

Beware witchdoctors

Are you a victim of placebo's evil twin? **Helen Pilcher** reports

Late one night in a small Alabama cemetery, Vance Vanders* had a run-in with the local witch doctor, who wafted a bottle of unpleasant-smelling liquid in front of his face, and told him he was about to die and that no one could save him.

Back home, Vanders took to his bed and began to deteriorate. Some weeks later, emaciated and near death, he was admitted to the local hospital, where doctors were unable to find a cause for his symptoms or slow his decline. Only then did his wife tell one of the doctors, Drayton Doherty, of the hex.

Doherty thought long and hard. The next morning, he called Vanders's family to his bedside. He told them that the previous night he had lured the witch doctor back to the cemetery, where he had choked him against a tree until he explained how the curse worked. The medicine man had, he said, rubbed lizard eggs into Vanders's stomach, which had hatched inside his body. One reptile remained, which was eating Vanders from the inside out.

Doherty then summoned a nurse who had, by prior arrangement, filled a large syringe with a powerful emetic. With great ceremony, he inspected the instrument and injected its contents into Vanders' arm. A few minutes later, Vanders began to gag and vomit uncontrollably. In the midst of it all, unnoticed by everyone in the room, Doherty produced his *pièce de résistance* – a green lizard he had stashed in his black bag. “Look what has come out of you Vance,” he cried. “The voodoo curse is lifted.”

Vanders did a double take, lurched

backwards to the head of the bed, then drifted into a deep sleep. When he woke next day he was alert and ravenous. He quickly regained his strength and was discharged a week later.

The facts of this case from 80 years ago were corroborated by four medical professionals. Perhaps the most remarkable thing about it is that Vanders survived. There are numerous documented instances from many parts of the globe of people dying after being cursed.

With no medical records and no autopsy results, there's no way to be sure exactly how these people met their end. The common thread in these cases, however, is that a respected figure puts a curse on someone, perhaps by chanting or pointing a bone at them. Soon afterwards, the victim dies, apparently of natural causes.

Voodoo nouveau

You might think this sort of thing is increasingly rare, and limited to remote tribes. But according to Clifton Meador, a doctor at Vanderbilt School of Medicine in Nashville, Tennessee, who has documented cases like Vanders, the curse has taken on a new form.

Take Sam Shoeman*, who was diagnosed with end-stage liver cancer in the 1970s and given just months to live. Shoeman duly died in the allotted time frame – yet the autopsy revealed that his doctors had got it wrong. The tumour was tiny and had not spread. “He didn't die from cancer, but from believing he was dying of cancer,” says Meador. “If everyone treats you as if you are dying, you

buy into it. Everything in your whole being becomes about dying.”

Cases such as Shoeman's may be extreme examples of a far more widespread phenomenon. Many patients who suffer harmful side effects, for instance, may do so only because they have been told to expect them. What's more, people who believe they have a high risk of certain diseases are more likely to get them than people with the same risk factors who believe they have a low risk. It seems modern witch doctors wear white coats and carry stethoscopes.

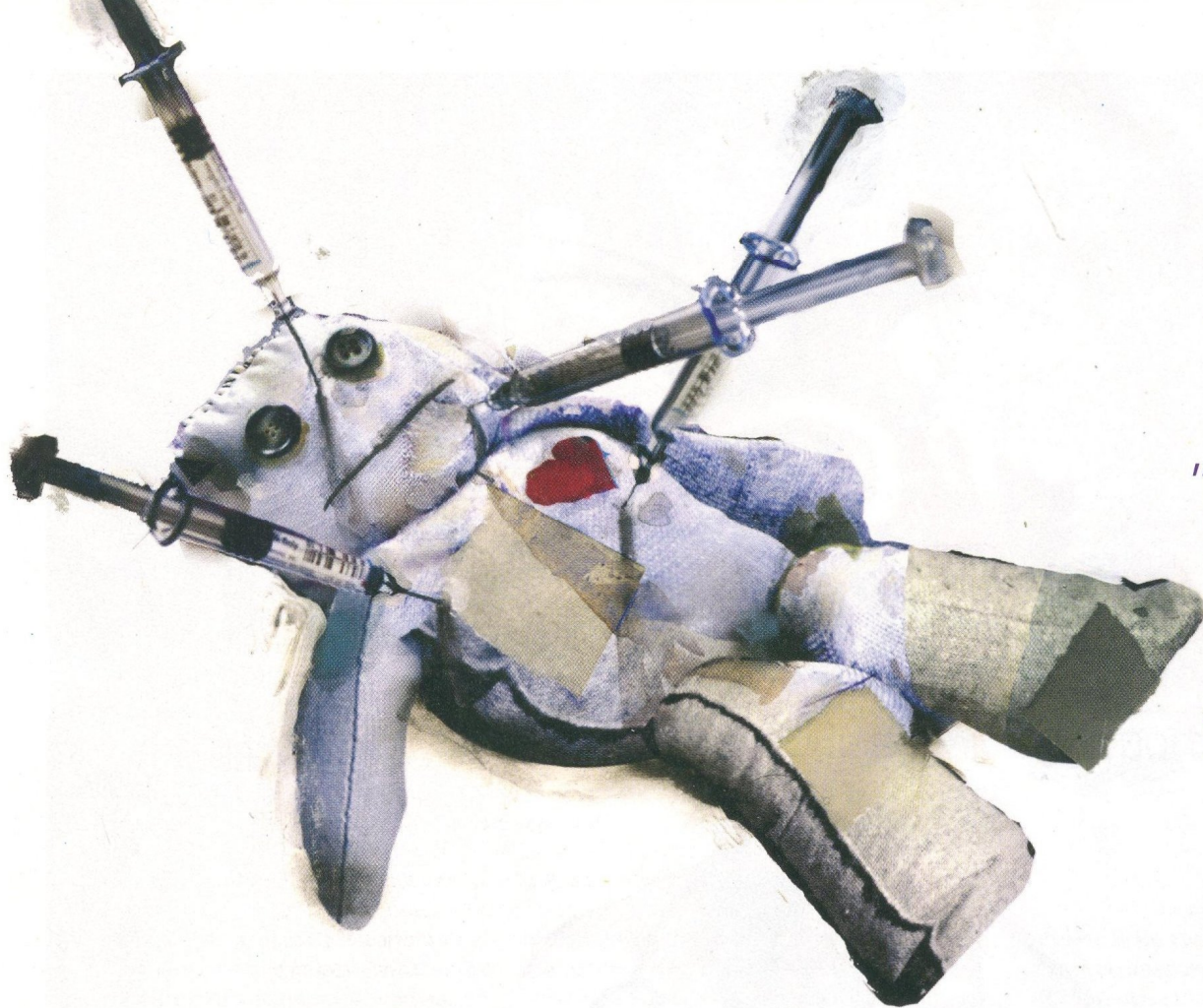
The idea that believing you are ill can make you ill may seem far-fetched, yet rigorous trials have established beyond doubt that the converse is true – that the power of suggestion can improve health. This is the well-known placebo effect. Placebos cannot produce miracles, but they do produce measurable physical effects.

The placebo effect has an evil twin: the nocebo effect, in which dummy pills and negative expectations can produce harmful effects. The term “nocebo”, which means “I will harm”, was not coined until the 1960s, and the phenomenon has been far less studied than the placebo effect. It's not easy, after all, to get ethical approval for studies designed to make people feel worse.

What we do know suggests the impact of nocebo is far-reaching. “Voodoo death, if it exists, may represent an extreme form of the nocebo phenomenon,” says anthropologist Robert Hahn of the US Centers for Disease Control and Prevention in Atlanta, Georgia, ►



DAVID HOLLERBACH



“He didn’t die from cancer but from believing he was dying of cancer”

who has studied the nocebo effect.

In clinical trials, around a quarter of patients in control groups – those given supposedly inert therapies – experience negative side effects. The severity of these side effects sometimes matches those associated with real drugs. A retrospective study of 15 trials involving thousands of patients prescribed either beta-blockers or a control showed that both groups reported comparable levels of side effects, including fatigue, depressive symptoms and sexual dysfunction.

A similar number had to withdraw from the studies because of them.

Occasionally, the effects can be life-threatening (see “The overdose”, below). “Beliefs and expectations are not only conscious, logical phenomena, they also have physical consequences,” says Hahn.

Nocebo effects are also seen in normal medical practice. Around 60 per cent of patients undergoing chemotherapy start feeling sick before their treatment. “It can happen days before, or on the journey on

the way in,” says clinical psychologist Guy Montgomery from Mount Sinai School of Medicine in New York. Sometimes the mere thought of treatment or the doctor’s voice is enough to make patients feel unwell. This “anticipatory nausea” may be partly due to conditioning – when patients subconsciously link some part of their experience with nausea – and partly due to expectation.

Alarming, the nocebo effect can even be catching. Cases where symptoms without an identifiable cause spread through groups of people have been around for centuries, a phenomenon known as mass psychogenic illness. One outbreak (see “It’s catching”, right) inspired a recent study by psychologists Irving Kirsch and Giuliana Mazzoni of the University of Hull in the UK.

They asked some of a group of students to inhale a sample of normal air, which all participants were told contained “a suspected environmental toxin” linked to headache, nausea, itchy skin and drowsiness. Half of the participants also watched a woman inhale the sample and apparently develop these symptoms. Students who inhaled were more likely to report these symptoms than those who did not. Symptoms were also more pronounced in women, particularly those who had seen another apparently become ill – a bias also seen in mass psychogenic illness.

THE OVERDOSE

Depressed after splitting up with his girlfriend, Derek Adams* took all his pills... then regretted it. Fearing he might die, he asked a neighbour to take him to hospital, where he collapsed. Shaky, pale and drowsy, his blood pressure dropped and his breaths came quickly.

Yet lab tests and toxicology screening came back clear. Over the next 4 hours Adams received 6 litres of saline, but improved little.

Then a doctor arrived from the clinical trial of an antidepressant in which Adams

had been taking part. Adams had enrolled in the study about a month earlier. Initially he had felt his mood buoyed, but an argument with his ex-girlfriend saw him swallow the 29 remaining tablets.

The doctor revealed that Adams was in the control group. The pills he had “overdosed” on were harmless. Hearing this, Adams was surprised and tearfully relieved. Within 15 minutes he was fully alert, and his blood pressure and heart rate had returned to normal.

The study shows that if you hear of or observe a possible side effect, you are more likely to develop it yourself. That puts doctors in a tricky situation. "On the one hand people have the right to be informed about what to expect, but this makes it more likely they will experience these effects," says Mazzoni.

This means doctors need to choose their words carefully so as to minimise negative expectations, says Montgomery. "It's all about how you say it."

Hypnosis might also help. "Hypnosis changes expectancies, which decreases anxiety and stress, which improves the outcome," Montgomery says. "I think hypnosis could be applied to a wide variety of symptoms where expectancy plays a role."

Is the scale of the nocebo problem serious enough to justify such countermeasures? We just don't know, because so many questions remain unanswered. In what circumstances do nocebo effects occur? And how long do the symptoms last?

It appears that, as with the placebo response, nocebo effects vary widely, and may depend heavily on context. Placebo effects in clinical settings are often much more potent than those induced in the laboratory, says Paul Enck, a psychologist at the University Hospital in Tübingen, Germany, which suggests the nocebo problem may have profound effects in the real world. For obvious reasons, though, lab experiments are designed to induce only mild and temporary nocebo symptoms.

Real consequences

It is also unclear who is susceptible. A person's optimism or pessimism may play a role, but there are no consistent personality predictors. Both sexes can succumb to mass psychogenic illness, though women report more symptoms than men. Enck has shown that in men, expectancy rather than conditioning is more likely to influence nocebo symptoms. For women, the opposite is true. "Women tend to operate more on past experiences, whereas men seem more reluctant to take history into a situation," he says.

What is becoming clear is that these apparently psychological phenomena have very real consequences in the brain. Using PET

IT'S CATCHING

In November 1998, a teacher at a Tennessee high school noticed a "gasoline-like" smell, and began complaining of headache, nausea, shortness of breath and dizziness. The school was evacuated and over the next week more than 100 staff and students were admitted to the local emergency room complaining of similar symptoms.

After extensive tests, no medical explanation for the reported illnesses could be found. A questionnaire a month later revealed that the people who reported symptoms were more likely to be female, and to have known or seen a

classmate who was ill. It was the nocebo effect on a grand scale, says psychologist Irving Kirsch at the University of Hull in the UK. "There was, as far as we can tell, no environmental toxin, but people began to feel ill."

Kirsch thinks that seeing a classmate develop symptoms shaped expectancies of illness in other children, triggering mass psychogenic illness. Outbreaks occur all over the world. In Jordan in 1998, 800 children apparently suffered side effects after a vaccination and 122 were admitted to hospital, but no problem was found with the vaccine.

scans to peer into the brains of people given a placebo or nocebo, Jon-Kar Zubieta of the University of Michigan, Ann Arbor, showed last year that nocebo effects were linked with a decrease in dopamine and opioid activity. This would explain how nocebos can increase pain. Placebos, unsurprisingly, produced the opposite response.

Meanwhile, Fabrizio Benedetti of the University of Turin Medical School in Italy has found that nocebo-induced pain can be suppressed by a drug called proglumide, which blocks receptors for a hormone called cholecystokinin (CCK). Normally, expectations of pain induce anxiety, which activates CCK receptors, enhancing pain.

The ultimate cause of the nocebo effect, however, is not neurochemistry but belief. According to Hahn, surgeons are often wary of operating on people who think they will die – because such patients often do. And the mere belief that one is susceptible to a heart attack is itself a risk factor. One study found that women who believed they are particularly prone to heart attack are nearly four times as likely to die from coronary conditions than other women with the same risk factors.

Despite the growing evidence that the nocebo effect is all too real, it is hard in this rational age to accept that people's beliefs can kill them. After all, most of us would laugh if a strangely

attired man leapt about waving a bone and told us we were going to die. But imagine how you would feel if you were told the same thing by a smartly dressed doctor with a wallful of medical degrees and a computerful of your scans and test results. The social and cultural background is crucial, says Enck.

Meador argues that Shoeman's misdiagnosis and subsequent death shares many of the crucial elements found in hex death. A powerful doctor pronounces a death sentence, which is accepted unquestioningly by the "victim" and his family, who then start to act upon that belief. Shoeman, his family and his doctors all believed he was dying from cancer. It became a self-fulfilling prophecy.

"Bad news promotes bad physiology. I think you can persuade people that they're going to die and have it happen," Meador says. "I don't think there's anything mystical about it. We're uncomfortable with the idea that words or symbolic actions can cause death because it challenges our biomolecular model of the world."

Perhaps when the biomedical basis of voodoo death is revealed in detail we will find it easier to accept that it is real – and that it can affect any one of us. ■

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*Names have been changed