

## From the Editor

### The placebo effect

*I have great success with placebos.*

Dr Clifford Hawkins, physician and raconteur  
(1915–91)

The origin of the word ‘placebo’, although in everyday use and with a clear meaning, remains obscure. A positive response to placebo treatment is common, but there is a wide variation in the rate of this response. The variation is in part due to random chance and differs with the sample size in the placebo and treatment groups.<sup>1</sup> How does the placebo response exert its effect?

In controlled trials of medical treatment for organic disease, a positive response is usually found in the placebo-treated group. Such positive responses in both the treatment and placebo groups, although variable in degree, are often reported in the meta-analysis of specific medical treatment, for example in active Crohn’s disease. It can be found in trials of specific medical treatment and also in meta-analysis of the placebo rates of remission and response in clinical trials of all active treatments for Crohn’s disease.<sup>2,3</sup> Overall remission rates in the placebo-treated group were 18% (95% confidence interval 14–24%) with response rates in the placebo group of 19% (95% confidence interval 13–28%).<sup>4</sup>

In these studies the placebo response rates varied according to the study duration, the number of study visits and disease severity at entry to the study, but no single factor could account for all the heterogeneity.<sup>4</sup> Spontaneous remission as part of the natural history of the underlying disorder may explain some of the improvement observed in both the treatment and placebo groups.

The nature of the placebo response and how it might be harnessed to good effect in functional disease and pain relief has recently received particular attention.<sup>5</sup> The kindly general practitioner

of old, listening carefully and patiently while prescribing either the red or green placebo medicine, appreciated the importance of some aspects of the placebo response. One patient recently encapsulated this aspect by commenting after his examination, ‘Thank you, doctor, I feel much better now’.

Can the nature and the power of the placebo response be harboured and applied in current day practice? Miller and Rosenstein from the Department of Clinical Bio Ethics at the National Institute of Health believe that it can.<sup>6</sup> For subjective outcomes, eg pain, we might expect patients to feel better after placebo treatment if the doctor or nurse were kind to them, appeared authoritative, or if the placebo was given, for example, as a large red pill instead of a small white one. An injection rather than a tablet might also exert a more positive effect. Exceedingly large trials, however, would be needed to show any effect independent of random chance.<sup>1</sup> The reality is that random chance alone can produce a wide range of responses.<sup>7</sup>

Ingenious attempts have been made by meta-analysis to compare the outcome in controlled trials where the control was either ‘placebo treatment’ or ‘no treatment’. Disappointingly, there was no evidence that placebo intervention (as compared to no treatment) had any clinically important effects. A possible benefit in outcome, particularly for treatment of pain, could not be clearly distinguished from random bias.<sup>8</sup> These data have recently been updated and the original findings confirmed.<sup>9</sup>

The other approach is to compare treatments which include care, attention and time but limited medical benefit with placebo treatment. In such controlled studies of homeopathy, for example, there was weak evidence for the specific effect of homeopathic remedies, but the findings were compatible with the notion that the clinical effects of homeopathy are placebo effects.<sup>10</sup>

Studies of the placebo response may include

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linguistics, philosophy<sup>11</sup> and psychology.<sup>12</sup> Those interested in pursuing the topic can do no better than read the review by McQuay and Moore from the Pain Research Unit, Department of Anaesthetics, University of Oxford.<sup>1</sup>

What was the nature of Clifford Hawkins' perceived success with placebo? He had a particular interest in functional bowel disease and was patient, tolerant, sympathetic and good humoured. Of course, only an exceedingly large controlled trial could determine whether this was the basis of his success!

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ROBERT ALLAN