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## Prescription drugs: legal and lethal

### **Forget heroin and cocaine. The dangerous drugs claiming the lives and minds of the stars are prescription painkillers and a new class of happy pills that doctors are handing out by the million**

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What finally killed Heath Ledger wasn't heroin or cocaine. Despite his well-publicised problems with illegal hard drugs in the past, the potentially lethal compounds found in the Manhattan apartment of the 28-year-old Hollywood actor after his death in January had all been legally prescribed. Just another victim of the American private-health system, you might think, the prescription-on-demand culture that wiped out Elvis Presley and Marilyn Monroe. Not our problem.

Think again. Of the six sedatives, painkillers and anti-anxiety drugs Ledger was taking, three had been prescribed here during his recent spell filming in London. In common with a growing number of young serial drug abusers – including his fellow film star Owen Wilson, whose attempted suicide last year was attributed to a three-day binge on the legal painkiller OxyContin – Ledger had moved on from street drugs. Having been caught on film two years ago at the Chateau Marmont in LA snorting a white powder, he had discovered a less troublesome, if no less dangerous, route to oblivion.

That most of us haven't yet registered this shift reflects the fact that when it comes to thinking about drugs, we're like a broken record. We think about the drugs governments are prone to declare "war" on. So it is that the argument about the dangers of cannabis drags on, while the tabloids feast on pictures of Pete Doherty and Amy Winehouse with their crack pipes, or speculate that Britney Spears might be a victim of the new "drug scourge" methamphetamine, better known as "crystal meth". But beneath the media headlines and moral panics, the ground is shifting. The problem with drugs is moving nsidiously closer to home. All of our homes.

In one of its less sensational aspects, our escalating fondness for taking drugs that won't get you arrested can be measured in the 10% annual rise over the past three years in the use of antidepressants, notably our old friend Prozac. The NHS issued 31m scripts for Prozac in 2006, a blanket figure that, however it breaks down

in terms of the numbers of users referred to, suggests that a lot of people are regularly taking a powerful antidepressant. Then there are the Valium guzzlers. The Council for Involuntary Tranquilliser Addiction (Cita), run by Liverpool University, guesstimates that there are as many as 1.5m nervous types in this country who have become accidentally addicted to benzodiazepines, the family of tranquillisers to which Valium belongs. Others take them knowingly, for fun. According to Professor Heather Ashton of Newcastle University, author of a pamphlet on addiction to benzodiazepines, these

“are now taken illicitly in high doses by 90% of drug abusers worldwide. They are part of the drug scene”. So well integrated are they that abusers will crush the pills and snort or inject them, the same way they might cocaine or heroin.

More worrying in a way, because they attract less attention, are those habit-forming drugs that can be bought without prescription at high-street pharmacies. Concern about these has given rise to a new coinage in the world of drug dependency, “OTCs”, an abbreviation for painkillers bought “over the counter”. This usually refers to the more powerful varieties of OTCs, such as codeine, which contains synthetic opiates. At a conference of the General Medical Association in 2004 it was suggested that there might be 50,000 OTC addicts in Britain today. The authorities are also concerned about OTC drugs causing suicidal tendencies: the European Medicines Agency is calling for OTC drugs to come with a “suicide rating”.

A few words of reassurance at this point for those concerned that they might be developing a dependency on analgesics, anti-inflammatories, hay-fever tablets or other popular remedies. Drugs that carry a risk of addiction do so because they alter the binding of neurotransmitters to receptors in the brain. In short, they are, in different ways, mood-enhancers. A couple of aspirin cannot affect your Monday-morning feeling nor induce a sense of numbness the way synthetic opiates do.

We could, though, get hooked on other readily available painkillers. The comedian Mel Smith publicly confessed to having developed a dependency on Nurofen Plus – the enhanced version that adds an opioid to ibuprofen, the active ingredient – while treating himself for gout. Smith suffered a seven-year addiction he referred to as his “dark secret”. “They didn’t make me feel high. They helped me to relax.” His 50-tablet-a-day habit landed him in hospital with two burst stomach ulcers. The pharmacists’ trade body, the Royal Pharmaceutical Society, has become increasingly insistent that its members check the symptoms of anybody asking for OTCs; the move was prompted by a survey of its members in Scotland that revealed that nearly half suspected they had sold painkillers to customers with something other than pain relief in mind.

But would this help a user such as Mark, an IT manager from the Midlands in his forties? His OTC drug problem began after he contracted MRSA while in hospital with severe pneumonia. The excruciating pain he felt eventually passed, and he was discharged; but then a chest infection set in, reawakening memories of his MRSA agony. As he didn’t have a good relationship with his GP, he asked a chemist for the strongest pain relief available. He came away with co-codamols, which contain codeine. For years Mark carried on taking these tablets – primarily for migraine symptoms – until in 2004 he was diagnosed with high blood pressure. Signed off from work, he soon realised it wasn’t the anxieties of his job that were causing his blood pressure to soar: it was the stress he felt without his painkillers. “I managed to get them down to eight a day, but I couldn’t cut them out totally. I went on like this for about four months.” Luckily, the doctor he eventually confided in worked part-time with the South Derbyshire Substance Misuse team.

Clean for four years, Mark now helps to run Codeine Free, one of the websites that have sprung up recently to offer advice and discussion forums on OTC drug addiction. The best-known of these, Over Count, was set up in Dumfries by David Grieve, a former policeman who spent £18,000 over a two-year period getting hooked on a popular proprietary cough medicine with a synthetic opiate base.

The prescription drugs causing most concern are antidepressants. Prozac, which has been around for 20-odd years, is old news. The two newcomers currently causing medical debate are the branded drugs Efexor and Cymbalta. These are classed as “selective serotonin and noradrenaline reuptake inhibitors”, or SSNRIs. The added “N” is what makes them special. Unlike Prozac and other SSRIs, these drugs do

not simply increase levels of serotonin, the brain chemical that makes us feel more sociable and relaxed. They also boost adrenaline, making us more energetic and sometimes slightly manic.

Cymbalta was developed by Eli Lilly after its patent on Prozac ran out in 2001, which meant that the latter could now be manufactured as a “generic” drug and sold more cheaply. During the clinical trials of Cymbalta in 2003, one of the paid guinea pigs, a female student, committed suicide; but it was approved for medical use in the US in 2004, and a year later was generating \$1 billion worth of sales. In the UK, Cymbalta has only just started to be prescribed. In America it’s a phenomenon, one of the pharmaceutical industry’s greatest hits. The financial analysts at Merrill Lynch, which part-owns Eli Lilly, have estimated that the market for Cymbalta will be worth over \$3 billion in 2009, overtaking the original SSNRI drug it was modelled on, Efexor.

Currently prescribed in the UK for conditions that range from chronic depression to hormonally related hot flushes, Efexor is less common but more controversial than Prozac. One of its most prominent former users is Robbie Williams. Hooked on cocaine and alcohol for most of the 1990s, Williams was back in rehab in February 2007 for what he described as “prescription-drug addiction”, the chief of these being his favourite antidepressant, Efexor. Whether Williams realised what was happening when he began taking pills prescribed by his LA psychiatrist is not clear. But he must have had an inkling that keeping depression at bay was not the only role Efexor played in his ostensibly sober life. He compared the feeling of taking it to “coming up on an E” (ecstasy tablet), and spoke glowingly to George Michael about its energising effect on his live performances – both of which endorsements were reported in Chris Heath’s biography of the star, *Feel*.

Efexor, which has been around for a decade, has become a cause for concern since an online petition was started in America in 2001. It now contains over 15,000 aggrieved signatories. There are complaints that doctors gave no indication, or flatly denied, that the drug carried any significant side effects or risk of dependency. For its part, the drug’s manufacturer, Wyeth, acknowledges that Efexor may cause unpleasant side effects such as nausea, insomnia and raised blood pressure in a small number of cases – its data suggest around 10%. The online complaints about the withdrawal symptoms go further, listing raging headaches, panic attacks, night sweats and vomiting. One petitioner writes: “I have lived my life saying ‘no’ to drugs. Now I’m having withdrawals from something my doctor gave me. This is a crime.”

It does at least suggest how hazy the line is that separates the gear you buy from a dealer on the street and the stuff prescribed by the guy in a white coat. Plenty of British doctors, however, disagree. One Harley Street GP with several highly stressed celebrity patients says Efexor is “a formidable agent that can change people’s lives in ways that are wonderful. To demonise it is wrong”. Efexor dependency is manageable, and ultimately avoidable, he says. The key lies in careful administration and monitoring to minimise the problems. “It’s like having a brilliant chainsaw. You don’t try to have a shave with it.”

When predicting the future for prescription-drug abuse in this country, all eyes are on America, where the situation has been barrelling out of control for decades. It was reported last year that prescription drugs in the States are responsible for more deaths than either cancer or road accidents. Tranquillisers abused by recreational users enjoy a high profile there thanks to Xanax. Designed to combat anxiety, but widely taken in excess with alcohol – whose effects it mimics and intensifies – Xanax is as common as Prozac, and far more socially troublesome. It has become synonymous, in law-enforcement circles, with wildly uninhibited behaviour and late-night call-outs to suburban addresses. It was one of the six prescription drugs found, along with empty bottles of booze, in Heath Ledger’s apartment.

The real worries, though, surround painkillers. Dihydrocodeine, or DF118, as it is referred to in the UK, is the preferred American alternative to diamorphine, the pharmaceutical name for heroin. In the US, which outlawed heroin in the 1920s, dihydrocodeine is the active ingredient in the popular branded painkiller Vicodin. Recently identified by the US Drug Enforcement Administration as the fourth most widely abused drug in the country – after cocaine, heroin and marijuana – Vicodin has seeped into American popular culture. The rapper Eminem wears a Vicodin tattoo on his arm. Celebrity abusers have ranged from Ozzy Osbourne to the ultra-conservative chat-show host Rush Limbaugh, who began taking it for back pain and went on to spend \$300,000 on it in three years. Or at least that's what his former housekeeper told the National Enquirer.

An English film producer who works in LA, and does not consider himself a druggie, was prescribed Vicodin for a back problem. "There was no warning that it was addictive," he says. "But I knew it was dangerous the first time I took it. It gives you this warm feeling which is rather delicious, and I am very careful not to take it now unless the pain is serious." His view is that in LA today the misuse of prescription drugs is "not about getting out of it. They keep you going. They encourage a hyper work ethic". The epidemic of prescribed antidepressants he holds in similar regard. "There's an incredible stigma against depression in California, where it's regarded as worse than bad breath."

The actor Owen Wilson had his own prescription for a bout of severe depression last year: OxyContin (oxycodone). Manufactured in the UK, but only sparingly prescribed here while its effects are monitored by our Medicines and Healthcare products Regulatory Agency (MHRA), this powerful opiate offers a dystopian glimpse of future drug abuse. Its rocketing popularity with the recreational crowd derives in no small part from its superior design. Like many of the new prescribed substances, OxyContin is, by comparison with the powders that are traded on mean streets, a smart drug. Whereas a shot of heroin will deliver its entire opiate charge at once, with possibly fatal results, OxyContin is released in stages over six to eight hours. For the cancer sufferers for whom the drug was developed, this means longer and more effective pain relief. For an abuser, it means a longer, more consistent high, with a reduced risk of an overdose.

In the US, OxyContin is now regarded as the most dangerous substance in the recreational arsenal, widely tipped to take over from heroin as America's favourite opiate. In its first year on the market, sales of OxyContin were worth \$40m. Four years later the manufacturers were shipping \$1 billion worth of a drug that had acquired the nickname "hillbilly heroin" because of its popularity among poor rural communities in the Appalachians. Sales of OxyContin have roughly doubled in America in this century. Since the cost of it is often covered in the first instance by health-insurance plans, it offers a double whammy for the potential abuser: a long, strong high that is both highly addictive and cheap.

This new pharmaceutical order has been vigorously embraced in the US, particularly by the young. Several studies have shown an alarming hike in prescription-drug abuse in the under-25s. A National Household Survey in 2001 discovered a doubling of the numbers of 12- to 17-year-olds reporting an interest in Xanax and Vicodin between 1996 and 2000. Wherever youth pitches its tent, a new slang takes root. "Pharming" is consuming a cocktail of prescription drugs. "Doctor shopping" is visiting several physicians to fulfil a medicines wish list. And if that doesn't pan out, there are always "pill ladies", elderly prescription-holders who take advantage of the difficulties experienced by the young in obtaining heavy-duty drugs created to ease chronic back pain or the suffering of cancer patients. And for the truly desperate, the practice of robbery has acquired a new subdivision: "prescription theft".

The most vivid insight into the transmission of the new drug culture has been provided by the stars of the real-life soap The Osbournes. The head of the family, metal guru Ozzy, was for years addicted to Vicodin, a subject he explored on his latest album, Black Rain. His children have long since overtaken

him. His daughter Kelly entered a rehab clinic at the end of the TV series claiming: “They found 500 pills in my room when they cleaned it.” His son Jack started popping Vicodin aged 14. At 17 he was a multiple prescription-drug addict. Street drugs he never bothered with. After he cleaned up, Jack Osbourne spilt his guts on MTV, naming nine medications that he used on a regular basis. His favourite was OxyContin. Evidence of just how deeply entrenched over-medication currently is in the US unfolded in the LA courtroom where Phil Spector stood trial last year for the murder of Lana Clarkson.

In one of the pre-trial hearings, his lawyers argued that the police, who kept their client locked in a cell for most of the day after the fatal incident, had acted unlawfully. Their reason was that Spector, at the time, was a prescription junkie, suffering withdrawal symptoms from seven named medicines. Two of these were powerful benzodiazepines. One, Klonopin, is a tranquilliser much more potent than Valium.

It is notoriously dangerous when taken with alcohol: users become quite unhinged. Which was why Spector’s lawyers were so insistent that although the accused spent a lot of time in bars on the night of Clarkson’s death, and ordered a number of alcoholic cocktails, he didn’t actually drink them. That Clarkson was, at the time, buzzing lightly on Vicodin, the painkiller she was still taking two years after breaking both of her wrists, was another twist in the tale. Spector and Clarkson were a very modern American couple: plain-clothes druggies whose habits were known only to their doctors. The situation in the UK is nowhere near as bad, but it does seem to be getting worse. In the same week last year that Robbie Williams went public with his prescription-drug habit, a private GP was banned for nine months for prescribing addictive or dangerous drugs from his website, e-med. The General Medical Council ruled that Julian Eden had adopted a “cavalier” approach to patients who contacted him online. In particular, the GMC was appalled by the case of a 16-year-old boy, with a history of self-harming and mental instability, who tried to kill himself after Eden issued him with a prescription for the beta-blocker propranolol. Another woman, a mother of three, obtained a year’s supply of dihydrocodeine and Valium. A third “patient” received 51 repeat prescriptions for two so-called “hypnotic” sedatives similar to the date-rape drug Rohypnol.

Eden’s activities came to light after he was exposed by two undercover reporters, both of whom were prescribed drugs that usually require a full medical consultation within minutes of logging on to e-med. Making matters worse, the GMC said, was the fact that Eden made no attempt to contact the GPs of his online clients.

Eden is, or was, a real doctor. As anybody with a broadband connection on their computer knows, prescription drugs of the more popular kind are now being sold from thousands of websites by anonymous peddlers. Every day I receive spam e-mails offering unlimited quantities of, say, the tranquilliser Xanax, or the highly addictive and widely abused sleeping pill Ambien. The asking price is usually \$2 a tab. This dodgy online pharmacy is invariably just a click and a credit-card payment away.

According to a report published in 2006 by the United Nations’ International Narcotics Control Board, the misuse of pharmaceutical drugs now outstrips the trade in illicit substances globally. As many as a tenth of these “medicines” the UN estimates to be counterfeits – crude, even dangerous, chemical copies of generic drugs manufactured by criminals in the Third World. The UN report explains this growth as a guerrilla response to the “war on drugs” fuelled by improved electronic communications.

Parliament is at last waking up to the problem. Dr Brian Iddon MP, chair of the House of Commons all-party group on drugs misuse, is carrying out the first proper assessment of prescription and OTC drug abuse in this country. A scientist by training, with degrees in chemistry, Iddon understands the problem better than most MPs. He reports a surge in intravenous Valium and Prozac abuse by crack

addicts in his Bolton constituency who use tranquillisers and antidepressants to soften their comedown. Iddon's group hopes to publish its report in the spring.

Iddon, whose committee is considering the findings carefully and has already received evidence from many users and their families, says: "Whatever happens in the USA comes to the UK, usually about 5-10 years later. So my guess is that we're heading for the rates of misuse of legal substances that the USA is seeing now. The internet supplies the drugs if doctors will not, or if patients do not want their doctors to know what they are up to. Anything is available on the internet, and there is little control of internet pharmacies or wholesale suppliers.

"The DoH has produced guidance for doctors which is still being ignored. For those who become addicted there should be more access to treatment. The NTA [National Treatment Agency] should treat all those with problems caused by 'misuse' of any substance – legal or illegal, including prescription medicines and OTCs, as well as alcohol."

But the pharmaceutical companies have a responsibility too. The MHRA yellow-card scheme is slow to pick up problems and, even when adverse reactions to a new medicine start to come in to the MHRA, it has little power to take action against the drugs companies. Not that a parliamentary report will do a lot to tackle the root of the matter: our proclivity as a species to seek chemical solutions to our chronic discontents. Harry Shapiro, who heads DrugScope, a British charity that offers advice on addiction issues, blames the rise in prescription and OTC drug abuse on our increasing tendency "to medicalise feelings which can't simply be wished away by swallowing a pill". Then again, depriving the desperately unhappy of what may turn out to be bad solutions won't work either, Iddon believes. "What on earth do we prop these people up with, then?" This is not a purely rhetorical question. Iddon has seen blue-sky policy documents, so-called "foresight programmes", drawn up by the old Department of Trade and Industry, that call on drugs companies to invent a "safe" recreational drug: a happy high with no side effects and no risk of dependency. It could signal the beginning of the end of the war on drugs. It could also take us one step nearer to the zonked anaesthesia of Aldous Huxley's *Brave New World*. More soma, anyone?