

Hong Kong Journal of Paediatrics

香港兒科醫學雜誌 (New Series)

An Official Publication of

Hong Kong College of Paediatricians &

Hong Kong Paediatric Society

c/o Hong Kong College of Paediatricians, Room 801,

Hong Kong Academy of Medicine Jockey Club Building,

99 Wong Chuk Hang Road, Aberdeen, Hong Kong.

Editorial Board

Chief Editor

CHEUNG Yiu Fai (張耀輝)

Associate Editors

HON Kam Lun (韓錦倫)

Ip Patrick (葉柏強)

Honorary Secretary

FUNG Cheuk Wing (馮卓穎)

Members

BUT Wan Man (畢慧文)

CHAN Chi Fung (陳志峰)

CHAO Sih Yin (趙式言)

FUNG Po Gee (馮寶姿)

KWAN Yat Wah (關日華)

KWONG Ling (龔玲)

LAM Hung San (林鴻生)

LEE Mun Yau (李敏尤)

LEE So Lun (李素輪)

LEUNG SY (梁詩彥)

LIU Sze Wai (廖思維)

Lo Fai Man (盧輝文)

LUK Chi Kong (陸志剛)

WONG Hiu Lei (王曉莉)

YEUNG Wai Lan (楊慧蘭)

Honorary Advisors to the Editorial Board

Andrew BUSH, *United Kingdom*

Don M. ROBERTON, *Australia*

David K. STEVENSON, *USA*

GUI Yong-Hao, *China*

Business Manager

Tsoi Nai Shun (蔡迺舜)

Publisher

Hong Kong Journal of Paediatrics is published by Medcom Ltd, Flat E8, 10/F, Ka Ming Court, 688-690 Castle Peak Road, Kowloon, Hong Kong SAR. Tel: (852) 2578 3833, Fax: (852) 2578 3929, Email: mc1@medcom.com.hk

Indexed in EMBASE/Excerpta Medica, Science Citation Index Expanded (SCIE) and Scopus

Website: www.hkjaed.org

ISSN 2309-5393 (online)

ISSN 1013-9923 (print)

Editorial

Small Kids with Big Data

Kids can no smaller than neonates and infants. For the word 'neonate', *neo* is from Greek meaning new, and '*natal*' is from Latin meaning to be born. Nothing can be happier than the celebration of the birth of healthy babies, who mature in no time to become infants. 'Infant' comes in turn from the Latin word '*infans*', which means speechless. These babies, albeit speechless, confer immense joy that nothing can compare with. As William Blake wrote in his poem *Infant Joy*, "I have no name, I am but two days old, what shall I call thee, I happy am, joy is my name, sweet joy befall thee". There are times, however, when giving birth to a child may bring forth moments of unhappiness and even feelings of pain and sorrow. Not surprisingly, in his counterpart poem *Infant Sorrow*, Blake wrote vividly "My mother groan'd, my father wept, into the dangerous world I leapt, helpless, naked, piping loud, like a fiend hid in a cloud, struggling in my father's hands, striving against my swaddling bands, bound and weary I thought best to sulk upon my mother's breast." These counterpart descriptions may well fit into the worries that babies were born into the world of despair in the days of Blake, but at all times, the concerns of the well-being of babies must be in the eyes and minds of their parents.

The original articles included in this issue of the Journal described clinical conditions that concern neonates and infants. Bakal et al reviewed the outcomes of neonates after surgery for esophageal atresia in Turkey and revealed still relatively high morbidity and mortality (>30%) due primarily to sepsis and pneumonia in a developing area.¹ Lee et al from this locality evaluated the benefit of increasing calcium intake in parenteral nutrition for premature infants less than 1200 grams and found that increasing the calcium dose in parenteral nutrition from 1.3 to 2 mmol/kg/day improved bone health of premature infants.² The study by Arda et al once again demonstrated the benefits of exclusive breast feeding in lowering the infection rate in infants and children in the first two years of life.³ Basturk performed a double-blind placebo-controlled randomised study and showed that the use of *Lactobacillus reuteri* DSM 17938 in infants with infantile colic significantly reduced crying episodes and restlessness.⁴ While reading through these articles, two key elements that are conducive to better care and management of medical issues in neonates and infants emerge: 1) the need to understand the rapid postnatal changes in newborn babies, and 2) the importance of making sense out of large datasets to overcome the challenges in clinical research in these smallest kids of all.

As paediatricians, we are aware of the rapid postnatal changes in growth and development. The growth parameters and developmental milestones can perhaps be envisaged as the composite outcomes of underlying complex biological processes. The possibility of incorporating systems medicine to paediatrics and the understanding from a holistic perspective of the body networks in operation, from genome to phenome, from cells to organ, and from molecules to individuals has already been alluded to in one of the previous editorials of the

Journal.⁵ Indeed, this approach has more recently been adopted to unravel the dynamic developmental trajectory of molecular changes over the first week of life based on transcriptomic, proteomic, metabolomic, cytokine/chemokine, and single cell immune phenotyping data.⁶ The generation in this study of big datasets on early life immune ontogeny in small babies based on this novel systems biology approach have provided important observations based on which genetic, epigenetic, environmental, and microbial influences on immune development can be determined. This is one of the early examples and it is anticipated that a future direction of neonatal research that lies in meaningfulness collection of the multi-omics dataset, generation of bioinformatics platform, and translational application of findings based on critical analysis of the big dataset.

As paediatricians, we are also acutely aware of the limitations of evidence generated from clinical research conducted in these smallest kids of all, given the relatively small number of research subjects, the ethical challenges, and the complex interactions among the early determinants of health and diseased conditions. Pooled analysis of data through systematic review and meta-analysis and establishment of registry and consortia have been used to address some the concerns and challenges being faced.⁷ Nonetheless, with the increasing amount of data being collected, a new hurdle is how to make clinical sense out of these data and how to generate novel perspectives from the sea of data. The urge to apply machine learning and artificial intelligence in the medical arena is unprecedented and exploration of their application in the exploitation of big data for the recognition of new disease phenotype has just begun. In the field of cardiovascular medicine, for example, machine learning with unbiased clustering analysis has been applied to identify novel distinct phenotypes, so-called phenomapping, of the heterogeneous clinical syndrome of heart failure with preserved ejection fraction.⁸ Recently, machine-learning of datasets based on systolic and diastolic functional data, mechanics and clinical parameters of children with dilated cardiomyopathy has identified distinct groups that were associated with differing proportions of

death of transplantation.⁹ The novel phenomapping approach based on big datasets has shown promise in shedding new lights on disease mechanisms, prognostication, and therapeutic strategies.

As the saying goes, small things can have big influence. The real-world life journey begins when newborn babies take their first breath. Gathering and phenomapping of big datasets of the early life dynamic developmental, environmental, and multi-omics trajectory would unveil a hitherto unknown much bigger picture of these smallest kids of all.

YF CHEUNG
Chief Editor

References

1. Bakal U, Ersoz F, Sarac M, et al. Post-operative prognosis of the patients with esophageal atresia: the 22-year experience of a reference hospital. *HK J Paediatr (new series)* 2022;27:163-9.
2. Lee RSY, Yue EKT, Lee JCY. Benefits of providing 2 mmol calcium/kg/day in parenteral nutrition for premature infants: a cohort study on biochemical markers of metabolic bone disease of prematurity. *HK J Paediatr (new series)* 2022;27:170-6.
3. Arda DB, Gur E, Erener-Ercan T, Can G. The effect of breastfeeding on the rate of infections in the first 2 years of life. *HK J Paediatr (new series)* 2022;27:177-81.
4. Basturk A. Investigation of the effectiveness of *Lactobacillus reuteri* DSM 17938 in the treatment of infantile colic: a double-blind placebo-controlled randomised study. *HK J Paediatr (new series)* 2022;27:182-7.
5. Cheung YF. Editorial: bringing systems medicine to paediatrics. *HK J Paediatr (new series)* 2021;26:1-2.
6. Lee AH, Shannon CP, Amenogbe N, et al. Dynamic molecular changes during the first week of human life follow a robust developmental trajectory. *Nat Commun* 2019;10:1092.
7. Stingonea JA, Mervisha N, Kovatcha P, McGuinness DL, Gennings C, Teitelbaum SL. Big and disparate data: considerations for pediatric consortia. *Curr Opin Pediatr* 2017;29:231-9.
8. Shah SJ, Katz DH, Selvaraj S, et al. Phenomapping for novel classification of heart failure with preserved ejection fraction. *Circulation* 2015;131:269-79.
9. Garcia-Canadilla P, Sanchez-Martinez S, Marti-Castellote PM, et al. Machine-learning-based exploration to identify remodeling patterns associated with death or heart-transplant in pediatric-dilated cardiomyopathy. *J Heart Lung Transplant* 2022;41:516-26.