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“Legal highs” should be regulated as medicinal products

PERSONAL VIEW Michael Evans-Brown, Mark A Bellis, Jim McVeigh

In the United Kingdom legislators are using the term “legal highs” as shorthand for emerging psychoactive substances that are not controlled under the Misuse of Drugs Act 1971 but that in their opinion cause similar harm to those that are.¹ It assumes defined causal links between the use of such substances and serious harm to individuals and society. This is compounded by anecdotal accounts in the media of widespread use and (suspected) serious adverse drug reactions that are presented as typical experiences. The term is misleading in defining the problem and its solution, to the exclusion of other policy measures that may be more effective and efficient, such as the medicines regulatory framework.

In such an environment fear and panic can weaken the ability to collect the data needed for risk assessments—it is of limited value if we can't discriminate between pharmacological effects, nocebo (undesirable placebo) effects, or other causes.^{2,3} The opportunity for rational debate and effective policy making is also limited.⁴ Policy measures that reflect such errors may be seen as disproportionate and illegitimate by the sections of society that are the intended focus, which could bring about unintended harmful consequences.^{5,6}

Pragmatic compromises ... should allow us to respond proportionately and with legitimacy to protect public health

The apparently rapid spread of substances such as BZP (1-benzylpiperazine), cannabinoid receptor agonists such as the Spice brand, and mephedrone has raised concerns that the 1971 act is insufficient to protect society from harm.¹ The government is seeking an amendment—temporary class drug orders—to give powers to regulate emerging substances until advice can be given on whether they should be brought under “permanent” control of the act.⁷ There is no requirement to show that use of such substances may lead to a “social problem”—a key criterion for “permanent” control under the act.^{7,8} During this interim period, class B penalties would apply to the production, intent to supply, and supply of such substances without authority—that is, imprisonment for up to 14 years and an unlimited fine on indictment.



ROB WHITE

Simple possession would not be an offence; the government has stated that it doesn't wish to criminalise users.^{1,7}

Although the government's proposal is well intended, it may be regarded by some as arbitrary. Will drug orders prejudice the existing risk assessment process? In other words, once it has been determined that an order is required, is “permanent” control a given? Will the orders place the courts at a disadvantage, particularly in relation to sentencing, given the lack of data on harms? Such questions are especially important given the criticisms over the application of the 1971 act, particularly in relation to drug classification.^{9,10,11}

Pragmatic compromises to deal with the problem of emerging substances are needed. They will not be a panacea, but they should allow us to respond proportionately and with legitimacy to protect public health. One such compromise could be the use of the medicines regulatory framework: if a substance is classed as a medicinal product (determined by the Medicines and Healthcare Products Regulatory Agency) then it would be

an offence to manufacture or import, market, or advertise it without authority. The maximum penalty under the Medicines Act 1968 is two years' imprisonment and an unlimited fine.¹²⁻¹⁶

Although some substances, such as BZP, have been regulated in this way, creative strategies such as marketing products as “not for human consumption”—widely believed to achieve compliance with the framework—have led to the belief that this approach cannot work. Review of judgments from the European Court of Justice on those factors that must be considered when classifying any substance (such as its familiarity to consumers),¹⁷ as well as the classification of Spice products and mephedrone as medicinal products by some European Union member states, suggest otherwise.^{18,19} Also, section 104 of the Medicines Act 1968 provides a catch-all to deal with such strategies: any articles or substances “appearing” (as the act puts it) to be used for a medicinal purpose—which includes “preventing or interfering with the normal operation of a physiological function”—can be regulated.^{20,21}

A synergy between compliance and deterrence through responsive regulation would need to be found.²² The principal goal would be to prevent harm (through compliance) rather than punish after an offence has been committed (deterrence). Better use of the pharmacovigilance system, including the yellow card scheme, may also help identify and reduce harms. Importantly, this framework will not compromise the UK's obligations to the European Union and to international treaties, nor, if necessary, the control of such substances under the 1971 act.

Whether taken for psychotropic or somatic effects, all drugs may pose risks to the individual and society. Progress requires debate in an environment that is free from fear, panic, and knee jerk reactions.

References and competing interests are given on bmj.com.

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REVIEW OF THE WEEK

Poet turned patient

Doctors can make the difference between a horrific and a tolerable experience of illness. **Leyla Sanai** found parallels with her own life in this memoir about a rare autoimmune disease



The Two Kinds of Decay
An autobiographical memoir by Sarah Manguso
Granta, £6.99, 192 pp
ISBN 978-1847083098
Rating: ★★★✿

Imagine losing power and feeling in your arms and legs. This is what happened to Sarah Manguso when she was 21 and a student at Harvard, when she noticed an inability to walk straight, and her hands and feet became paraesthetic. Fearing that her fellow students would assume she had an alcohol problem, she contacted her parents, who fetched her and sought medical advice.

Manguso's first diagnosis was Guillain-Barré syndrome. She was given daily apheresis (plasma exchange) in intensive care for a week and then discharged. But the symptoms returned. She was initially told that it was a minor hiccup, but, as is often the case, the patient knew better. Manguso's problems worsened, and she was soon back for more apheresis. It turned out that her illness was not Guillain-Barré after all but a related autoimmune disorder, chronic inflammatory demyelinating polyradiculoneuropathy, in which similar antibodies are made to the myelin sheaths of neurones. Unlike Guillain-Barré, the disorder may recur.

Manguso's memoir is a collage of her memories of her illness: remissions and relapses; different doctors and nurses; the effect on her of their kindness or arrogance; her return to Harvard; and her long, slow recovery. Manguso has published poetry, and her writing reflects this; her prose is spare, stark even. So much lingers in the cool spaces between her words, in thoughts unsaid but hinted at, often with dry, sardonic wit. The difference made by doctors and patients who are kind and empathic is known to every patient, but Manguso gives us concrete examples. There is the misplaced optimism of the neurologist who wouldn't believe her symptoms; the astounding paternalism of the doctor who told her that she must be wrong about her symptoms because they didn't follow the academic pattern; the nurses who would chivy the apheresis machine along

by injecting more heparin as a short cut; the vascular surgeon who, after Manguso sobbed on being told she needed another central line, told other doctors within her earshot that she was "the kind of patient who took things very hard."

It's easy for me, looking from both a doctor's and a patient's point of view, to see the source of these clashes: to a busy vascular surgeon a patient crying about the need for a central line may seem extreme. To Manguso, who had just been torn from university at the age of 21 by a debilitating and frightening illness with an uncertain prognosis and in whom a previous central line insertion had been a trial, with her parents blanching as blood oozed during repeated attempts, a central line insertion would be traumatic. But Manguso is also generous in her praise for doctors and nurses who made a difference.

She describes immediately loving the neurologist who made the correct diagnosis; the wonderful nurturing of the nurse who brought in sweets for her each day while she was receiving apheresis to counteract the bitter taste of infused albumin; of the nurse who, filling in observations about her complexion, didn't simply copy the "pale" parroted by previous nurses but listened to Manguso explain that she was naturally pale. It's details like these—clinicians listening, showing compassion, and treating the patient as an intelligent individual—that make the difference between a horrific and a tolerable experience of illness.

Manguso's considerable intellect allows her to snarl at those who displease her, and occasionally she is too hard. One family doctor is spurned because his voice quavered with emotion as he told her what an ordeal she had been through.



Manguso: "took things very hard"

Whether it was the perceived negativity (which I interpreted as an attempt to tell her how brave she'd been) or the obvious emotion, Manguso's response seems harsh: if we want our doctors to be empathic we must forgive occasional overemotion or clumsiness.

Sometimes too her capacity for consideration is dubious. In the depression that follows her illness she drives the wrong way up a road into a van of children as a suicide attempt, and when at her parents' home for months she would wake from nightmares and scream repeatedly even though she knew that she was awake. She describes her devoted parents becoming haggard with stress; their distress at watching her have a central line inserted as she had asked for them to be present; a friend of her father's telling him he had aged 10 years in the first year of Manguso's illness; and her resentment when her parents' daily hospital visits coincided with her favourite television show. And she takes their absolute dedication for granted, saying that if she'd had a relapse without insurance her parents would have been homeless within a year. She will one day realise how lucky she is to have such loving parents, and perhaps increased maturity will bring some of the protective instinct about them that they have unflinchingly shown towards her.

Some doctors may balk at apparent overegging of the pudding, as Manguso tells us that insertion of a central line is "vascular surgery" and that of a Hickman line is "a long surgery." Her description of the sob inducing pain of electromyography is horrific, but I've had it and thought it all right. But then maybe I've become inured to these things because my own autoimmune disease has necessitated three laparotomies with removal of large bowel; loss of dominant thumb and several fingertips; five lumbar sympathectomies, a bilateral thoracic one, and digital and radial ones; numerous other procedures and operations; a need for 72 long days every year receiving vile infusions in hospital and 18 other drugs; and nine years (and counting) of an indwelling central line. But Manguso was so young when she became ill, and her formative years were blighted by being incapacitated. People are different: for me physical illness is so much more tolerable than emotional pain, which crushes me completely—whereas for Manguso, courageous through the break-up of a long term relationship before her illness, it may be the reverse.

Manguso's descriptions of the procedures she experienced are lucid and cogent, there being only two tiny errors. Manguso has combined black humour, sparkling acuity, and wisdom beyond her years to produce a piercing, powerful memory album of the experience of her illness and recovery.

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BETWEEN THE LINES Theodore Dalrymple

Malice, intention, patience, and resource

There was a time when doctors wrote their memoirs and the public bought them. Whether doctors were better writers in those days or the public had fewer amusements to choose from I cannot say; but Halliday Sutherland's memoir, *The Arches of the Years*, published in 1933, was reprinted in Britain at least 34 times and was translated into eight European languages.

Sutherland (1882-1960) was an interesting figure. He spent most of his professional life working on the prevention of tuberculosis, and he wrote books on the subject. He made the first health education film in Britain. He became a firm Catholic and wrote pamphlets against artificial contraception. In 1923 he was sued for libel by the pioneer of birth control, Marie Stopes. He was alleged to have implied in his book, *Birth Control: A Statement of Christian Doctrine Against the Neo-Malthusians*, that Stopes took advantage of the ignorance of the poor to conduct experiments on them. He won his case (which is still cited by lawyers) two years later in the House of Lords. Stopes called him the most cocksure man in the British empire.

Not long after he qualified Sutherland went to Spain as an assistant to his uncle, who had a medical practice in Huelva. It seems that the young Sutherland was much less troubled by bureaucracy in taking up practice in a foreign country than the average British doctor now has in obtaining a hospital car park permit. In his memoir he recounts how he tried to develop passive immunisation there against leprosy by injecting leprosy material into a goat and then using its serum.

It worked, but not in the sense intended. The patients did not get better, but a servant of Sutherland's started to steal the goat's milk. Sutherland told him that he had injected leprosy material into the goat, and the theft of the milk ceased at once.

[Halliday Sutherland] recounts how he tried to develop passive immunisation there against leprosy by injecting leprosy material into a goat and then using its serum



Marie Stopes: sued Sutherland for libel

Before devoting himself to bacteriology Sutherland also worked for a short time in an asylum (his father had been a deputy commissioner for lunacy in Scotland). "Mrs H... was a stout, elderly, white-haired lady with the staring eyes of mania, and she disliked me," Sutherland recalls. She hid a stocking about her person, filled it with earth, stones, and nails that she found in the grounds, and then one day attacked Sutherland with it. "In her action," writes Sutherland, not without a certain admiration, "there was malice, intention, patience and resource." But he realised that, as he put it, this branch of medicine was not for him.

This anecdote took me back to the days when I first worked in prison. There was still a large square battery in existence called a PP9, and prisoners could buy it for their radios. Some, however, bought it for other purposes: they put it in a sock and attacked their enemies with it. "Could you see Smith, sir?" a prison officer would ask me. "He's just been PP-nined."

I was never PP-nined in the manner of Dr Sutherland, and the battery was withdrawn, at least from prison circulation. It was replaced briefly, as a weapon, by tins of mandarin oranges. "Could you see Smith, sir?" a prison officer would ask me. "He's just been mandarinnd."

Yes indeed, malice, intention, patience, and resource.

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Obituary (*BMJ* 1960;1:1368-9)

MEDICAL CLASSICS

Long Day's Journey into Night

A play by Eugene O'Neill, first published 1956

The US playwright Eugene O'Neill (1888-1953) wrote his autobiographical play, *Long Day's Journey into Night*, in 1940, but it was not published until 1956. Posthumously it won him his fourth Pulitzer prize in 1957. The play, whose themes include addiction, tuberculosis, and depression, stretches over one April day in 1912.

Mary and James Tyrone have been married for 35 years and are parents to Jamie and Edmund (modelled on O'Neill) and to Eugene, who died of measles in infancy. Mary has always blamed her eldest son, from whom the baby must have caught the infection. She has been battling morphine addiction for 23 years, is referred to as a "dope fiend," and has just undergone withdrawal at a sanatorium. She ostensibly takes morphine for arthritic pain, but she also seeks to retreat into the past, symbolised by the rising fog outside, to avoid blaming her family for her addiction, loneliness, and unhappiness.

The men, also in denial, drink whiskey heavily and habitually to blot out their frustration at not being more successful. James and Jamie are actors, and Edmund has the makings of a writer. Caught in a cycle of self hatred, blame, frustration, cynicism, and rage, they paint a convincing portrait of alcoholism. And to make things worse Edmund has contracted tuberculosis, which is also met with denial, especially by Mary, whose father died from the disease. James's stinginess is blamed for Mary's addiction as well as

Edmund's potential death, because he is not willing to pay for medical help. But the real villains are two doctors who never appear in the play.

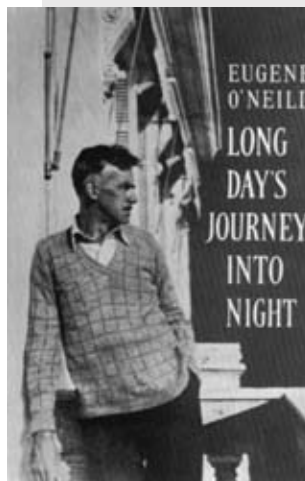
The doctor who gave Mary morphine after Edmund's birth is blamed repeatedly for her state. And another, Dr Hardy, is appreciated by James, but his family suspect James of preferring this physician because he is cheap. Dr Hardy invites a specialist to advise Edmund about his tuberculosis and give him hope. Mary says, "Doctor

Hardy! I wouldn't believe a thing he said, if he swore on a stack of Bibles! I know what doctors are. They're all alike. Anything, they don't care what, to keep you coming to them." To her it's almost as if the doctor were the addiction rather than the drug.

James concedes that Edmund can choose any sanatorium, within reason. The men move forward to confront their destiny; Mary regresses to her school days to escape the present and future: "It [the medicine] kills the pain. You go back until at last you are beyond its reach. Only the past when you were happy is real." The play's climax shows Mary remembering how she wanted to be a nun but fell in love and how happy she was for a time—before this long day's journey into darkness and despair.

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The number needed not to treat

FROM THE
FRONTLINE
Des Spence



After finishing training for general practice I applied for an academic position for a year. I wrote a proposal on an observation I had made, that individual doctors generate much of their own workload. But as we say in Glasgow, “What’s for you won’t go by you,” and I wasn’t interviewed. My observation still holds true, however.

Doctors are aware of the NNT (number needed to treat), the number of patients who need to be treated for one to benefit from the intervention. (Remember that the NNT may be for many years of treatment, and when given per year the number may be far less impressive.) Fewer doctors are familiar with a more important concept, the NNNT (the number needed not to treat). The best example of an NNNT is the use of antibiotics for sore throat. If doctors don’t prescribe antibiotics, one in four patients will stop believing that antibiotics are effective, and a large percentage will not return with a sore throat again (www.medicine.ox.ac.uk/bandolier/band44/b44-4.html). Extrapolated and compounded over time this clearly reduces pressure on medical appointments. And this observation is true of every self limiting illness.

This non-interventional effect is seen in almost all medical situations. Consider a doctor taking a blood test (often on the pretext of reassuring the patient but in reality to reassure the doctor). The patient tells everyone, “There is something wrong; they’re running further tests.” He or she

waits anxiously to have the blood taken and then for the doctor to comment on the result. “Normal levels,” however, are but confidence intervals, so by definition some normal results lie outside this range. This then leads to further tests. Cue yet more anxious waiting, and, “The doctor must be really worried about me.” Should the “abnormality” persist, many patients are referred “just in case.” A simple routine blood test sets off a cascade of medical consumption, clogging general practice appointments and outpatient departments. This pattern is being repeated all the time all over the country. So, wide variation among doctors’ clinical practice leads to wide variation in their workload.

This is a fact. Use of healthcare and health seeking behaviour is directly affected by doctors’ behaviour. Doctors’ behaviour is linked directly to how they are paid. A private, fee for service system encourages medicalisation and consumption; a socialised system of capitation does not. This largely explains the huge cultural and international variations in the use of healthcare. The less doctors do, the lower our workload. Better still: the less we intervene, the less health anxiety we generate, and the more we promote self caring. There is more to healthcare than illness. A wider understanding of NNNTs would directly reduce our workload.

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Bombs and tunnels

IN AND OUT OF
HOSPITAL
James Owen Drife



Visiting Vietnam in 2011 produces mixed feelings if you were a student in the 1960s. The “American war,” as of course the Vietnamese people call it, was beginning when I entered medical school and ending when I graduated. The British prime minister had resisted US pressure to send troops (those were the days, eh?) but did not denounce America’s epic struggle to save the world from communism.

As our cruise ship approached Hai Phong I felt more than my usual guilt at being a tourist in a developing country. Hai Phong and Da Nang were names I had last heard in news bulletins filled with casualty figures. US student demonstrations had helped stop the killing, but it never occurred to me to join Vanessa Redgrave and other lefties protesting outside the US embassy in London.

Vietnam had seemed a small

country, but now it has 87 million people, most of them too young to remember the war. The nation is used to fighting. It expelled its Chinese overlords a thousand years ago and did not take kindly to French colonialism in the 19th century. Independence from France was the main goal of Ho Chi Minh, whose little body is still on display in a huge Soviet-style mausoleum in Hanoi.

After the Japanese left in 1946 the United Kingdom and the US could have supported Vietnamese self determination. Instead they helped the French to return. Ho turned to Moscow, and the stage was set for decades of appalling carnage in Vietnam and Cambodia. Northern Vietnam is dotted with war cemeteries, but the country is surprisingly low on bitterness.

The south has a guerrilla theme park with a grisly display

of man traps. Visitors can enter a hidden tunnel, now somewhat enlarged. I lasted three metres before retreating and lingering beside mannequins showing how improvised explosive devices were made from undetonated US bombs. For me, it seems, the horrors of war are preferable to a touch of claustrophobia.

Today the Communist Party is in charge, but the country is socialist in name only. Nobody speaks French or Russian any more. Capitalism and the internet are everywhere. Education is expensive, and there is no free healthcare for the poor. It feels as if the US won. They might have done so without all those expensive bombs if they’d listened to Vanessa.

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