.2%, respectively) and lower among surgical infants (23.8 and 0%, respectively). Diagnosis included visualizing air in infusion lines or retinal vessels, a decrease in the end-tidal carbon dioxide levels, and radiographic, doppler ultrasound, transesophageal echocardiography, or computed tomography (CT) imaging. The prognosis for neonatal air embolism is poor, especially for preterm infants requiring mechanical ventilation. Prevention is key and treatment is supportive.

Keywords

- vascular air embolism
- neonates
- preterm infants

Key Points

- Vascular air embolism is a rare but often fatal neonatal condition that is often underrecognized.
- Preterm infants on mechanical ventilation and with air leak syndromes are at particular risk.
- Prognosis is poor, prevention is key, and treatment is supportive.

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Vascular air embolism is a rare but often fatal condition in neonates.[1] It occurs commonly, but not exclusively, in preterm infants who are on mechanical ventilation. The literature about neonatal vascular air embolism comprises mainly case reports and does not lend itself to any meaningful estimation of prevalence. There are few comprehensive systematic reviews about neonatal vascular air embolism, and available ones are dated.[1,2] Its rarity and the lack of awareness among clinicians compound the difficulties associated with prompt diagnosis and effective management. The objective of this systematic review was to examine all case reports of neonatal vascular air embolism to date and provide up-to-date information about the patient characteristics, clinical presentations, outcomes, pathogenesis, diagnosis, prevention, treatment, and prognosis of neonatal vascular air embolism. This will increase clinician awareness and understanding about neonatal vascular air embolism, and facilitate early diagnosis and effective treatment to achieve optimum outcomes.

Materials and Methods

Since Lee and Tanswell[1] conducted a literature search for cases prior to 1989, we conducted a literature search from 1986 to 2024, for case reports of neonatal vascular air embolism published in the English language, using MEDLINE, CINAHL, and EMBASE, and the keywords "neonates," "newborns," "newborn infants," "preterm infants," "air embolism," "venous embolism," and "arterial embolism." The search generated 173 results. We excluded six inaccessible articles and duplicate cases. We reviewed all cases, including cases identified by Lee and Tanswell,[1] and tabulated them according to patient characteristics, clinical presentations, and outcomes. We summarized the results and presented them together with a review of the pathophysiology, diagnosis, prevention, and treatment. For statistical analysis, the chi-square test was used to examine differences in incidence rates, using the Social Science Statistics chi-square calculator.[3] Patients or the public were not involved in the design, conduct, reporting, or dissemination plans of our research. This study does not involve human participants.

Patient Characteristics

We identified 117 cases of neonatal vascular air embolism from 63 single case reports and 16 case series (►**Supplementary Material S1** [available in the online version]).[1,2,4–26] The mean gestational age (GA) was 30.4 weeks (range 23–40), mean birth weight (BW) was 1,422 g (range 250–3,400), and a median age of occurrence was 2 days (range 1–540) after birth (►**Table 1**). The majority were preterm (75.2%, $n = 88$) and male (62.7%, $n = 64/102$), among those with documented GA and sex. Most of the vascular air embolism events occurred in the neonatal intensive care unit (82%, $n = 96$), and the remainder occurred during surgery (17.9%, $n = 21$). At the time of vascular air embolism, 90.5% ($n = 106$) of infants were on assisted respiratory support, including hand bagging (1%), continuous positive airway pressure (4.2%), intermittent mechanical ventilation (73.5%), and high-frequency oscillatory ventilation (3.4%). Reasons for assisted respiratory support included respiratory distress syndrome, meconium aspiration, viral pneumonia, amniotic fluid aspiration, congenital alveolar dysplasia, and surgery. Air leak syndrome was present in 52.9% ($n = 62$); these included pulmonary interstitial emphysema (PIE) in 34.1% ($n = 40$), pneumothorax in 27.3% ($n = 32$), pneumomediastinum in 11.1% ($n = 13$), pneumopericardium in 10.2% ($n = 12$), and pneumoperitoneum in 3.4% ($n = 4$). Preterm infants were more likely to have air leak syndromes compared to term infants (64.7 vs. 24.1%).

Clinical Presentation

The cause of vascular air embolism was attributed to lung injury/assisted respiratory support in 70% ($n = 82$), introduction of intravascular air during a surgical procedure in 17.9% ($n = 21$), accidental intravenous (IV) or catheter injection of air in 8.5% ($n = 10$) infants, necrotizing enterocolitis in 1.7% ($n = 2$), cardiopulmonary resuscitation (CPR) in 1% ($n = 1$), and trauma in 1% ($n = 1$; ►**Table 2**). Infants with lung injury/assisted respiratory support were predominantly preterm, low BW, and male, whereas surgical infants were mostly term and equal in sex distribution.

The most common presentation was acute clinical deterioration, with desaturation, bradycardia, hypotension, collapse, and drowsiness. A cry or gasp of short duration was reported in two infants and was likely a response to hypoxia and air hunger.

Cyanosis, pallor, and mottling were commonly associated with non-specific generalized skin discolorations and reflected hypoperfusion and oxygen deprivation resulting from circulatory collapse. Non-specific localized transient skin discolorations, including blanching, blue-black, red, or vivid patches, and migrating areas of pallor in the extremities, were reported in six infants (7.3%) with lung injury/assisted respiratory support and one infant (5%) with surgery, but not among infants with accidental IV air injection or other causes. Non-specific skin discolorations are likely the result of vasospasm and vasodilation of cutaneous blood vessels as they redistribute blood in response to cutaneous hypoperfusion and hypoxia during circulatory collapse. Air bubbles can also cause transient skin discoloration through blood vessel occlusion or spasm induced by irritation of the gas.[1,2] Petechiae were noted in one infant but they appeared before the onset of vascular air embolism and are likely due to other causes.

There are few pathognomonic cutaneous signs of vascular air embolism in infants. Lee's sign[1,4] (pink red blood vessels superimposed on the cyanosed background) is a specific skin discoloration that has only been reported in infants with vascular air embolism and is attributed to direct oxygenation of erythrocytes adjacent to free air in the vascular system, while the tissues continue to be poorly perfused and oxygenated. Liebermeister's sign[5] (sharply defined area of pallor in the tongue) has been described in decompression sickness but has not been reported in neonates with vascular air

Table 1 Characteristics, associated phenomena, and outcomes of infants with air embolism

	All infants ($n = 117$)		Preterm ($n = 88$)		Term ($n = 29$)	
Characteristics	**Value**	**Range/*N***	**Value**	**Range/*N***	**Value**	**Range/*N***
Gestation (mean weeks; *n*)	30.4 ($n = 94$)	23–40	28.8 ($n = 77$)	23–36	39.5 ($n = 14$)	37–40
Birth weight (mean grams; *n*)	1,422 ($n = 91$)	830–3,400	1,214 ($n = 77$)	250–2,660	2,875 ($n = 11$)	1,400–4,150
Male:female ratio (N = male:female)	1.6:1	$N = 64{:}38$	1.8:1	$N = 49{:}26$	1.2:1	$N = 15{:}12$
Embolism age (median days; *n*)	2 ($n = 107$)	1–540	2 ($n = 77$)	1–260	45 ($n = 27$)	1–540
Surgery (*n*; %)	21	17.9%	7	7.9%	14	48.2%
Associated phenomena	*n*	Percentage (%)	*n*	Percentage (%)	*n*	Percentage (%)
Air leak syndrome	64	54.7	57	64.7	7	24.1
Interstitial emphysema	40	34.1	39	44.3	1	3.4
Pneumothorax	32	27.3	27	31.6	5	17.2
Pneumomediastinum	13	11.1	12	13.6	1	3.4
Pneumopericardium	12	10.2	11	12.5	1	3.4
Pneumoperitoneum	4	3.4	3	3.4	1	3.4
Abnormal EKG	7	5.9	5	5.6	2	6.8
Air withdrawal from central catheter	12	10.2	6	6.8	6	20.6
Outcomes						
Death	85/117	73.9	72/88	81.8	14/29	48.2
Adverse neurological sequelae in survivors	5/30	16.6	5/16	31.2	0/14	0

Abbreviation: EKG, electrocardiogram.
Note: *n* denotes infants with documented gestation, birth weight, sex, and embolism age.

embolism. Air in the retinal vessels was reported in one infant.

Cardiac arrhythmia and electrocardiogram abnormalities, including tachycardia, bradycardia, ST elevation, arrhythmia, ventricular fibrillation, and asystole, were reported in 5.9% ($n = 7$). A millwheel murmur and diminished heart sounds were heard in some cases. Air bubbles were withdrawn from a central catheter in 10.2% ($n = 12$). A decrease in end-tidal carbon dioxide concentration ($EtCO_2$) was noted in 9.4% ($n = 11$), reflecting reduced cardiac output and volume-related hypotension. Inappropriate high arterial oxygen concentration was recorded from an intra-aortic oxygen electrode in one case.

Pathogenesis

Neonatal vascular air embolism can be spontaneous or iatrogenic.[1,2] Spontaneous vascular air embolism is mostly arterial in nature and commonly occurs when air is injected into the pulmonary veins by mechanical ventilation,[9] especially in preterm infants with respiratory distress syndrome. Air leak syndromes, including PIE, pneumothorax, pneumomediastinum, pneumopericardium, pneumoperitoneum, and necrotizing enterocolitis, preceded vascular air embolism in 52% of reported cases. Barotrauma from high intrabronchial pressures during mechanical ventilation can cause microscopic alveolar rupture and fistularization distal to the terminal bronchioles,[2] creating a direct communication between the airway, interstitium, and small vascular channels. Air may enter into the intrapleural space and cause air leak syndromes, or into the pulmonary veins and cause vascular air embolism. Air can also gain access to the systemic venous system via the lymphatic ducts.[10] The amounts of air required to cause fatal embolism could be as little as 3 to 5 mL/kg[11] in infants. Air can often be found in both the arterial and venous system because of retrograde flow into the right heart through an incompetent pulmonary valve, and passive retrograde flow of gas bubbles because of their buoyancy.[1]

Iatrogenic vascular air embolism is usually venous in nature. Air can be introduced into the venous circulation through IV lines because of inadequate flushing, infusion sets running "dry," cracks in the tubing, or the use of infusion pumps without pressure or air-sensing technology.[2,4–12] Lung laceration has been reported in 25 to 30% of chest tube insertions and may favor reversal of the intrabronchial pressure pulmonary venous pressure gradient, resulting in pulmonary vascular air embolism.[1,13] During cesarean

Table 2 Clinical presentation and outcomes of vascular air embolism in infants by causative categories

	Lung injury/assisted respiratory support	Surgery	Accidental IV injection of air	NEC/other
Number (*n*)	82	21	10	4
Characteristics				
Gestation (wk)	29.2 (range 23–40)	36.4 (range 32–40)	31 (range 25–40)	36.6 (range 30–40)
Birth weight (g)	1,325 (range 250–4,150)	2,527 (range 1,000–3,400)	1,140 (range 830–1,760)	2,525 (range 2,350–2,700)
Sex	47M/25F	11M/8F	6M/2F	0M/3F
Presentation				
Desaturation	6	7	1	0
Bradycardia/arrhythmia	9	3	1	0
Hypotension	6	4	0	0
Collapse	4	1	2	1
Cry/Gasp	1	0	1	0
Drowsy	0	0	1	0
Skin discoloration				
Nonspecific generalized	15 (18.2%)	1 (5%)	2 (20%)	0
Cyanosis	11	1	1	0
Pallor	4	0	1	0
Mottling	2	0	1	0
Nonspecific localized	6 (7.3%)	1 (4.7%)	0	0
Blanching	2	0	0	0
Blue-black patches	1	1	0	0
Red patches	1	0	0	0
Livid discoloration	1	0	0	0
Migrating areas of pallor in extremities	1	0	0	0
Specific				
Lee's sign	2	0	0	0
Outcome				
Death	70 (85.3%)	5 (23.8%)	7 (70%)	1 (100%)
Neurological sequelae among survivors ($n = 30$)	5 (41.6%)	0	0	0

Abbreviations: F, female; IV, intravenous; M, male; NEC, necrotizing enterocolitis.

section, air can enter the cut lumen of large veins and sinusoids during incision of the placenta, and cause vascular air embolism.[14] CPR may also cause neonatal vascular air embolism.[15] Halbertsma et al[27] reported an 89% incidence of vascular air embolism in a postmortem study of unsuccessful CPR in newborn infants and postulated that frail pulmonary alveoli may rupture into blood vessels during neonatal CPR. Finally, air can enter the vascular system during ECMO or surgical procedures,[28] including repair of congenital heart disease, ventriculostomy, ventriculoperitoneal shunt, cranial remodeling, foramen magnum decompression, removal of brain tumor, duodenal surgery, ileostomy, fundoplication, liver transplantation, peritoneal dialysis, arthrogram, intraosseous infusion, and abscess irrigation.[6,16–26] Venous air embolism typically results in right-sided cardiac air but in neonates, venous air can access the arterial systemic circulation through the patent foramen ovale, especially in the face of raised pulmonary vascular pressures.[1,2]

Injuries resulting from vascular air embolism are mostly due to the mechanical effects of bubbles occluding flow in the circulatory system, together with the spasm of the vessels induced by irritation of the gas.[1,2] Air bubbles in the heart can cause an air lock that disrupts the circulation of blood. Occlusion of blood vessels supplying major organs can cause organ damage, for example, coronary arteries (myocardial ischemia and infarction, arrhythmia) and cerebral arteries (seizures, stroke, hypoxic–ischemic encephalopathy).[2] Vascular air embolism can also induce acute injury to the microvasculature through the release of oxygen free radicals from activated neutrophils, leading to increased permeability and pulmonary edema, the release of thromboxane A2, pulmonary vasoconstriction, and increased vascular

resistance and lung lymph flow.[28–31] Animal studies show that much of the brain dysfunction that follows vascular air embolism may be due to the effects of air on vascular endothelial cells, causing vasoconstriction and reduction in cerebral blood flow, rather than the effects of bubble entrapment.[32]

Outcomes

The overall mortality was 73.9% ($n = 85$) and the incidence of adverse neurological sequelae (cerebral palsy, severe [grade 3 or higher] intraventricular hemorrhage, hypoxic–ischemic encephalopathy) among survivors was 16.6% ($n = 5/30$). However, the outcomes depend on the maturity, cause, and setting of the vascular air embolism event.

Preterm infants compared to term infants had significantly ($p < 0.05$) higher incidence of mortality (81.8 vs. 48.2%) and adverse neurological sequelae among survivors (31.2 vs. 0%; ►Table 1). This is not surprising as preterm infants are more likely to have respiratory distress syndrome, require assisted respiration, and have air leak syndromes which predispose to spontaneous vascular air embolism. Lee and Tanswell[1] observed a correlation between the timing of vascular air embolism and GA or BW, but no relationship with inflation pressure, suggesting that barotrauma is inflicted earlier in the more immature lung and that the development of vascular air embolism is determined as much by the physical characteristics of the lung being inflated as by the characteristics of the inflation.

In contrast, surgical cases compared to non-surgical cases had significantly ($p < 0.05$) lower incidence of mortality (23.8 vs. 84.3%) and adverse neurological sequelae among survivors (0 vs. 35.7%). This may be because surgical patients were less likely to be preterm, vascular air embolism was more likely to be promptly diagnosed and treated in the intensively monitored and equipped environment of the surgical operating room, and some surgical patients were already on extracorporeal membrane oxygenation or cardiopulmonary bypass.

Venous air embolism is potentially less harmful than arterial air embolism because air bubbles are filtered out in the microvasculature of the lung and do not enter the arterial vasculature to cause organ failure. In infants, however, the small lung sizes can be overwhelmed by as little as 3 to 5 ml of air, and air can enter the arterial vasculature through the patent ductus arteriosus. In this cohort, the mortality rate was 85.3% among infants with arterial air embolism (lung injury/assisted respiratory support) and 70% among infants with venous air embolism (accidental IV air injection), while the incidence of neurological sequelae among survivors was 41.6 and 0%, respectively.

Diagnosis

Diagnosis requires awareness and a high index of suspicion.[1,2] In some cases, columns of air or a frothy mixture of blood and air, were withdrawn with blood from the umbilical arterial catheter. An inappropriate high arterial oxygen concentration recorded using a transcutaneous oxygen monitor, or from intra-aortic oxygen electrodes; and an abrupt decrease in the end-tidal carbon dioxide levels, demonstrated by capnometry, have been reported.[1,6] Air bubbles in retinal blood vessels were observed in one case of an infant undergoing eye surgery.[7] Radiography, doppler ultrasonography, transesophageal echocardiography, or computed tomography (CT) imaging are diagnostic, and free air may be seen in the arterial and venous systems, as well as in the heart, brain, or portal system.[1,2] Imaging should be performed antemortem. Postmortem radiographs need to be interpreted with caution as intravascular air may appear as early as 25 minutes after death.[8]

Prevention and Treatment

Nursing protocols to prevent vascular air embolism should be adopted.[33] These include priming of IV infusion sets, use of pressure or air-sensing technology in IV pumps and 0.2-micron in-line filters in IV infusion lines, employing head-down position and the Valsalva maneuver during insertion and removal of infusion lines, ensuring that an injection cap is attached to each lumen of central venous catheters, securely luer-locking all connections, clamping the catheter when opening the IV system, withdrawing any air within the injection site cap/catheter prior to injecting any fluid, avoiding use of scissors to remove IV line dressings, and clamping proximal to the damage if an IV line becomes disconnected or damaged. Avoiding high airway pressures and barotrauma, and minimizing the need for mechanical ventilation, are helpful strategies.[1,2] Using soft rubber catheters, instead of stiff plastic chest tubes, for drainage of pneumothoraces, may be less traumatic to the lung and reduce the risk of vascular air embolism.[1,13]

Awareness is critical for prompt diagnosis and treatment is largely supportive.[1,2] Prompt CPR, volume expander, and vasopressor support should be given as needed. The source of vascular air embolism should be promptly stopped, for example, clamp an IV line that is infusing air. If an umbilical artery or central catheter is present, air should be aspirated if possible. This may remove air bubbles causing airlock in the heart. The infant should be placed in a Trendelenburg and left decubitus position to reduce the risk of air bubbles embolizing the cerebral and coronary arteries and allow the entrapped air in the heart to be stabilized within the apex of the right ventricle, thereby relieving the obstruction of the pulmonary outflow tract. The infant should be given 100% oxygen to correct hypoxemia and increase the diffusion gradient for nitrogen out of the bubbles, causing them to shrink. Hyperbaric oxygen may be of benefit but there is a lack of clinical trials evidence to support this. Head or total body cooling may provide neuroprotection. Corticosteroids and/or barbiturates may also be considered.

Limitations

As this is a review of a small number of case reports, it is not meaningful for estimating prevalence, there is potential for reporting bias, and generalizability is limited. The review does not include case reports published in other languages than English.

Prognosis

The prognosis for neonatal air embolism is poor, especially for preterm infants requiring mechanical ventilation, who have a mortality rate of 81.8% and adverse neurological sequelae among survivors incidence of 31.2%. Prevention is key and treatment is largely supportive.

Authors' Contributions

Q.Z.: Conceptualization, methodology, investigation, data curation, writing—original draft. S.K.L.: Conceptualization, methodology, supervision, writing—review and editing.

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Conflict of Interest

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References

1 Lee SK, Tanswell AK. Pulmonary vascular air embolism in the newborn. Arch Dis Child 1989;64(4 Spec No):507–510
2 Smith J, Els I. Intracardiac air–the 'hospital killer' identified? Case reports and review of the literature. S Afr Med J 2003;93(12):922–927
3 Social Science Statistics. Chi-Square Test Calculator. November 13, 2018. Accessed January 8, 2025 at: https://www.socscistatistics.com/tests/chisquare2/default2.aspx
4 Kim MJ, Yu HJ, Lee CG, et al. A case of pulmonary vascular air embolism in a very-low-birth-weight infant with massive hydrops. Clin Exp Pediatr 2009;52(12):1392–1395
5 Durant TM, Oppenheimer MJ, Webster MR, et al. Arterial air embolism. Am Heart J 1949;38(04):481–500
6 Keidan I, Givon U, Berkenstadt H, Perel A. Venous air embolus during arthrography in a child: vital signs changes illustrated by the automated data recording system. Paediatr Anaesth 2002;12(04):362–364
7 Bradley LM, McDonald AG, Lantz PE. Fatal systemic (paradoxical) air embolism diagnosed by postmortem funduscopy. J Forensic Sci 2021;66(05):2029–2034
8 Quisling RG, Poznanski AK, Roloff DW, Borer RC. Postmortem gas accumulation in premature infants. Radiology 1974;113(01):155–159
9 Gregory GA, Tooley WH. Gas embolism in hyaline-membrane disease. N Engl J Med 1970;282(20):1141–1142
10 Booth TN, Allen BA, Royal SA. Lymphatic air embolism: a new hypothesis regarding the pathogenesis of neonatal systemic air embolism. Pediatr Radiol 1995;25(Suppl 1):S220–S227
11 Beluffi G, Perotti G. Air embolism in the newborn: rare complication of intensive care therapy in children. Am J Perinatol 2009;26(05):393–397
12 Levy I, Mosseri R, Garty B. Peripheral intravenous infusion–another cause of air embolism. Acta Paediatr 1996;85(03):385–386
13 Moessinger AC, Driscoll JM Jr, Wigger HJ. High incidence of lung perforation by chest tube in neonatal pneumothorax. J Pediatr 1978;92(04):635–637
14 Allen JR, Carrera GM, Weed JC. Neonatal death due to embolism. JAMA 1969;207(04):756–757
15 Qazi AQ, Haider ZA, Najam Y. Fatal systemic air embolism in a neonate after cardiopulmonary resuscitation. APSP J Case Rep 2015;6(01):11
16 Reinhartz O, DeSilva AM, Hanley FL. Management of neonatal bronchovenous fistula after cardiopulmonary bypass. Ann Thorac Surg 2002;73(04):1320–1322
17 Bala R, Pandia MP. Venous air embolism during endoscopic third ventriculostomy. Asian J Neurosurg 2018;13(02):431–432
18 Pandia MP, Chablani DD, Bithal PK, Rath GP. Atypical presentation of air embolism in an infant undergoing ventriculoperitoneal shunt surgery. Paediatr Anaesth 2013;23(02):201–202
19 Felema GG, Bryskin RB, Heger IM, Saswata R. Venous air embolism from Tisseel use during endoscopic cranial vault remodeling for craniosynostosis repair: a case report. Paediatr Anaesth 2013;23(08):754–756
20 Fuzaylov G, Woods B, Driscoll W. Documentation of resuscitation of an infant with pulseless electrical activity because of venous air embolism. Paediatr Anaesth 2008;18(11):1121–1123
21 Lalwani K, Aliason I. Cardiac arrest in the neonate during laparoscopic surgery. Anesth Analg 2009;109(03):760–762
22 Schwartz N, Eisenkraft JB. Probable venous air embolism during epidural placement in an infant. Anesth Analg 1993;76(05):1136–1138
23 Huang D, Yang L, Yu W, Qi B. A 7-month-old girl with a suspected air embolism complication during a living-donor liver transplantation procedure: a case report. Front Pediatr 2023;11:1271925
24 DiChiacchio L, Cappiello CD, Greenspon J. Extracorporeal cardiopulmonary resuscitation in a neonate after air embolism during insufflation for laparoscopic peritoneal dialysis catheter placement. J Surg Case Rep 2018;2018(06):rjy119
25 van Rijn RR, Knoester H, Maes A, van der Wal AC, Kubat B. Cerebral arterial air embolism in a child after intraosseous infusion. Emerg Radiol 2008;15(04):259–262
26 Schwab C, Dilworth K. Gas embolism produced by hydrogen peroxide abscess irrigation in an infant. Anaesth Intensive Care 1999;27(04):418–420
27 Halbertsma FJJ, Mohns T, Bok LA, Niemarkt HJ, Kramer BW. Prevalence of systemic air-embolism after prolonged cardiopulmonary resuscitation in newborns: a pilot study. Resuscitation 2015;93:96–101
28 Flick MR, Perel A, Staub NC. Leukocytes are required for increased lung microvascular permeability after microembolization in sheep. Circ Res 1981;48(03):344–351
29 Fineman JR, Wong J, Mikhailov T, Vanderford PA, Jerome HE, Soifer SJ. Altered endothelial function in lambs with pulmonary hypertension and acute lung injury. Pediatr Pulmonol 1999;27(03):147–156
30 Tanus-Santos JE, Moreno H Jr, Moreno RA, Martins ML, Pereira R, de Nucci G. Inhaled nitric oxide improves hemodynamics during a venous air infusion (VAI) in dogs. Intensive Care Med 1999;25(09):983–989
31 Berner ME, Teague WG Jr, Scheerer RG, Bland RD. Furosemide reduces lung fluid filtration in lambs with lung microvascular injury from air emboli. J Appl Physiol 1989;67(05):1990–1996
32 Helps SC, Parsons DW, Reilly PL, Gorman DF. The effect of gas emboli on rabbit cerebral blood flow. Stroke 1990;21(01):94–99
33 Gorski LA. Reducing the risk of air embolism. J Infus Nurs 2009;32(02):71–72

