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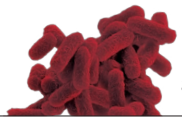

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More scrutiny for herbal remedies

New laws that promote centuries-old traditional medicines are a backwards step for China. Only controlled clinical trials can satisfy concerns.

In the 1990s, dozens of women who had taken Chinese herbs as part of a weight-loss programme ended up with kidney failure. Some died, and others became dependent on dialysis or transplants. Investigations blamed aristolochic acid, a natural ingredient of many traditional Chinese medicines (TCMs) that was quickly tied to other syndromes, including bladder cancer. Many countries across the world, from Japan to Canada, banned its use. China and the United States issued warnings, but allowed sales to continue. As use of the plant extract persists, so does the characterization of its dangers. In October, researchers published a report linking it to liver cancer (A. W. T. Ng *et al. Sci. Transl. Med.* **9,** eaan6446; 2017).

All drugs carry a risk, and doctors who give out TCMs argue that poisoning by aristolochic acid is an unfortunate and rare side effect caused by misuse of the medicines. But such risks are supposed to be balanced by benefits, and the benefits in this case are far from clear.

Evidence-backed use of medicines demands tests for efficacy and safety in rigorous clinical trials, so that health-care officials can decide whether treatments should be used. China, however, is moving in the opposite direction. As we discuss in a News story this week (page 552), new draft guidelines would scrap clinical-testing requirements for those TCMs that are made according to classical recipes. Advocates of TCMs say that this will align China's system with that of the United States, where supplements and herbal preparations need not pass the tests of the US Food and Drug Administration (FDA) before going on sale. That is true, but the US system is not one to emulate.

A 1994 US law lists such supplements as a separate category — neither food nor drug — and the FDA can try to ban them only if the agency proves them to be dangerous. The FDA has been playing catch-up ever since: even after fatal cases, all it can do is recommend that unsafe remedies be removed from the market. The law was a boon for the ballooning herbal and supplement business, but a major loss for science and for consumers, who often experienced adverse consequences.

There are major differences between the situation in the United States and in China. US companies, unlike their Chinese counterparts, are not supposed to say that herbal remedies cure disease. In China, by contrast, TCMs are often prescribed for specific diseases. The Chinese health ministry, for example, recommends an injectable herbal drug called Xiyanping for treating the H1N1 strain of influenza A (swine flu) and hand, foot and mouth disease. (In September, the China Food and Drug Administration pulled certain batches of Xiyanping from the shelves following reports of adverse effects.)

Demand for herbal remedies in China starts at the very top. President Xi Jinping has thrown his weight fully behind TCMs, which he says are crucial to the development of China's health care. This is understandable: he has pledged to spread health care to everyone in the country, and Western health care — which currently dominates the market — is too expensive to roll out quickly. TCMs are also good business for Chinese companies, and sales at home and abroad have grown steadily over the past two decades. But political and economic expedience is no basis for health policy. Worse, the tighter embrace of TCMs from the country's political elite is closing down debate among China's medics and public over whether the remedies work.

The new approach stands in contrast to efforts over the past decade or so by the government and Chinese companies to demonstrate efficacy as part of a modern and international approach towards TCMs.

"Fast and cheap cannot be the goal of drug regulation."

Following this agenda, and rules to encourage a more evidence-based approach, the drug company Tasly in Tianjin finished a phase III controlled study of a Chinese herbal remedy for the heart condition chronic stable angina pectoris in December 2016. The company claims it is the world's first compound Chinese herbal drug to have been shown to be safe and effective in "FDA-prescribed global multicenter phase-three clinical trials".

Many doctors on the side of TCMs argue that the remedies cannot be tested because they have to be tailored on the basis of the doctor's intuitive interpretation of patients' needs, and are usually used in combination. That is not convincing. Just because standardized trials are difficult or expensive is not a reason to say they can't be done — fast and cheap cannot be the goal of drug regulation. The world needs more such rigorous trials of herbal remedies, not a carte blanche for manufacturers to sell them to vulnerable patients.

The new regulations could have a bright side. Physicians hope that the rules will force manufacturers to be more careful about the composition of the drugs, which are often found to be adulterated. Ensuring the remedies are pure would be a positive step, but still wouldn't answer the questions of whether they work and whether their effect is worth the risks. Such answers cannot be assumed. Hundreds of years of use in clinics that don't standardize or analyse the clinical data are no match for blinded, controlled studies. ■

Opioid agonies

The staggering scale of painkiller abuse defies easy solutions.

Drug overdose is now the leading cause of death for the under-50s in the United States. More than 60,000 people succumbed last year, and millions more are addicted. When compared with other nations, the statistics are shocking. According to a report this year from the United Nations Office on Drugs and Crime, America has 4% of the world's population but some 27% of its overdose deaths.

The bulk of these people have taken opioid drugs — both legally and illegally sourced. Americans consume some 50,000 prescribed doses of opioid painkillers per million people each day — almost double those handed out in the next-highest-prescribing nation, the neighbouring Canada, with just over 30,000.

US President Donald Trump has rightly drawn attention to what he has called a national public-health emergency. (Although he notably failed to declare the situation a national emergency, which would have released extra funds and other resources to tackle it.) Just this month, a report from the White House Council of Economic Advisers said that the opioid epidemic cost the nation half a trillion dollars in 2015. And last week, the Food and Drug Administration (FDA) released guidelines to steer drug companies towards opioid painkillers that are harder to abuse.

The opioid crisis is a slow-motion emergency unfolding in real time. The issue has pushed its way onto the political agenda but has yet to provoke a satisfactory response, partly because there is no easy solution to its convergence of social, cultural and medical factors. (While Americans are dying from overuse of legal opioid painkillers, millions of people with cancer in nations, such as India, with strict narcotics controls have died in agony because they can't get them.)

The misuse of a valuable resource is partly to blame for opioid addiction and deaths. (The semantics are important here: whereas abuse of a drug seeks a high, its misuse aims to redirect clinical benefit at an inappropriate target. Crudely, abuse is more severe.) Opioid prescriptions in the United States ballooned in the 1990s, when lobbyists and companies succeeded in broadening the range of conditions the drugs could be used for — they were once restricted to pain following surgery or due to late-stage terminal cancer. A study in *Nature Reviews Gastroenterology and Hepatology* reports this month, for example, that opioid misuse to treat the pain of gastrointestinal conditions (for which there is no good evidence of benefit) has become endemic (E. Szigethy *et al. Nature Rev. Gastroenterol. Hepatol.* http://doi.org/cgp8; 2017). More than half of people with chronic pancreatitis and almost one-fifth with irritable bowel syndrome are reckoned to be opioid users.

"It is too simple to blame overprescribing, not least because there are few other options."

It's difficult not to have sympathy for desperate people seeking relief from enduring pain. And it's easy to see why so many front-line doctors are willing to write an off-label prescription when asked. (The above article also said that many medics feel pressured to agree when patients ask for opioids because they fear negative feedback and consequent criticism from managers.) It is too simple to blame overprescribing, not least because there are few other options. Efforts to tackle opioid misuse in medicine can work only if combined with broader re-education and a concerted effort to find alternatives.

Reducing the damage of opioid abuse is a different issue — and probably an even more difficult one. The FDA's new guidelines urge drug manufacturers to make generic opioid painkillers that are more difficult to grind up and snort, among other measures. But, as the agency admits, it's not clear that such 'abuse-deterrent' formulations will prove effective. Science and medicine can play their part in tackling this crisis, but the rest of society needs to wise up — and fast. ■

Babble fusion

London researchers are the latest workers to deal with noisy distraction.

In 1797, an unexpected visitor to the English cottage of the poet Samuel Taylor Coleridge became a literary metaphor for unwanted distraction that disturbs creativity. The arrival of the so-called Person from Porlock, Coleridge wrote, caused him to forget the rest of *Kubla Khan* — the words of which he had been busy transcribing after they came to him in a productive dream — and the poem ends incomplete after 54 lines.

Porlock is almost 200 miles from central London, but plenty of people are still knocking on the doors of the Francis Crick Institute, which opened as a base for biomedical research in the capital last year. And some of them are bringing distraction. Scientists working there, in spaces arranged around a central atrium, have complained that the open-plan design is too noisy and they can't concentrate.

Teething troubles? Probably, and the Crick is far from alone in trying to balance the promised benefits of open-plan office space — collaboration and idea sharing — with the inevitable downsides, including disturbances and lack of privacy. For although the trend in recent years has been firmly towards open-plan design (offices are much more modern-looking and cheaper without all those bulky internal dividing walls), evidence is mounting that such workplaces typically come with a drop in productivity.

Asked what bothers them, open-plan workers say that they resent being on display and grumble about temperature, but they most commonly complain about noise. And their most distracting noise — simply defined as unwanted sound — is often the human voice. (Not all office sounds are considered noise, and some workers say that they find the clatter of keyboards motivating and reassuring.)

To explain the distracting nature of overheard speech, most acoustics experts rely on the changing-state hypothesis, which suggests that sound that arrives in a series of contrasting segments is harder to ignore, and so more likely to be considered noise, than steady sound. Hence a series of spoken words, with intonation, emphasis and pauses, takes attention away from a task more than does a constant drone of air conditioning.

Importantly for open-plan offices, acoustic design theory assumes that as more voices are added to the noise, the distracting peaks, troughs and gaps start to overlap, cancelling and smoothing each other out. At a certain point, simultaneous voices merge into non-segmented babble. So, a single speaker makes distracting background noise, but several speakers, in theory, produce a more soothing background sound.

Not convinced? Some experts agree with you. This year, architects at the University of Sydney in Australia published a challenge to the way in which their colleagues account and allow for unwanted speech in open-plan offices. Specifically, they argue that the relevant international standard — ISO 3382-3:2012 — is flawed because it rigidly follows this acoustic-design logic and assumes that the most problematic noise is the voice of a single speaker (M. Yadav *et al. Appl. Acoust.* **126,** 68–80; 2017). In tests, the architects found that combining four voices made the effect worse for an unfortunate worker asked to sit at a desk and concentrate. Differences between the separate voices might themselves act to segment the sound, the authors suggest.

What's to be done? Some scientists at the Crick (like workers in countless offices around the world) have been spotted wearing chunky headphones. Music can bring its own distractions (any sensory input that demands attention must drain cognitive power), but the overall effect is complicated because it can also serve as a powerful influence on motivation. What's more, as any office drone who has tried it will confirm, people are less likely to approach you if you are wearing headphones, whether music is playing or not. So an open-plan office of workers with headphones on would seem to go against the hoped-for creative cooperation of chance collaboration.

Even unmolested concentration and effort, of course, is no guarantee of success — in science or in anything else. Some scholars claim that Coleridge got stuck on *Kubla Khan* and then invented the Person from Porlock to excuse its fragmentary composition. That might be true — but go on, keep the sounds, noise and babble down a bit. Some of us are trying to think. ■