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The antibiotics crisis isn't the fault of science – it's market failure

The WHO has warned of rising drug-resistant infections, and Singapore has just updated its action plan on this. But it cannot fight this alone.

Hsu Li Yang

Dying from a bacterial infection after injuries sustained during an air raid in the Second World War, UK policeman Albert Alexander was the first person to be treated with penicillin.

Desperate doctors, who had already had to remove an eye, treated him with the antibiotic on Feb 12, 1941, and he rapidly recovered. However, the limited supply ran out, and he died – a reminder that antibiotics save lives only when we have them, and when they still work.

It's timely to reflect on that, as – ironically – superbugs that resist antibiotics such as penicillin are in the news.

The Government has reviewed and updated its National Strategic Action Plan (NSAP) on antimicrobial resistance rate (AMR) on Nov 12. AMR refers to the phenomenon wherein microbes evolve to survive the drugs and chemicals used to kill them leading to the rise in drug-resistant infections. The first NSAP was launched in 2017 to reduce the AMR here.

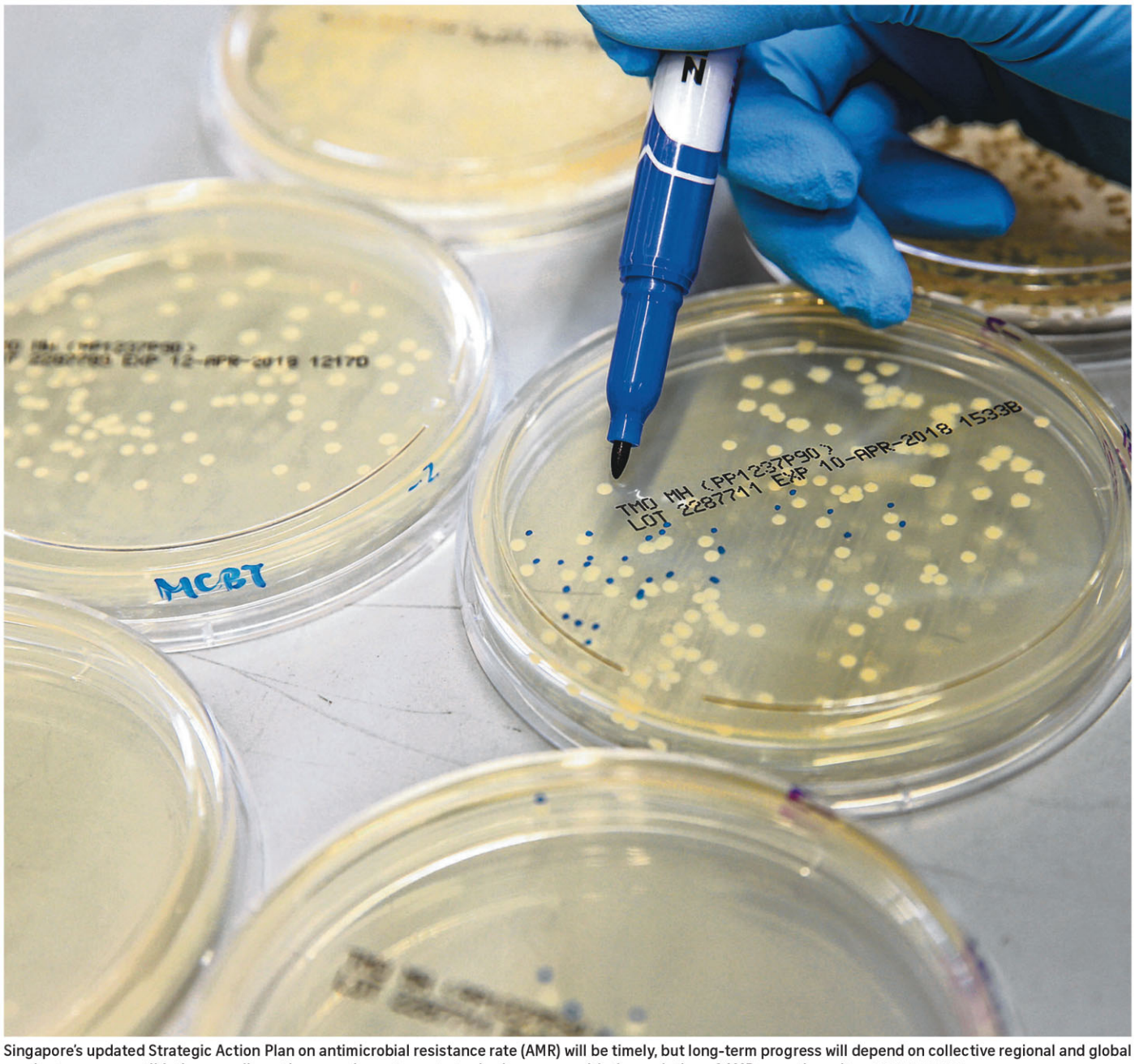
The move comes even though Singapore's drug-resistant bacterial infection rate is lower than globally, according to data submitted to the World Health Organisation (WHO). But a few days before the Government's announcement, the WHO had issued a warning that, globally, the number of drug-resistant infections is soaring. One in six bacterial infections worldwide – out of over 4.5 million such infections reported by 104 countries in 2023 – was caused by drug-resistant bacteria, a WHO study found.

Low and middle-income countries (LMICs), including most Asean and South Asian states, had higher rates of drug-resistant infections compared with wealthier countries such as Australia, Germany and the United States.

This mirrors a study in the Lancet journal that there were 4.71 million deaths associated with drug-resistant infections in 2021, again concentrated in LMICs.

While the numbers are worrying, there is a deeper challenge: antibiotic resistance is as much about access and economics as it is about biology.

How serious is the problem, and to what extent does the global situation impact Singapore?



Singapore's updated Strategic Action Plan on antimicrobial resistance rate (AMR) will be timely, but long-term progress will depend on collective regional and global resolve to ensure antibiotics as well as other complementary strategies keep pace with the evolution of AMR, says the writer. ST FILE PHOTO

THE RISE OF DRUG-RESISTANT BACTERIA

Most antibiotics today are derived from molecules produced by the microbes themselves in competition or collaboration with each other. Take penicillin – it was discovered thanks to mould growing on Alexander Fleming's laboratory dish.

When bacteria become resistant to commonly used antibiotics, the infections they cause become more difficult and costly to treat. The risks of complications and even death increase for major surgery, cancer treatment, transplants and other medical advances we take for granted. Even minor injuries and common infections can turn deadly.

An increasing number of drug-resistant infections has become untreatable. This happens either because the bacteria have become resistant to all antibiotics – which is rare – or more commonly, patients have limited access to the rare few antibiotics that might still work.

Newer antibiotics like ceftazidime/avibactam (Zavicefta) or ceferidocol, for example, are either not licensed or too expensive in many LMICs worldwide.

AMR was recognised early on by Fleming. He warned about the risk of inappropriate antibiotic use during his Nobel Prize lecture in 1945.

For some time, that warning spurred innovation. Drugmakers raced to outsmart evolving microbes – until they found richer rewards elsewhere.

THE PHARMA SWITCH TO BIG-MONEY DRUGS

The private sector was initially able to keep pace in the ensuing "antibiotic-microbial arms race". Indeed, AMR became a driving force for the development of new antibiotics by many multinational pharmaceutical companies in the 1960s and 1970s.

But in the 1980s to early 2000s, most of these companies quit antibiotic research and development (R&D) due to tighter regulations including for licensing trials, coupled with a management focus on maximising shareholder value. They switched to higher-profit, non-infectious drugs such as Ozempic (for diabetes) and Keytruda (cancer). Global sales estimates alone for Keytruda in 2024 were US$29.5 billion (S$38.4 billion).

The current estimated return on investment – or net present value – for new antibiotics stands at negative US$50 million, meaning that companies developing antibiotics will lose money.

A report by the Biotechnology Innovation Organisation in 2022 highlighted that venture investment in companies developing new antibiotics in the US was US$1.6 billion between 2011 and 2020, about 16.5 times less than investments in new cancer drugs over the same period.

The negative market and investor sentiment worsened following the bankruptcies or exits at a loss of a handful of small and medium-sized biotechnology enterprises developing antibiotics.

Ideally, healthcare needs a steady supply of new antibiotics that will keep pace with AMR at a minimum, and that are affordable to people in the LMICs where the problem of drug-resistant infections is worse.

Also, in an ideal world, the use of antibiotics would be restricted in order to slow down the inevitable development of resistance and conserve their longer-term effectiveness.

Unfortunately, this makes little economic sense to investors. The markets may have failed, but policymakers and philanthropists are beginning, belatedly, to fill the gap.

The silver lining is that there is now greater attention and interest than ever on the issue of AMR. Last September, all member states unanimously adopted the political declaration on AMR at the United Nations General Assembly (UNGA) High-Level Meeting in New York.

For the first time, there was a commitment to a hard target of reducing deaths due to drug-resistant infections by 10 per cent by 2030, from the baseline estimates of 2019. This was in addition to other commitments, including reducing the use of antimicrobials in agriculture and increasing investments in AMR surveillance and research.

Governments, non-governmental organisations and philanthropic organisations have also stepped in to increase the future supply of antibiotics. These efforts include funding and technical expertise for early stage antibiotic development, clinical trials and commercialisation of

CONTINUED ON PAGE B2

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Singapore's strengths can contribute to regional and global efforts

FROM B1

future antibiotics.

The three largest philanthropies – Novo Nordisk, Gates Foundation and the Wellcome Trust – entered into a partnership in 2024 to support science and innovation that tackle the most pressing health issues of the day, including AMR.

There have also been attempts to try different reimbursement models for antibiotics, rather than the traditional model for drugs which is purely dependent on volume of sales.

The most well known of these is undoubtedly UK's Netflix-style subscription model which was trialled in 2020, providing pharmaceutical companies with new antibiotics a guaranteed pre-agreed revenue that is delinked from the volume of antibiotic sales.

But for such strategies to be successful, it is important that most, if not all, of the large market economies will have to adopt similar models to influence the pharmaceutical industry.

It is too early to assess the impact of all these different efforts, although one positive sign is that there are now more antibiotic products in the early stage of development compared with over a decade ago.

While most of these experiments are unfolding abroad, Singapore has built its own defences, with results worth noting.

WHAT ABOUT SINGAPORE?

Singapore's lower AMR (or drug-resistance infection rate) did not occur purely by chance, nor just because of higher socioeconomic status. Investments in infection prevention including hospital design, provision of evidence-based high-quality healthcare by trained professionals and AMR R&D have blunted the rise and impact of superbugs here.

The update to the Strategic Action Plan against AMR will be launched later in 2025. Nonetheless, although we are able to mitigate against the worst impact of drug-resistant infections, it is clear that AMR – like most other infectious diseases – cannot be successfully tackled by one country alone.

We will always be vulnerable to the importation of drug-resistant bacteria from other countries and are too small a market to influence multinational pharmaceutical companies to invest more in new antibiotics.

Singapore's scientific, regulatory and implementation strengths can, however, contribute to regional and international efforts against AMR. These include increasing Asean and global AMR surveillance, continuing to invest in R&D – including alternative approaches that slow the spread of AMR or complement traditional antibiotic treatment – and supporting global financing models to make new antibiotics viable.

In 1941, the UK policeman's life was briefly prolonged by a then miracle drug, but he could not be saved because it could not be produced at scale.

Today, the challenge is reversed: We have the scientific and manufacturing capacity to develop and produce new antibiotics at scale, but have not exercised this to the fullest. This is not due to scientific failure, but market failure and the lack of an alternative widely adopted economic strategy.

Singapore's updated Strategic Action Plan will be timely, but long-term progress will depend on collective regional and global resolve to ensure antibiotics as well as other complementary strategies keep pace with the evolution of AMR.

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