in other types of enantioselective catalytic reaction[2]. The active catalyst recognizes one face of the planar cation, shielding it so that only the opposite face can interact with an approaching nucleophile. The products of this S_N1 reaction are thus obtained predominantly as one enantiomer.

Not only does Wendlandt and co-workers' study transform an S_N1 reaction into a catalytic, enantioconvergent process, but it also constitutes a powerful synthetic route for preparing molecular motifs called quaternary carbon centres[3,4], which are notoriously challenging to make enantioselectively. Quaternary carbon centres have four different carbon-based substituents attached to a central carbon atom, and are commonly found in biologically active, naturally occurring compounds, such as morphine or various steroids. A great deal of structural diversity could be generated by varying each of the four substituents, making quaternary carbon centres valuable starting points for drug discovery. The authors' study is a breakthrough in that it allows readily accessible racemic mixtures (one-to-one mixtures of enantiomers) of starting materials to be quickly processed to make structurally complex molecular scaffolds containing these motifs.

Wendlandt *et al.* exemplify their reaction using substrates that contain structural groups specifically chosen to stabilize the intermediate cation. However, the underlying concept is general, and will certainly be translated to related classes of reaction. The reported products are striking because the carbon atoms attached to the central atom in the quaternary centre represent a diverse range of electron orbitals (*sp*, sp^2 and sp^3). This means that the groups attached to the central atom have markedly different geometries and reactivities. Future work in which the four groups are varied will therefore produce highly versatile libraries of molecules that could be used in a wide range of reactions for synthesis, and allow the exploration of a large amount of 'chemical space' — the vast array of all possible molecules. ■

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EPIDEMIOLOGY

A broader look at paediatric HIV infection

An epidemiological study of adolescents who had acquired HIV around the time of birth highlights how high-income countries benefit from the ability to begin treating all infected children in the first years of life.

PATRICIA M. FLYNN

It is estimated that more than 2.1 million children under 15 years of age are living with HIV infection worldwide (see Statistical Tables at go.nature.com/2qqvksh). Almost all of these children received the retrovirus from their mother, either around the time of birth (the perinatal period) or through breastfeeding. Writing in *PLoS Medicine*, the CIPHER (Collaborative Initiative for Paediatric HIV Education and Research) Global Cohort Collaboration[1] has shed light on the population of children who survive perinatal HIV infection, living into adolescence and beyond. The collaboration's far-reaching epidemiological study emphasizes the importance of early antiretroviral therapy (ART) for improving survival rates and clinical outcomes.

Before the availability of ART, the mortality rate of babies perinatally infected with HIV was 25% by 2 years of age[2]. Today, a much higher percentage of perinatally infected children survive into adolescence, but this population is little studied compared with other cohorts of people with HIV. Furthermore, it has been unclear whether or how perinatally acquired HIV might differentially affect adolescents living in different parts of the world.

The CIPHER investigators combined data from researchers in 12 regions of the world who followed adolescents with perinatal HIV infection. For a total of 38,187 adolescents, the authors report factors such as the age at which ART began, the person's growth record, whether or not they dropped out of their treatment programme, and survival. Individuals were tracked from their first clinic visit and first ART treatment until 15 years of age, and data were collected from the 1980s or 1990s (depending on region) until 2014.

These data allowed the CIPHER researchers to compare adolescents in different countries, regions and country income levels. Their analysis demonstrates that country income level is associated with the stage of life at which ART typically begins. Not surprisingly, the initiation of both care and ART occurred much earlier in the high-income countries included in the study (14 European countries and the United States) than in other areas of the world. Specifically, children first visited a clinic at a median of 1.1 years of age and began ART at a median of 2.5 years in high-income countries, compared with 7.1 years and 8.0 years, respectively, in the low-income countries studied (26 countries in sub-Saharan Africa).

Growth is delayed in children with HIV infection[3], and was markedly different between high- and low-income countries. The authors found that height-for-age scores were higher in high-income countries than in countries at other income levels at the times when the person first visited the clinic and began ART. In all regions, growth levels began to catch up after ART began. But the height-for-age scores achieved by children in high-income countries at the age of 10 and at the time of the last recorded clinic visit were similar to those of children and adolescents who did not have HIV. By contrast, height-for-age scores for

SOURCE: UNICEF

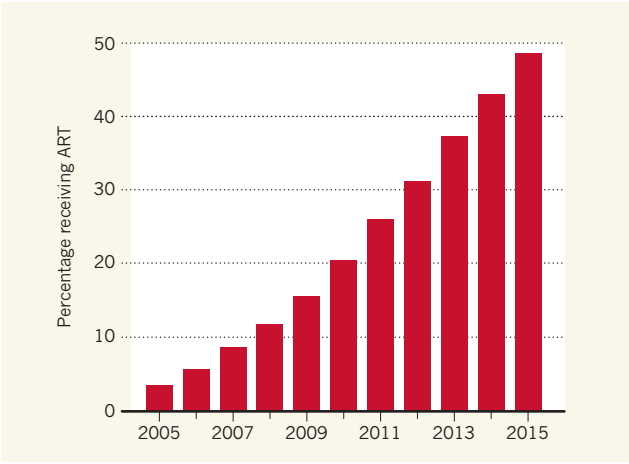

Figure 1 | Prevalence of antiretroviral therapy (ART) for children living with HIV in low- and middle-income countries. Between 2005 and 2015, the percentage of children under 14 years of age who were living with HIV in low- and middle-income countries and who were receiving ART rose from less than 5% to 49%. But the CIPHER Global Cohort Collaboration[1] reports that these children typically began ART later in life than their counterparts in high-income countries.

children living in regions with lower incomes remained below average, probably because ART began significantly later in life. In addition, the cumulative incidence of mortality by age 15 was approximately 3 times greater in low-income countries than in high-income ones (2.6% and 0.9%, respectively).

This data set will no doubt improve our understanding of the population of young people living with HIV infection, in no small part owing to its impressive size and breadth. Previously, the only available data sets included many fewer children and adolescents, and were limited to regional or national cohorts. However, the work also comes with caveats. For instance, the cohorts studied in different parts of the world were established for different reasons — some were national registries, whereas others were groups followed as part of other research. As such, there could be some biases in the study. In addition, there were some differences in the data elements that were collected in different regions. Future studies looking at specific aspects of the data might therefore be limited to fewer adolescents.

The CIPHER investigators' work adds to previous evidence[4,5] for the benefits of early ART. Together, these key studies demonstrate that early ART can save lives and preserve normal growth and development in children with HIV infection. However, the scale-up of ART for infected children has lagged woefully behind that for adults. Data from the United Nations' children's agency Unicef (see go.nature.com/2qqc5gt) show improvements in the availability of ART for children under 15 years of age since 2005, but there is still much to be done. In 2015, fewer than half of infected children were receiving ART (Fig. 1).

There are many barriers to the optimal provision of ART for children in low-income countries[6]. For instance, problems with infrastructure, including a lack of medical personnel and insufficient drug stocks, are common in many areas of the world. Drug development is challenging, because the physiological changes that occur during childhood can affect drug absorption, distribution, metabolism and excretion, and much work is therefore typically required to make drugs safe and effective for children of all ages. ART consists of three drugs that, in adults, can be given in one pill — but this is trickier in children, because the appropriate ratios of the drugs might vary with age. Finally, infant- and child-friendly formulations that do not require refrigeration and are easy to transport are currently lacking.

"Early antiretroviral therapy can save lives and preserve normal growth and development in children with HIV infection."

Because advances in preventing perinatal HIV infection have markedly decreased the numbers of infected children, there is unfortunately no longer a market benefit to developing paediatric ART, making it an unattractive focus for pharmaceutical companies. The current paper's clear demonstration of the benefits of early ART demands that efforts to develop optimal drugs and formulations be increased. In addition, infrastructure must be put in place to make ART consistently available to the more than one million children with HIV infection who do not currently have adequate access to these live-saving drugs. ■

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OCEAN SCIENCE

Shrimp cause a stir

Brine shrimp (*Artemia salina*) are a type of tiny crustacean that lives in swarms and has a daily pattern of vertical migration. In a paper online in *Nature*, Houghton *et al.* report that such group migration generates water eddies with the potential to cause substantial mixing of the water column (I. A. Houghton *et al. Nature* https://doi.org/10.1038/s41586-018-0044-z; 2018).

The ability of individuals or groups to alter their physical environment has long fascinated biologists. Indeed, Charles Darwin's final book, *The Formation of Vegetable Mould through the Action of Worms* (Murray, 1881), reported his analysis of the changes that could occur through the repeated actions of small creatures. This work was a fitting finale for a career spent showing how small changes could, given the time and opportunity, have large effects. As with worms, so, too, with shrimp.

In laboratory-conducted experiments, Houghton and colleagues studied the effect of *A. salina* group migration (pictured: a time-lapse image in which the vertical tracks made by suspended particles provide a way of monitoring water flow). They found that shrimp movement created a water jet that caused mixing of the water column on a scale three orders of magnitude more effective than the mixing that occurs by diffusion. Ocean mixing can be caused by wind or currents. Small marine organisms might also contribute to perceptible ocean-mixing changes, if the phenomenon reported by Houghton and colleagues is relevant for tiny crustaceans called krill, which swarm in vast numbers in climatically sensitive parts of the world, such as the Southern Ocean. **Henry Gee**

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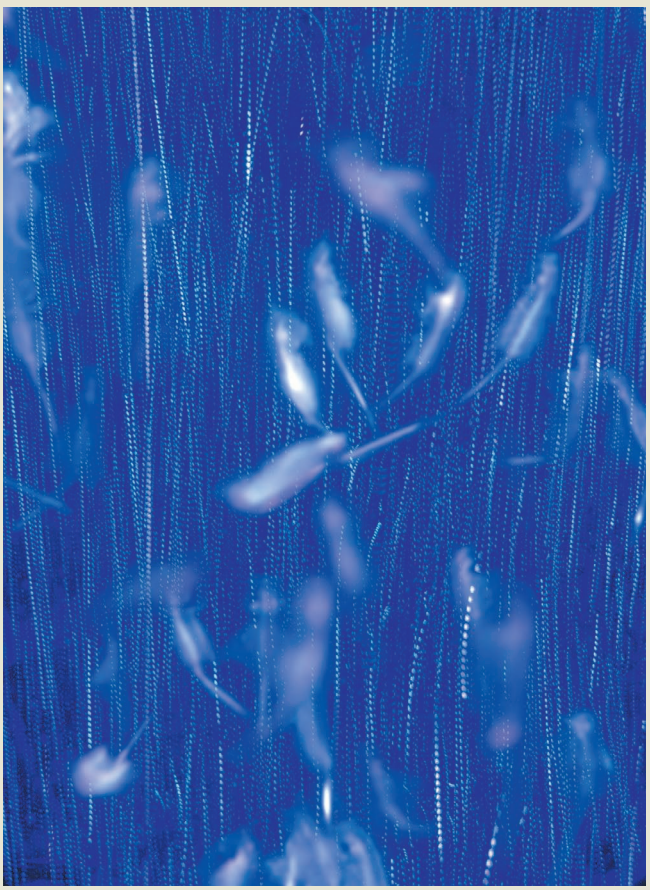

ISABEL HOUGHTON