time to knockdown or mortality in existing bioassays. Molecular markers of resistance to these new active ingredients should be identified to help predict the potential for cross-resistance, as well as contribute to our understanding of how rapidly resistance will spread and intensify in mosquito populations. These efforts will require more support for entomological capacity in the field and for national malaria control programmes to gather the data and advocate for action based on those data.

Finally, although the GPIRM is in need of updating, its recommendation to use nets with non-pyrethroid active ingredients as soon as they become available is suddenly relevant. They are available now and it is time to use them. However, we must do so judiciously to maintain the efficacy of these new active ingredients and to avoid the crisis we have faced with pyrethroid resistance.

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50 years of oral rehydration therapy: the solution is still simple

50 years ago, the first study showing that an oral solution of glucose and electrolytes was effective for replacing water and electrolyte losses in cholera was published in *The Lancet*.[1] The 4·6 million annual deaths from diarrhoea in children younger than 5 years estimated in 1980[2] has fallen to under 500 000 in 2018,[3] despite a 70% increase in the world's population. Although several factors contributed to this reduction, as of 2007 it was estimated that oral rehydration therapy (ORT) alone had prevented 54 million diarrhoeal deaths.[4] In addition, ORT helped reduce the nutritional impact of diarrhoea. In the past, patients with acute watery diarrhoeal diseases often received only sips of water without food, euphemistically called "resting the stomach", which contributed to iatrogenic marasmus.[5] The resumption of nutritional intake immediately after rehydration, which became standard practice at the Cholera Research Laboratory in Dhaka (now the International Centre for Diarrhoeal Disease Research, Bangladesh—icddr,b) during the 1960s, and a component of the ORT approach, greatly reduced this problem in countries with ORT programmes. A 1978 *Lancet* Editorial noted that the recognition that glucose enhanced sodium and water absorption, which led to the development of ORT, "was potentially the most important medical advance this century".[6] Since the developmental history of ORT is well documented,[7] we focus here on five lessons from 50 years of ORT use (panel).

The first lesson is that high-quality scientific evidence is crucial for the development, acceptance, and use of clinical or preventive innovations. Physiological and pathophysiological studies formed the basis for ORT's development. The solution formula, however, had to be coupled to a validated, effective clinical method based on either intake and output measurements or clinical signs. The latter were later simplified for use by mothers of affected infants.

The second lesson is the importance of doing research in the affected areas. Having investigators in

endemic areas facilitated recognition of the necessity of developing an effective oral solution of glucose and electrolytes for cholera, and an effective method of delivery. Intravenous fluid was the standard treatment for severe dehydration but, along with trained medical practitioners, was often absent or unaffordable in affected areas.

Third, field trials and international support were essential components of this research. It was crucial to broaden hospital-based studies and follow-up with field trials[8] to show the effectiveness of ORT in rural clinics and households, where most treatment began. ORT use by all age groups, for all causes of acute watery diarrhoeal diseases, and to correct dehydration and acidosis alone with no intravenous fluids added to its value as a primary treatment.[9–11] Confirmation of the first successful trial in Dhaka, Bangladesh, by an additional clinical trial in Kolkata, India, enhanced the credibility of ORT.[12] Use of ORT under disastrous conditions in cholera-stricken refugee camps in India during the Bangladesh independence war in 1971 gave further evidence to support global application.[13] International support was necessary to overcome scepticism among physicians and to promote use of packets of oral solution of glucose and electrolytes to be added to a litre of water. Studies using a so-called pinch and scoop method for preparing 500 mL of a sugar and salt solution proved effective where packets were unavailable. Mothers could now prepare the solution at home to maintain the child's hydration status from disease onset.[14]

The fourth lesson is the importance of continuing innovation for treatment. Later studies evaluated rice or cereal-based oral solution of glucose and electrolytes, adding glycine to improve absorption in cholera, reducing sodium content, and using zinc to reduce recurrences of diarrhoea. Some changes proved impractical, whereas others have been incorporated into national programmes. However, the bedrock of safe, effective ORT remains the aggressive use of a physiologically sound and effective oral solution of glucose and electrolytes to adequately replace diarrhoeal water and electrolyte losses.

Finally, the success of ORT programmes in many countries validates the urgent need to extend ORT training to countries where its impact remains unrealised. Major cholera outbreaks in Haiti and Yemen have refocused interest on ORT in disaster situations.[15,16]

***Panel:* Key lessons from 50 years of ORT**

- The ORS formula was based on physiological and pathophysiological studies coupled with sound clinical methodology providing the foundation for its effective clinical use.
- Addressing the right questions and conducting research relevant to the problem are enhanced if investigators are embedded in affected communities.
- It is important to continue refining the treatment and its application even during implementation, attracting international organisations' support, and adapting methods for maternal use.
- ORT remains underused in some critically affected countries, and programmes to promote its use should be funded to halt deaths from cholera and other acute watery diarrhoeal diseases. ORT is also underused in high-income countries, and should be promoted to reduce costs and involve family members to improve patient care.
- ORT use for Ebola virus disease and other conditions that cause dehydration and electrolyte disturbances needs further clinical study to optimise such applications.

ORT=oral rehydration therapy. ORS=oral solution of glucose and electrolytes.

In Haiti in 2010 and 2011 thousands of people died, especially early in the outbreak, when neither ORT nor intravenous fluids were widely used.

ORT use in high-income countries is disappointingly low, due possibly to greater remuneration for intravenous therapy than when ORT is used in hospital or home and the added nursing time if mothers don't participate in care. In 2007, at icddr,b, more than 42 000 diarrhoea patients (>40% cholera cases) were treated over 9 weeks, predominantly with rice ORT administered by family members after brief instruction by nurses, with no deaths from diarrhoea (Cash RA, personal communication). ORT implementation with the participation of family members could enhance care, contribute to family health education, and reduce costs. A shortage of intravenous saline has resulted in a renewed US interest in ORT.[17]

Looking to the future, ORT would be expected to be increasingly used to treat conditions besides acute watery diarrhoeal diseases. ORT can prevent and treat dehydration among older people, common especially in summer, and is credited with reducing global deaths from dehydration-induced kidney diseases.[18] ORT is now considered an essential element of treatment for Ebola virus disease,[19] although clinical studies are still needed.

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We led the pivotal initial clinical studies demonstrating that ORT could greatly reduce or eliminate the need for intravenous fluids in patients with cholera or other potentially lethal acute watery diarrhoeal diseases. We declare no other competing interests.

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Initiation of Global Burden of Animal Diseases Programme

A consistent and comparable description of animal diseases, the risk factors associated with them, and the effectiveness of intervention strategies to mitigate these diseases are important for decision making and planning. The economic impact of a pathogen or animal disease is a function of disease frequency, infection intensity, the effect of the disease on mortality and productivity in animals and its effects on human health, and efforts to respond to the disease.[1] All of these factors can vary over time between species and the contexts in which people and animals live, and need to be measured to understand the patterns of impact at local, national, and global levels. Animal health has major impacts on human health directly through zoonotic disease transmission, or indirectly through nutritional availability and environmental management.[2,3]

For human health, the Global Burden of Disease (GBD) study has created a comprehensive dataset of diseases, injuries, and risk factors that is used to measure epidemiological levels and trends worldwide.[4] There is no equivalent dataset for animal diseases. The burden of individual animal diseases, such as foot and mouth disease,[5] and of multiple diseases in geographical regions such the UK are estimated to be high.[6,7] Estimates range from a 20% reduction in the global production of animal-source food[8] to animal production losses of up to 50% in developing countries.[9] However, there is no systematic way to capture and measure losses associated with animal diseases, and data on expenditure for disease mitigation are not analysed in a way that allows comparisons to be made. These data gaps limits animal health policy making to individual disease reviews of impact at best, and anecdotal evidence at worst.[10]

A system is required that regularly collects, validates, analyses, and disseminates information on livestock production and animal health economic effects to achieve evidence-based policy making and impact on the Sustainable Development Goals on health, nutrition, environment, and poverty.

A workshop, led by the University of Liverpool and the N8 Agrifood Resilience Programme, was held to initiate a programme for the Global Burden of