

## Sustainable Development Goals (SDGs) 2030 – disappointing progress

**S**ustainable Development Goals include reducing premature mortality globally by improving nutrition and social protection, the provision of adequate housing, and safe learning environments for all children. The SDGs may have been idealistic, and perhaps even unrealistic, from their inception, but the COVID-19 pandemic, the very real and the negative effects of global warming, and other avoidable humanitarian disasters occurring in Afghanistan, Ukraine, and elsewhere have made them seem even more unachievable, especially within the ten-year timeframe that remains.

Nevertheless, a recent article published in the *Lancet* calls for ‘action to make children central to the development agenda and to identify several priority actions’. Of course, a major barrier to progress is funding and it is difficult to see where cash-strapped governments will find the spare cash for such worthy aims. Neither do the authors consider the difficulty of ensuring compliance from countries run by corrupt and self-serving regimes. If you are interested in global health, then there is a rich bibliography associated with this article.<sup>1</sup>

1. Bhutta, ZA et al. Optimising child and adolescent health and development in the post-pandemic world. 7 May 2022. [bit.ly/SDGsLancet](https://doi.org/10.1016/S0140-6736(22)00444-4)

## chronic stress – epigenetic effects on the digestive system

**M**edical students probably know better than anyone that long-term stress can cause digestive sensitivity, discomfort, and conditions like irritable bowel syndrome and even stomach ulcers, but the mechanism for these effects was not well understood. Recent studies revealed significant changes to gene expression in the colon epithelial cells of rats subjected to stress, resulting in reduced ability to maintain gut health, with an increase in the production of inflammatory cytokines and chemokines.<sup>1</sup>

A sub-set of these rats showed quite significant levels of altered gene expression, which may account for the fact that some people suffer more under conditions of sustained stress than do others.

1. Wiley J et al. Chronic psychological stress alters gene expression in rat colon epithelial cells promoting chromatin remodeling, barrier dysfunction and inflammation. 29 April 2022. [bit.ly/ratstudy](https://doi.org/10.1016/j.ratsstudy.2022.04.001)

## epigenetics and drug development

**E**pigenetic changes modify genetic information without altering the DNA sequence.<sup>1</sup> As highlighted by the rat study on the effects of chronic stress on gene expression in the colon, dysfunction of the epigenome can cause serious disease, ranging from cancers to autoimmune disorders. ‘Increasing knowledge of the role of epigenetics in disease and the reversibility of these modifications explain why pharmacological intervention is an attractive strategy for tackling epigenetic-based disease.’

Research into effective drug therapies for epigenetic changes leading to disease is complex and focuses on first identifying and understanding ‘the role of proteins responsible for writing, reading, and erasing epigenetic marks in disease’, then developing and trialling compounds that inhibit or modulate their action.

1. Holdgate G et al. Drug discovery for epigenetics targets. April 2022. [bit.ly/eptherapy](https://doi.org/10.1016/j.eptherapy.2022.04.001)

## why Alzheimer’s causes sleepiness

**A**lzheimer’s patients are often drowsy during the day, but it’s not because they don’t sleep well at night. A recent clinical trial that monitored the sleep patterns of a group of Alzheimer’s patients and then examined their brains after death, revealed that the cause is a loss of neurons whose function is to keep us awake.<sup>1,2</sup> One of the study’s co-lead authors is a medical student at the University of California, Joseph Oh. He explained: ‘You can think of this system as a switch with wake-

promoting neurons and sleep-promoting neurons, each tied to neurons controlling circadian rhythms.'

The study was aided by comparing the brains of Alzheimer's patients with those suffering from a neurodegenerative condition that makes sleep difficult, called progressive supranuclear palsy (PSP), as well as with healthy brains.

Another key finding of the research is that tau proteins, and not beta amyloid, are 'a critical driver of sleep disturbances'. It is hoped that the study will enable better ways of managing sleep disturbances for both Alzheimer's and PSP patients.

1. Medicine Net. New Insights Into Why Alzheimer's Can Bring Drowsiness. 8 April 2022. [bit.ly/Alzheimerstudy](https://bit.ly/Alzheimerstudy)
2. Oh, JY. Subcortical Neuronal Correlates of Sleep in Neurodegenerative Diseases. 4 April 2022 [bit.ly/sleepneurology](https://bit.ly/sleepneurology)

## and why it doesn't pay to pull 'all nighters' when preparing for exams

It will come as no surprise to medical students that sleep deprivation causes cognitive impairment.

Once again, genes are involved, and it seems that 'the temporal and spatial oscillations of circadian genes are severely disturbed after sleep deprivation, leading to a progressive loss of their physiological rhythms, which in turn affects memory function.'<sup>1</sup> Sounds pretty serious. And it is, with chronic sleep deprivation potentially leading to neurodegenerative disease and even accelerated aging. Yet there has been little research into how circadian genes affect memory and the immune system with a view to finding suitable therapies. This is especially important given that the fast pace of modern life often militates against healthy sleep patterns.

Research on sleep-deprived mice at the cellular level has greatly increased understanding of the 29 genes involved in regulating the circadian rhythm, of which seven were identified as being particularly influential. And with better understanding comes the possibility of developing treatments to both prevent and mitigate the effects of sleep deprivation, an

occupational hazard for most healthcare workers involved in clinical work.

1. Ke, P et al. Relationship between circadian genes and memory impairment caused by sleep deprivation. 21 March 2022. [bit.ly/SDgenes](https://bit.ly/SDgenes)

## Covid variants play 'hide and seek'

Although Covid may feel like 'old news' now that the worst appears to be over, at least in the UK, the virus in its various forms continues to be of concern globally. Two studies conducted by an international research team and recently published in *Nature Communications*<sup>1</sup> speculate that 'People suffering from COVID-19 could have several different SARS-CoV-2 variants hidden away from the immune system in different parts of the body'. The mechanism by which the virus achieves this appears to be a 'pocket' on the spike protein which persists within the different variants because it allows the spike protein to change its shape depending on which organ it invades and thus evade the immune system.

'Our results showed that one can have several different virus variants in one's body. Some of these variants may use kidney or spleen cells as their niche to hide, while the body is busy defending against the dominant virus type. This could make it difficult for the infected patients to get rid of SARS-CoV-2 entirely,' reports Dr Kaptil Gupta, lead author of the study. However, the ubiquity of the pocket in the different variants also offers hope. Research at the University of Bristol is seeking to develop a pocket-binding antiviral that works against all variants of the Covid virus. (Additional references provided for those interested in the scientific details of this research.<sup>2,3</sup>) ■

1. Drug Discovery Today. SARS-CoV-2-infected individuals could have different variants hidden in different parts of the body. 1 March 2022. [bit.ly/clevervirus](https://bit.ly/clevervirus)
2. Gupta K et al. Structural insights in cell-type specific evolution of intra-host diversity by SARS-CoV-2. January 2022. [bit.ly/clevervirus2](https://bit.ly/clevervirus2)
3. Staufer O et al. Synthetic virions reveal fatty acid-coupled adaptive immunogenicity of SARS-CoV-2 spike glycoprotein. 14 February 2022. [go.nature.com/3N2JgnB](https://go.nature.com/3N2JgnB)