Verdi's medical classic, p 1017

VIEWS & REVIEWS

It's time to put the placebo out of our misery

PERSONAL VIEW **Robin Nunn**

We need to stop thinking in terms of placebo. Apparently almost anything can be a placebo, and a wide variety of medical conditions respond to it. Placebos are not even needed to generate placebo-like effects. Secretly injecting morphine, for instance, seems to be less effective than doing the same thing and telling the patient about it (*Nat Rev Neurosci* 2005;6:545-52). When placebo, or any other construct, can be virtually anything, then it just may turn out to be virtually nothing.

Nobody who came and saw the placebo has conquered its definition. This is more than a hint that something is fundamentally wrong. Definitions have failed because attempts to capture the notion of placebo are like attempts to graft more epicycles on an earth centred theory of the universe. No matter how accurate the attempts, the placebo, like the earth, is not at the centre of any meaningful construct. It's time to stop greasing the rusty gears of old notions with placebo oil, time to shift into something new.

Every way of looking at the placebo construct invites criticism, because it doesn't make sense. A placebo is something inert that has an effect. Or something effective that is inert. Of course, this oversimplification invites attacks on the notions of inert and effect. Similarly, to declare that a placebo is something with non-specific effects seems strange. If you can't specify the effects, then how do you know what they are? On the other hand, if you can specify the effects, then they're specific effects. Placebos are often the controls against which drugs are measured in trials. But there are no standard tests to determine that they are placebos.

If something cannot be defined and does not make sense no matter how it is viewed, it's time to ask if it's really there

If something cannot be defined and does not make sense no matter how it is viewed, it's time to ask if it's really there at all. This is not just a matter of words: it's about a whole world view. The placebo construct conceals more than it clarifies. Unfortunately, asking you not to think placebo is like asking you not to think zero.

BERT HARDY/HULTON/GETTY IMAGES

What makes audiences react, and what makes some audience members react more than others?

Here's a thought experiment to zero out the nothingness of the placebo. Imagine that you are a visitor from another world. You observe a human audience for the first time. You notice a man making vocal sounds. He is watched by an audience. Suddenly they burst into smiles and laughter. Then they're quiet. This cycle of quietness then laughter then quietness happens several times. What is this strange audience effect? Not all of the man's sounds generate an audience effect, and not every audience member reacts. You deem some members of the audience to be "audience responders," those who are particularly influenced by the audience effect. What makes them react? A theory of the audience effect could be spun into an entire literature analogous to the literature on the placebo effect. The notion of audience effect serves no purpose, and much of what passes between performer and audience is obscured by constructing an audience effect and related notions such as audience responders. We could learn more about what makes audiences laugh by returning to fundamentals. What is laughter? Why is "fart" funnier than "flatulence"? Why are some people just not funny no matter how many jokes they try? But let's leave the analogy with an audience effect and leap into the post-audience effect, post-placebo world of honest ignorance and clear inquiry.

You may justifiably be reluctant to abandon a notion with such a long history and one that may have served you well. But suppose there is no such unicorn as a placebo. Then what? Just replace the thought of placebo with something more fundamental. For those who use placebo as treatment, ask what is going on. Are you using the trappings of expertise, the white coat and diploma? Are you making your patients believe because they believe in you?

In a post-placebo era, experiments will simply compare something with something else. That is, they will compare experimental conditions: one group gets these conditions and another group gets those conditions. The report of every methodologically acceptable experiment will describe the conditions that have been compared, so that anyone reading the report may try to replicate them. We will reject from consideration any trials that are insufficiently described. Eventually we will have standard descriptions for commonly compared things. We gain transparency, honesty, and clarity.

If we put the placebo construct out of our misery, the implications and opportunities are huge. We need new literature, new textbooks, new training, and new laws that expunge the notion of placebo and replace it with something more fundamental, or we admit that we just don't know. Look clearly at the naked emperor and see the body beneath the nothing that covers it. Why wait?

Robin Nunn is lecturer, Institute for the History and Philosophy of Science and Technology, University of Toronto r.nunn@utoronto.ca

A longer version of this article with references is on bmj.com

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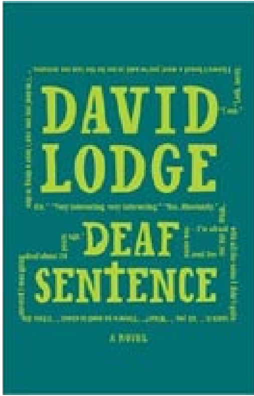
REVIEW OF THE WEEK

Pardon?

David Lodge's latest novel is the most interesting literary work on deafness since Oliver Sacks's *Seeing Voices,* says **John Quin**



Deaf Sentence
David Lodge
Harvill Secker, £17.99, pp 294
ISBN 978-1846551673
Rating: ★★★☆

What's that you say? Not another novel from David Lodge? Britain's answer to John Updike is back and on form. Critic, essayist, dramatist, and novelist, he is thus pompously labelled with all those poncy P words, like prodigious and protean. Now we learn in his acknowledgments that, more profoundly, he is hard of hearing. This then informs his new novel, which characterises deafness as essentially comic. Lodge has always been a funny guy—he's here to amuse us, and *Deaf Sentence* has its fair share of guffaws. Being by Lodge the book also gives you his persistent obsessions: the campus, Catholicism, literary theory, and linguistics are all present and correct. Obscure words such as "phatic" are casually placed for you to dig out the dictionary, and there's his guilt ridden sex, or as he might call it houghmagandy, that has troubled his texts since *How Far Can You Go?*

Professor Desmond Bates is our unreliable narrator, trapped in an unreliable auditory world and plagued by even more unreliable emails. He says "what" a lot: "Like most deaf people he's got into the habit of saying 'what?' automatically to every conversational gambit." Bates is a cranky curmudgeon, a grumpy old man who compares his trials to those of Goya and Beethoven and whose hero is Scrooge. His inner despair and his wretched deafness make him, like Beethoven, seem "outwardly" to be "such a grouchy unsociable bastard." In the late Goya he sees deafness as an "imminent, inevitable, inexorable suffocation."

Lodge is excellent on the farcical potential of hearing aids. He ruthlessly mocks their inefficiency and inconvenience, the duff batteries, the high pitched feedback

Bates finds retirement tougher than he thought; he misses the structure of his week and mildly resents his wife, Fred, in her ongoing success in an interior design business. Fred accuses him of avoiding conversation: "I know it was very noisy in there, but it sometimes seems to me that you've almost given up *wanting* to hear what other people are saying—deafness is a convenient excuse to switch off and follow your own school of thought." This has the authentic tone of something I suspect has been said at some point to the author.

Lodge is excellent on the farcical potential of hearing aids. He ruthlessly mocks their inefficiency and inconvenience, the duff batteries, the intermittent high pitched feedback, the horrors of a night at the cinema or the theatre, and the ultimate challenge: simply answering the phone. Bates/Lodge sees deafness as "a kind of pre-death, a drawn-out introduction to the long silence into which we will all eventually lapse." Puns on death/deaf are then piled on like so many handfuls of dirt on a grave, so we get as your starter for 10 points "deaf in Venice" and then bonus points for "deaf in the afternoon," "I had not thought deaf had undone so many," and "half in love with easeful deaf."

Bates sees an ear, nose, and throat consultant, Mr Hopwood, a "stout, moustached, bald-headed man with a slightly harassed manner" who sits "in his waistcoat behind a cluttered desk." Hopwood tells him cheerfully that the cause of his deafness is only of academic interest, as "there's no cure." In an aside Bates comments: "Interesting that 'academic' should have that meaning of 'useless.' Be careful then what you say to a linguist or a novelist as patient."

Bates, seemingly upstanding and rigid, rails against the inanities of the modern world and is pestered by a loopy American postgraduate called Alex, demanding help with her thesis on the linguistic structure of suicide notes. He struggles with temptation and a descent into shame and humiliation. If these trials were not enough, Bates also has had to juggle with caring for his increasing demented 80 something father, who is deaf too. Lodge is fine on male neglect here—the world of soiled cardigans, frayed shirts, trousers that can stand up by themselves, the rows of empty shelves in the fridge. Then there is the tiring hunt for a residential care home, the readmission after another stroke. A houseman, Wilson, says that the consultant, Dr Kannangra, will "probably suggest inserting a PEG tube." And then poor Bates realises that the decision puts the onus on him: "I have to decide whether he lives or dies." But then we learn that Bates has been here before, with his first wife, Maisie, who died of cancer. The author thus deftly introduces, late in the novel, the tricky subject of assisted suicide. Lodge almost casually introduces this ethical dilemma, which with a lightness of touch near conceals the immensity of the decision for a Catholic such as himself.

This is the most interesting literary work on deafness since Oliver Sacks's *Seeing Voices: A Journey into the Land of the Deaf* (1989). One star is docked, though, for the linguist Bates's persistent and irritating use of the word "thick" to describe accents from anywhere north of Watford—but then, as noted, he is unreliable.

John Quin is consultant physician, Royal Sussex County Hospital, Brighton **Jdquin@aol.com**

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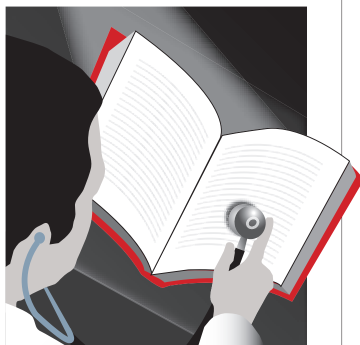
The cup of immoderation

BETWEEN THE LINES
Theodore Dalrymple



I hardly let a day go by without a glass or two of wine, and therefore I believe strongly (because I want to) in the J shaped curve of mortality versus alcohol consumption. Teetotallers are harming their health. As for moderation, its definition is clear: it is the habitual consumption of one drink more than the number I am drinking at the time.

Still, when I behold the scenes observable in the centre of every British town and city on Friday and Saturday nights, I begin to long for a revival of the temperance movement and for a reincarnation of the Reverend John Davis, who in 1843 delivered a lecture in Pembroke in Wales, later published in Haverfordwest, which he described modestly as "a Mite cast into the Teetotal Treasury with a view to promoting the prosperity of the cause of Total-Abstinence."

What fiery rhetoric, what eloquence! Replying to those who profit from the spirit, wine, and beer trades—maltsters, brewers, publicans, spirit merchants, and jerry lords, as he calls them—and who claim that there is no positive command in the Bible to abstain from drinking alcoholic beverages, he asks them, "And who has commanded [you] to carry on a traffic that is ruinous to bodies and souls?"

In other words, it is necessary to interpret the Bible in the light of reason and not literally.

The Reverend Davis reserves his greatest eloquence for the personage he calls Dr Moderation, who misleads people into supposing that there is no harm in a cup or two and who is in fact Abstinence's most dangerous enemy.

"The moderate drinker, however moderate . . . does himself harm, as he exposes himself to temptation, and throws himself liable to the snares where others have been caught and entangled. He is walking upon the very margin of the precipice; only one short step farther, one glass more, one additional cup and there he is a sot; he is precipitated into the abyss of drunkenness and ruin.

"He walks upon hot coals, he bears them in his bosom, and is he not in danger of being burnt? He is playing with the coiled serpent, and is he not in danger of being wounded by her sting, and poisoned by her venom? What is moderation? Or how far may a man go in drinking intoxicating fluids, and still keep within the bounds of moderation? Fix upon any quantity, say for instance, that he may take four pints, or four glasses, and still be a moderate man; well, now tell me what is the fifth pint, or the fifth glass? This of necessity must be the cup of immoderation, or of intoxication. O how short is the distance, how narrow the space between the superlative of moderation and the positive of immoderation? And indeed having taken the fourth glass, I would not be a surety that he will not take the fifth. Thus, certainly the moderate man does himself harm."

Nowhere does the Reverend Davis consider the possibility that alcohol might have some advantages that offset its disadvantages

Three things occur to me. The first is to wonder whether such eloquence is to be found in Pembroke today. The second is that nowhere does the Reverend Davis consider the possibility that alcohol might have some advantages that offset its disadvantages. The third is that he regards a danger of suffering a harm as equivalent to actually suffering it. And this, of course, is a permanent temptation to those who, like the Reverend Davis, ask whether, "if it is our duty to prevent evil, it is not our duty to expel evil, and banish it from our otherwise happy land?"

Theodore Dalrymple is a writer and retired doctor

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MEDICAL CLASSICS

Rigoletto By Giuseppe Verdi

First performed 1851

The eponymous hero of this 19th century Italian opera is a tragic, lonely, and self absorbed figure, embittered by society's prejudice against his physical disfigurement and paranoid from a curse brought on by mocking the misfortune of a man whose daughter was dishonoured. He's also a working class single parent with difficulty forming relationships; add to that a pathological grief reaction to his wife's untimely death and a stifling attachment to his teenage daughter, Gilda. Rigoletto may have a day job as a court jester, but he would make a meaty long case in any postgraduate psychiatry examination.

Verdi's most popular opera oozes sex and debauchery (either subliminal or in your face: the first act is variously depicted as "feast" or "orgy," depending on the libretto). It switches between the opulent courts in which Rigoletto performs to the backstreet hovel where he keeps his daughter locked up and to which he returns to guard her by night. Moving disjointedly between these worlds like the misfit he is, Rigoletto forms a powerful main character whose vulgarity, cynicism, and primal urges stand for the dark side in us all.

You don't need the whole plot to grasp the salient medical details. The courtiers find it unacceptable that Rigoletto should be keeping a beautiful "mistress" indoors when he's not only poor but has a spinal deformity and a mental health problem. They trick the hunchback into helping them kidnap Gilda, who ends up defiled, stabbed, and in a sack before the opera ends.

How should the imperfect be allowed to love?

ALASTAIR MUIR/REX FEATURES

With its debut performance in 1851, a sexual double standard came as standard. In Act III the playboy duke offers us "La donna e mobile"—"Fickle is woman fair/Like feather wafted/ Changeable ever/Constant, ah, never"—to justify his repeated conquests.

The question this opera raises (and perhaps the real reason why it was originally banned as obscene) is to what extent, and in what way, should the imperfect be allowed to love. At a time when it was not uncommon for people with severe deformities to be smothered at birth, Verdi's depiction of a twisted, passionate sexuality in such a person offered plenty to shock "decent" people.

Yet Rigoletto is also a tender father whose altruistic devotion to his daughter is, on another level, entirely respectable and admirable. The family income is modest, and he could do with an anger management course, but even the most assiduous social workers would find it hard to find serious fault with his parenting. In a scene where Rigoletto's richer, more able bodied rivals justify taking away his innocent and beautiful prize on the grounds that he himself is neither, Verdi manages to engender a sense of social injustice even in the most hardened aristocrats—and therein lies the opera's enduring message.

Trisha Greenhalgh, professor of primary health care, University College London p.greenhalgh@pcps.ucl.ac.uk

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Pride and prejudice

FROM THE FRONTLINE
Des Spence

The mind's inner eye struggles with the ageing reality in the mirror. For we are products of our time and end up as just rusting outdated models. Attempts to revamp our image with skinny jeans and haircuts are always an embarrassing disaster, so we revert to form: same haircut, same newspapers, same choices in restaurants, and same music. Likewise it is hard to change opinions forged in our youth, for these are based more on emotion than reason. Thankfully most of us have insight into these weaknesses. It is not, therefore, the prejudiced that I am weary of but those who claim to be without prejudice.

Can we change doctors' opinions about relations with the drug industry? A new online training programme, called Pharmalyzer ("Are you prescribing under the influence?"), attempts to do just this (http://pharmedout.org). The module runs through the techniques the industry uses to influence prescribing, though in the language of medical Americana: how to build brand loyalty, the "evergreening" of patents, cynical rebranding of racemic isomers, the "me too" drugs offering phoney improvements, marketing masquerading as postgraduate education, research tricks, disease mongering, and "friendship," the omnipresent foot in the door of drug selling.

Its conclusion is that that we should stop seeing drug company representatives, for contact is just bad medicine for doctors and patients alike. Can this education programme change anything? Most of the visitors to this module will be likeminded ideologues who will enjoy bolstering their cheerfully admitted prejudices against spivvy Big Pharma. But regrettably those that deny that they are personally influenced by the industry and who claim to be blessed with a superior intellect that can see through the marketing will rather spend their time being educated over a free pharma lunch.

We need something more direct than yet more education. This government, so intent on micromanaging and regulating our medical lives, hasn't acted, despite drug scandals and medicalisation. It is too weak to tackle a politically influential drug industry. So let our beleaguered institutions—the General Medical Council, the royal colleges, and the BMA—show political leadership and do the right thing by endorsing a no drug representative policy for all UK doctors. Until then, let the Pharmalyzer module at least be an interesting addition to our "validated stakeholder 360 degree" annual appraisal in this new era of tick box professionalism.

Des Spence is a general practitioner, Glasgow destwo@yahoo.co.uk

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Safe passage

THE BIGGER PICTURE
Mary E Black

All my life I have wanted to see the Panama canal, and last week I finally made it and stood, amazed, on the viewing dock above the two-stage Miraflores locks on the Pacific side. Container ships, after a patient wait in the holding area, are guided through the narrow channel by a team of four small silver trains, two on each side, with guy ropes tied to bow and stern. The actual transit is short, measured in minutes. It is a simple process yet highly skilled. The laden ships can float, but to avoid colossal damage they get a little help from time to time. It is an organisational miracle.

Which brings me to birth. Pregnancy is a period of preparation; and at the end women enter the waiting area knowing that birth is imminent but not exactly when (unless, like the ships that pay extra to get a defined date and jump the queue, you book an elective caesarian section). You hope that the passage is straightforward and your guides are expert. You hope you will not get stuck. I had better stop now as analogies can run too far.

I am not, by the way, advocating high tech, mechanised labour for all. I had two midwife led water births at home but with expert care minutes away and within health systems that had programmes for planned home delivery. In contrast my sister would have died in labour without the highest level of surgical delivery and hospital care. What we had in common was this: we were healthy and well cared for, our voices were heard, and we both entered the process of giving birth with a professional team in place to intervene as required.

The Panama canal is so well run that cases of damage to the boats that pass are remarkably few: passage might be a randomly awful experience; instead it is almost routine. Things can go wrong in pregnancy and childbirth, but most do not need to. Yet more than half a million women—one woman each minute—die from pregnancy related causes each year. Most deaths are in developing countries and have been medically preventable for decades: bleeding (25%), infections (13%), unsafe abortions (13%), eclampsia (12%), obstructed labour (8%), other direct causes (8%), and indirect causes such as malaria, anaemia, HIV and AIDS, and cardiovascular disease (20%). The underlying causes are also preventable: poverty, malnutrition, displacement, and discrimination against women. A third of pregnant women go into labour without a skilled attendant.

If we can build and run the Panama canal for our ships, and if pregnant women in the developed world can labour safely, why have we failed women in developing countries? Our boats and our babies should make passage safely.

Mary E Black is a public health physician, Belgrade, Serbia drmaryblack@gmail.com

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