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The better-than-nothing idea: debating the use of placebo controls

Later this month, participants at a national conference will attempt to craft a coherent policy on the use of placebo in randomized controlled trials, one that will iron out the inconsistencies that have plagued attempts to reconcile the *Declaration of Helsinki*, the *Tri-Council Policy Statement*, and the made-in-the-FDA guidance of the International Conference on Harmonisation.[1] The placebo debate, which has been smouldering since the lightning-strike of Rothman and Michels' critique in 1994,[2] has been described as a conflict between goal-based and duty-based thinking.[3] Arguments for the use of placebo posit scientific rigour as a goal that may, ethically, guide practice; the counterargument, expressed by Charles Weijer[4] among others (see page 603), is that the physician's duty to the research participant *qua* patient is paramount.

Of course, individual patients have a stake in medical progress, and physicians have a duty to foster the integrity of that progress. Research that has no hope of yielding useful results cannot be considered ethical. Placebo controls have been defended strenuously on methodologic grounds — e.g., that they permit smaller studies, thus exposing fewer participants to potential harm, and that they allow the placebo effect and side-effects to be distinguished more cleanly. Just as strenously, these claims have been disputed.[5] Emanuel and Miller[6] have attempted to define a middle ground, where placebo could be used in the presence of proven effective therapy, but only when it is methodologically compelling to do so and provisions are made to obviate potential harm. However, this middle ground seems firm only where risks are small — in trials of the treatment of allergic rhinitis, for example.

One might argue that to disallow exposure even to minimal risk in a placebo trial arm undermines the very notion of informed consent and assumes that patients who enrol in clinical trials have no altruistic concern for the patients of the future. At the same time, we should remember that science is a creature of our own making, invented to serve our own pragmatic purposes, such as helping ill people become well. Interesting that science in its pure (that is, imaginary) state is a creature so unlike us: without allegiance, opinion, ego or moral valence. Ultimately, the placebo debate seems to be about what kind of admittance this creature should gain into the clinic or hospital ward. For it is in the name of scientific rigour that psychotic patients have had their medications withheld and patients with parkinsonism have undergone the sham implantation of fetal cells, with the attendant risks of surgery, anesthesia and medication. For clinicians to deal in abstractions such as "the cause of science" sits uneasily with the primary duty of care; otherwise, as some commentators seem happy to imply, clinical researchers are ethically distinct from physicians.[6]

Ultimately, the best test of the appropriateness of including a placebo arm in a trial design will be whether the patient's consent to participate can be confidently given, and whether the clinician's request for that consent arises from a state of clinical equipoise and of moral equilibrium. — *CMAJ*

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