This paper outlines and analyses ethical issues associated with human (infection) challenge studies. Responding to the concern that challenge studies might be considered ethically objectionable because they involve intentional harm of research participants, it demonstrates why there should be no in-principle ethical objection to human challenge studies—and argues that this kind of research might even be ethically required. While numerous infamous historical examples of research involving human subjects involved the direct infection (and/or microbial exposure) of human participants, it was not intentional infection (and/or microbial exposure) of participants per se that made these studies wrong. Human infection challenge studies are nonetheless ethically sensitive, and thus warrant additional ethical vigilance—e.g. via establishment of specific research ethics guidelines and/or special review procedures.