

# Researchers as guinea pigs

## *Self-experimentation in Australia is alive and well*

MANY ADVANCES IN MODERN MEDICINE owe a great deal to human experimentation. Indeed, much of biomedical research is irrelevant to mainstream medicine unless its clinical utility is established through human experimentation, for, as observed by the English essayist Alexander Pope, “the proper study of mankind is man.”<sup>1</sup>

Today the circumstances and conduct of human experimentation are painstakingly policed by ethics committees, but even such strict surveillance cannot guarantee safety: “because experiments with humans are voyages into the unknown, an element of risk is always involved; the potential for death, injury, or illness can be reduced, but it can not be eliminated.”<sup>2</sup> It is this very uncertainty that presents a dilemma for researchers. Sir George Pickering, past Regius Professor of Medicine at Oxford, delineated this quandary: “The experimenter has one golden rule to guide him . . . Is he prepared to submit himself to the procedure? If he is, and if the experiment is actually carried out on him, then it is probably justifiable. If he is not, then [it] should not be done.”<sup>2</sup> In short, the researcher should be the guinea pig.

Risk-laden stories of researchers being guinea pigs abound in medicine’s heritage. They include that of John Hunter, the 18th-century English anatomist and surgeon, who allegedly inoculated himself with venereal pus. The symptoms of gonorrhoea and primary syphilis were soon apparent and during the last 15 years of his life he was plagued by a legacy of angina pectoris presumably due to tertiary syphilis.<sup>2,3</sup> Other celebrated accounts include that of Werner Forssmann, who, in the 1920s, catheterised his heart with ureteric tubes. This risk-laden technique lay fallow until the 1940s, when Cournand and Richards in the United States refined and employed it in ground-breaking work in cardio-respiratory physiology. In 1956, all three were awarded the Nobel Prize in Medicine or Physiology.<sup>2</sup>

In the 1950s the enthusiasm for self-experimentation within the Department of Internal Medicine at Washington University, St Louis, earned it the name the “Kamikaze School of Medicine”.<sup>2</sup> Bill Harrington, a young researcher, courted death from cerebral haemorrhage with profound thrombocytopenia after being infused with plasma from a patient with idiopathic thrombocytopenic purpura (ITP).<sup>2</sup> A fellow researcher, Tom Brittingham III, repeatedly injected himself with leukaemic white cells in an attempt to produce white-cell antibodies. He almost killed himself when he had an anaphylactoid reaction accompanied by profound hypotension and severe pulmonary oedema after being infused with plasma from a patient with aplastic anaemia.<sup>2</sup>

Nonetheless, these unsettling self-experiments established the immune basis of ITP and white-cell-associated transfusion reactions. Harrington’s work inspired Jan Dausset of Paris to pursue research into the immunology of ITP and white cells, which culminated in his being awarded the 1980 Nobel Prize for demonstrating human leukocyte antigen (HLA; the transplantation antigen) in white cells.<sup>2</sup>

Australian researchers have also succumbed to the human guinea pig syndrome.

In 1951, as the first wave of myxomatosis raced along the Murray River, its arrival in Mildura coincided with an outbreak of Murray Valley encephalitis in the surrounding district. The public was gripped by fear that the myxoma virus was responsible for the outbreak of encephalitis. This fear reached such heights that the chairman of Mildura Base Hospital challenged R G Casey, the Minister responsible for the Commonwealth Scientific and Industrial Research Organisation (CSIRO), and Sir Frank Macfarlane Burnet, Director of the Walter and Eliza Hall Institute (WEHI), to test the harmlessness of the myxoma virus on themselves!

Spurred on by intense media pressure, Macfarlane Burnet, Frank Fenner (Professor of Microbiology at the John Curtin School of Medicine, but working at WEHI) and Ian Clunies Ross (Director of the CSIRO) inoculated themselves with enough myxoma virus to kill 100–1000 rabbits. All three suffered no harm, and in true political style this fact was made public by Casey through an announcement in Federal Parliament.<sup>4</sup>

The culture of the Kamikaze School of Medicine was further manifest when Australian clinical researchers performed radiolabelled platelet studies on themselves,<sup>5</sup> or underwent unpleasant bone marrow aspirations to procure marrow cells for drug studies.<sup>6,7</sup> Finally, the experiments of Barry Marshall, who ingested *Helicobacter pylori*,<sup>8</sup> are now legend in medicine. His self-experiments eventually turned prevailing concepts of peptic ulcer causation and treatment on their head.

Now, in the new millennium, the report in this issue of the Journal (page 69) by Landmann and Prociw attests that self-experimentation in Australia is alive and well. In a series of self-experiments these investigators have shown that dog hookworm (*Ancylostoma caninum*) infection causing symptomatic eosinophilic enteritis is more likely to enter the body orally than percutaneously.<sup>9</sup>

What drives researchers to be their own guinea pigs? Lawrence Altman, in his delightful book *Who goes first? The story of self-experimentation in medicine*, proposes a number of motivating factors.<sup>2</sup> These include reliability (researchers being more likely to adhere compulsively to the research protocol), dependability (for observations and detecting problems with design), a spirit of adventure, first-hand experience, self-protection, convenience (avoiding the frustrations of recruiting and being involved in the nuances of informed consent) and experience (when the experiments involve risk, the experience of the researcher is important and many will risk exposing themselves rather than others).

However, self-experiments are subject to criticism.<sup>2</sup> Potential problems include loss of objectivity, cumulative exposure to risks and comorbidities in the self-researcher (including self-experimentation suicide), but particularly the inherent limitations of a research design focusing on a single subject.<sup>10</sup>

Despite all this, researchers who enlist as guinea pigs will continue to grace medical research. Modern research is increasingly complex, with sophisticated designs and statistics, bewildering technology and the added burden of the close monitoring of projects by ethics committees. This impersonal and mechanistic culture is far removed from the humanistic and romantic spirit of adventure embodied in altruistic self-experimentation. As long as human research is informed by the premise that “because we were venturing into the unknown... a man is entitled to risk his own life. He is not entitled to risk somebody else’s”,<sup>2</sup> researchers as guinea pigs will always be with us.

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Editor

*The Medical Journal of Australia*

1. Pope A. In: Parlington A, editor. The Oxford dictionary of quotations. Oxford: Oxford University Press, 1992: 552.
2. Altman LK. Who goes first? The story of self-experimentation in medicine. Berkeley: University of California Press, 1998: 299, 6-8, 313, 38-52, 273-282, 283-296, 288-316, 193.
3. Porter R. The greatest benefit to mankind. A medical history of humanity from antiquity to the present. London: Harper Collins, 1997: 280-281.
4. Burnet M. Changing patterns: an atypical autobiography. Melbourne: William Heinemann, 1982: 110-112.
5. Castaldi PA, Firkin BG. Studies of the life span and fate of platelets. *Aust Ann Med* 1963; 12: 333-341.
6. Van Der Weyden M, Rother M, Firkin B. Megaloblastic maturation masked by iron deficiency: a biochemical basis. *Br J Haematol* 1972; 22: 299-301.
7. Koutts J, Van Der Weyden MB, Firkin BG. Effect of trimethoprim on folate metabolism in human bone marrow. *Aust N Z J Med* 1973; 3: 245-250.
8. Marshall BJ, Armstrong JAY, McGeachie DB, Clancy RJ. Attempt to fulfil Koch's postulates for pyloric campylobacter. *Med J Aust* 1985; 142: 436-439.
9. Landmann JK, Prociw P. Experimental human infection with the dog hookworm, *Ancylostoma caninum*. *Med J Aust* 2003; 178: 69-71.
10. Jasienski M. Wishful thinking and the fallacy of single subject experimentation. *The Scientist* 1996; 10: 10. □

## books received

**Breast cancer screening.** Vainio H, Bianchini F (eds). Lyon: IARC Press, 2002 (xiii + 229 pp \$70) ISBN 9283230078.

**Cancer prevention manual. Simple rules to reduce the risks.** Stephens F. Oxford: Oxford University Press, 2002 (xiii + 138 pp \$29.95) ISBN 019852532X.

**Childhood asthma and other wheezing disorders.** Silverman M (ed). London: Arnold, 2002 (xii + 484 pp \$340) ISBN 0340763183.

**Clinical guide to inherited metabolic diseases.** Clarke JTR. Cambridge: Cambridge University Press, 2002 (xvi + 289 pp \$120) ISBN 0521890764.

**Complementary and alternative medicine secrets.** Kohatsu W. Philadelphia: Hanley and Belfus, 2002 (xiv + 456 pp \$95.15) ISBN 1560534400.

**Contraception health choices. A contraceptive clinic in a book.** Sydney: Choice Books, 2002 (xiv + 152 pp \$22) ISBN 1920705015.

**Cries unheard. A new look at attention hyperactivity deficit disorder.** Halasz G, Anaf G, Ellingsen P, Manne A, Salo FT. Altona, Vic: Common Ground, 2002 (x + 91 pp \$24) ISBN 1863354972.

**Differential diagnosis in obstetric and gynecologic ultrasound.** Bisset

RAL, Khan AN, Thomas NB. London: Elsevier Science, 2002 (xx + 452 pp \$122.98) ISBN 0702026816.

**Don't panic. Anxiety, phobias and tension.** Page A. Sydney: Australian Women's Weekly, 2002 (96 pp \$12.95) ISBN 1876624876.

**Drug interaction facts 2003.** Tatro DS (ed). St Louis: Wolters Kluwer, 2003 (xxviii + 1543 pp \$145.95) ISBN 1574391372.

**European health report 2002.** Copenhagen: World Health Organization, 2002 (v + 156 pp \$68.95) ISBN 9289013656.

**Family practice desk reference.** Driscoll CE, Bope ET (eds). Chicago: AMA Press, 2002 (xi + 1035 pp \$87.50) ISBN 1579471900.

**Get through MRCP Part 1: 1000 MCQs and best of fives.** Coales U. London: Royal Society of Medicine Press, 2002 (vi + 310 pp \$55.50) ISBN 1853155268.

**Good grub. Food for healthy people and a healthy planet.** Furnass B (ed). Canberra: Nature and Society Forum, 2002 (xii + 255 pp \$20) ISBN 0958567425.

**Management of alcohol and drug problems.** Hulse G, White J, Cape G (eds). Melbourne: Oxford University Press, 2002 (xx + 404 pp \$49.95) ISBN 0195513312.