

## Asthma in Singapore: Past, Present and Future

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The story of asthma in Singapore over the past 50 years mirrors the history of Singapore as it progressed from a third world to a first world country.<sup>1</sup> In 1965, infectious diseases such as tuberculosis, diphtheria and cholera were the main challenges to public health as a consequence of poor sanitation, overcrowding and malnutrition. Asthma was not a priority. Patients often used traditional remedies ranging from herbs (Chinese, Jamu or Ayurvedic) to animal products to “cure” asthma. In 1971, a very unfortunate incident occurred. A 28-year-old asthmatic died of arsenic poisoning from taking ‘Sin lak’ pills, a Chinese herbal remedy for asthma. Between 1972 to 1973, two astute clinicians, Drs Tay and Seah reported an outbreak of arsenic poisoning when they observed patients with skin hyperkeratosis and areas of hyperpigmentation associated with neurological involvement and skin malignancies, occurring in asthmatics taking ‘Sin Lak’.<sup>2</sup> ‘Sin Lak’ was subsequently banned in Singapore, a measure that undoubtedly saved many lives.

In that era, treatments for asthma were very diverse and included some that are no longer recommended. Private practitioners made home visits and tried to help patients with prescriptions of oral salbutamol, theophylline and steroids. Injections of subcutaneous adrenaline and intravenous aminophylline were commonly used for asthma attacks in hospitals. Inhaled corticosteroids, currently recognised as the most effective treatment for long-term control of asthma, became available in the late 1960s but were not widely accepted as the drug of choice, chiefly due to cost reasons. Asthma-related deaths were common then.

Coordination transformed this landscape. The 1980s and 1990s saw the amalgamation of dispensaries and clinics into polyclinics, which provided mass vaccination, programmes to promote health and standardised availability of drugs. Inhaled corticosteroids became more widely used and asthma mortality and admission rates fell correspondingly.<sup>3</sup> In 2001, the Singapore National Asthma Programme (SNAP) was launched to improve asthma control in the primary care by promoting treatment with inhaled corticosteroids

and asthma education to patients. A significant shift in the drug treatment of asthma away from episodic quick relief medication towards long-term daily preventative treatment with inhaled steroids took place.<sup>4</sup>

By the turn of the century, Singapore had gained first world economic status and its healthcare was rated amongst the best in the world.<sup>5</sup> Today, inhaled preventers are easily accessible. State-of-the-art treatment such as biologics and bronchial thermoplasty are available too, where appropriate.

So, perhaps we can rest on our laurels having defeated asthma? Evidence of a disturbing rise in prevalence, magnified by gaps in awareness, and subgroups of aggressive treatment-refractory disease suggest that victory is not at hand. To elaborate, the first factor is a rising tide of “allergy epidemic” in Singapore. Eighty percent of local university students have allergen sensitisation and 18% reported asthma,<sup>5</sup> making Singapore one of the highest asthma prevalence communities in the world. Non-residents in Singapore develop increasing rates of sensitisation and atopy year on year when they move here,<sup>5</sup> suggesting that the environment in Singapore is contributing to this allergic phenomenon. Second, despite the availability of asthma medications, our asthma mortality rate is 3 times that of other developed nations such as the United States and New Zealand.<sup>6</sup> Sixty-seven percent of patients who had fatal or near-fatal asthma had “untreated asthma”;<sup>7</sup> in other words, they were not receiving controller medications or regular follow-ups for asthma. In another survey of 2467 patients with asthma from 8 Asian countries which included Singapore, 73% of patients experienced 1 or more exacerbations in the past year yet 90% reported good control of asthma.<sup>8</sup> The mismatch between patients’ perception of asthma control and the reality of outcomes (fatality, near fatal experience, exacerbations) illustrate the issues of adherence, health literacy and misinformation. Third, a small but significant proportion of asthma individuals do not respond to high-intensity, guideline-recommended treatment, and continue to have recurrent exacerbations,

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frequent hospitalisations, declining lung function and poor quality of life. These patients with severe asthma make up 5% to 10% of total asthma population but contribute to the majority of the disease-specific healthcare burden and costs. Globally, the economic costs associated with asthma have exceeded that of tuberculosis and HIV/AIDS combined.<sup>9</sup> The cost of asthma includes direct cost of emergency care, inpatient and outpatient services and treatment. Indirect costs include costs resulting from missed work or school (by patients and caregivers), loss of productivity or premature retirement. Developed economies can also expect increase in economic cost of asthma by >50% every 10 years.<sup>10</sup>

What does the future hold for asthma in Singapore? Asthma shows no sign of abating and continues to rise in Singapore aggressively. Much of what we know of asthma is derived from Western cohorts where genetics, environment, exposure and culture differ significantly from Singapore. To address this, it is necessary to marry the tools of the future with disciplined coordination and astute clinical skills.

First, we must have strong clinical research. We must collaborate to gather data and meticulously phenotype our patients.

To reduce mortality, clinicians from several restructured hospitals (Changi General Hospital, National University Hospital, Singapore General Hospital and Tan Tock Seng Hospital) have joined forces in an ongoing audit and analysis of near-fatal and fatal asthma. In parallel, there are efforts to carefully characterise the spectrum of clinical patterns of asthma patients in Singapore, ranging from the fixed airways obstruction phenotype,<sup>11</sup> to the frequent exacerbator phenotype,<sup>12</sup> atopic sensitisation patterns,<sup>13</sup> and adherence behaviours.<sup>14</sup>

Second, we must have coordinated basic science research and strong translational effort to bring useful science into clinical practice. All 3 components have to be fused by cross-discipline collaboration and public-private partnerships. Clinicians, researchers, clinician-scientists, industry and patients need to undertake a concerted effort for the collection of “omics” data (e.g. genomic, proteomic, lipidomic and microbiome) in local patient cohorts. Such efforts can lead to the identification of novel molecular endotypes or pathways of disease, generate candidate biomarkers for diagnosis, monitoring and prognostication, and identify new targets of treatment, disease modification and even cure. Provision of adequate research funding and infrastructure, coupled with the spirit of globalisation and collaboration, researchers with inquisitive mind who uphold the highest level of research ethics are all important components for a successful research programme.

Third, intelligent and coordinated use of Information Technology with Big Data and Health Services Research

to perform predictive analytics for at-risk groups (e.g. children who are likely to develop problematic asthma in adulthood), high-risk groups (e.g. frequently exacerbating severe asthma) and provide information for precision medicine to individuals with special needs (e.g. biologics for severe uncontrolled asthma).

Asthma in Singapore since our independence has evolved from a low-prevalence, low-impact disease to a high-prevalence problem of significant magnitude. We are now faced with the challenges of a rising allergic epidemic, high asthma burden and high mortality but they are surmountable if we are united in our core mission to improve lives. Our pioneers have toiled to make us a world class healthcare system, so it is our turn to carry the torch and leave behind a legacy that our future generations will be proud of.

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