

Chapter 1

Introduction

Clifford D. Packer

Writing Case Reports

There are many good reasons to write case reports: to educate other trainees and physicians; to contribute evidence that could be useful to others for patient care; to learn (and teach) scholarly writing skills; to be the first to describe a new syndrome or a serious adverse drug reaction; to analyze clinical reasoning and decision-making; to propose new hypotheses on mechanisms of disease; to participate in innovative research in personalized medicine; to gain academic recognition and career advancement; and to take part in the historical tradition of case reporting that goes back almost 4000 years.

This book has two purposes. First, it can be used as a comprehensive handbook or guide for anyone interested in writing a medical case report. Chapters [5](#), [6](#), [7](#), [8](#), [9](#), [10](#), [11](#), and [12](#) cover every practical step from conception and case selection (“Is my case good enough?”) to obtaining consent, collecting images and other data, assembling a team of authors, defining a target audience, selecting a journal, and responding to peer review. Chapters [7](#), [8](#), [9](#), and [10](#) give detailed, step-by-step instructions on how to write traditional case reports, adverse drug reaction case reports, case series, n-of-1 case studies, clinical image or clinical quiz articles, clinical vignettes, and

clinical problem-solving cases. These chapters have numerous figures, tables, images, and excerpts of published case reports (including many written by the authors) to illustrate and reinforce the strategies that lead to publication.

The second purpose of this book is to give the interested reader some perspective on the historical, educational, social, and cultural aspects of case reporting. Chapter 2 traces the history of case reporting from ancient Egypt to the present day, focusing on the effects of culture and technology on the evolving form and structure of the case report. Chapter 3 discusses the educational benefits of reading and writing case reports, both for trainees and experienced physicians. Chapter 4 covers the practical benefits of case reporting, including contributing to the medical literature, career development, and better patient care. Chapter 13 explores postpublication issues: press releases and media exposure, peer review and editorial writing opportunities, indexing, citations, and use of social media to track article views and comments. Finally, Chap. 14 speculates on the uncertain future of the case report. We hope that readers who want to write case reports will go beyond the “handbook” and take the time to learn more about this ancient yet still vibrant form of medical communication.

The Violinist Who Lost His Vibrato

Case reports can arise in unexpected places. One of my first published case reports began with a conversation I had with a violinist at a chamber music party. On hearing that I was a physician, he began complaining to me about the side effects of one of his blood pressure medicines. Normally, this would elicit a polite nod or two, followed by a quick move to the opposite side of the room. However, something about his story intrigued me. When he was prescribed daily atenolol for hypertension, he began to have difficulty with initiating and controlling his *vibrato*, which

is produced by quick oscillations of the violinist's hand to create a pleasantly pulsating tone. The problem worsened, and finally came to a head when he began rehearsing the famous solo in Massenet's *Meditation from Thais*, a slow piece that requires varied and dramatic *vibrato* effects. Despite hours of practice, the *vibrato* was too slow, too "wide," and difficult to control. In desperation, he turned to a physician with experience in music medicine, who weaned him off the atenolol and started him on an angiotensin-converting enzyme inhibitor for hypertension. His *vibrato* quickly recovered, and his subsequent performance of the *Meditation* was completely successful. This conversation led eventually to a case report and review of the literature on beta-blockers, stage fright, and the paradoxical effects of atenolol on the "controlled tremor" of *vibrato* [1].

Another case report was born when a patient with unexplained hypokalemia rolled into my office with a 2 l bottle of cola in the front basket of his electric scooter. His potassium had been low and almost impossible to replete for 2 years; an extensive work-up had revealed nothing. As I looked at him, I suddenly realized that the big cola bottle was the "MacGuffin" in the case. When I asked him about it, he admitted to drinking 4 l per day. This led to a diagnosis of cola-induced hypokalemia, which was confirmed when his potassium normalized after he reduced his cola intake [2].

What did these two cases have in common? An unexpected association, a mystery solved, but also the excitement of discovery. Vladimir Nabokov, in his *Lectures on Literature*, wrote that "a wise reader reads the book of genius not with his heart, not so much with his brain, but with his spine." [3] In a very similar way, experienced physicians detect reportable cases with their spines, by the "telltale tingle" they feel when confronted with true novelty. The purpose of this book is to help physicians and students to sustain and preserve that initial *frisson* of excitement by learning to write up their cases for publication.

Evidence Value of Case Reports: “What Actually Happened”

“Case reports may remain the ‘lowest’ or ‘weakest’ level of evidence with respect to causality,” writes Riaz Agha, “but they remain the first line of evidence of what actually happened” [4]. Case reports derive their value as evidence from the real-world authenticity of the cases they describe. As Milos Jenicek reminds us, “Everything begins with the personal experience of the physician and his patient, at the office or hospital ” [5]. Randomized trials deal with populations of patients, under carefully controlled conditions; case reports deal with individual patients in the randomness of everyday life. Randomized trials are mainly confirmatory; they “bring a final quantification” of the evidence, Jan Vandenbroucke notes, “but offer little scientific novelty in themselves” [6]. Case reports are all about novelty, serendipity, new ideas, fresh hypotheses, and therapeutic surprises. Rather than providing confirmation, they provide inspiration. Case reports and case series supply most of the ideas and hypotheses that are tested and confirmed in randomized trials. Case reports are the lone prospectors who pan for gold and chip away at rocks with their hammers; randomized trials are the organized mining operations that rush in with their feeders and crushers and leaching tanks when the prospector finds a promising nugget.

Case reports are traditionally regarded as the base of the evidence pyramid, with randomized controlled trials at the top (see Fig. 4.1). Evidence-based medicine tells us to use these high-quality randomized trials to guide our decision-making. This is all very well when patients present with textbook illnesses, and do not have multiple comorbid conditions. However, if your practice involves patients with complex medical histories who present with confusing and atypical symptoms, you will soon discover that randomized trials do not have all the answers. Fortunately, there are more than 1.7 million case reports indexed in PubMed, and a literature

search will usually yield a handful of similar cases that may give some guidance on diagnosis and management. Thus, we turn the evidence pyramid on its head when randomized trials are lacking, and case reports and case series – “what actually happened” – become the best available evidence.

Impact of Case Reports

Those who consider writing case reports a quaint, outmoded, and marginal pursuit should consider the dramatic and continuing impact of case reports in the twenty-first century. Whereas randomized trials often take years to plan and execute, case reports can function as “reports from the frontline” with rapid publication and wide dissemination of critical information on the natural history, prognosis, and treatment of emerging diseases. For example, a recent case report, “Zika Virus Associated with Microcephaly” [7], describes the autopsy findings of the 29-week fetus of a woman with symptoms of Zika virus infection. The autopsy revealed microcephaly, almost complete agyria, hydrocephalus, and other major brain abnormalities. Zika virus was found in the fetal brain tissue on reverse transcriptase–polymerase chain reaction (RT-PCR) assay, and the complete Zika virus genome was recovered from the fetal brain. This report provided the best evidence to date that Zika virus infection in pregnant women causes fetal microcephaly. Case reports played a similar frontline role in the recent Ebola virus epidemic in Africa, with critical information on natural history, virology, common complications (including Gram-negative septicemia and encephalopathy), and optimal ICU treatment for survival [8]. Similarly, case reports and case series have made critical contributions in outbreaks of SARS [9], MERS [10], AIDS [11], toxic shock syndrome [12], West Nile Virus [13], and many others.

In addition to recognition and description of new diseases, case reports continue to play important roles in pharmacovigilance (see Chap. 8), hypothesis-generation and study of

mechanisms of disease (Chap. 7), medical education (Chaps. 3, 8, 9, and 10), researching rare disorders and outliers (Chap. 8), personalized medicine (Chap. 8), study of the history of medicine (Chap. 2), quality assurance, and solving ethical dilemmas [6, 14, 15].

Case Reports: Form and Function in the Twenty First Century

Over the centuries, case reports have evolved to fit the socio-cultural and technological contexts of their times. The twenty-first century has seen an expanding variety of roles for case reports (Fig. 1.1), probably arising from the rapid growth in computer technology, with increasingly powerful applications in research, education, imaging, and bioinformatics.

For example, the study of individual outlier cancer survivors has become one of the hottest areas in cancer research with the advent of rapid and inexpensive genomic sequencing; we can now sequence hundreds of these individuals to find the ones with mutations that predict response to a

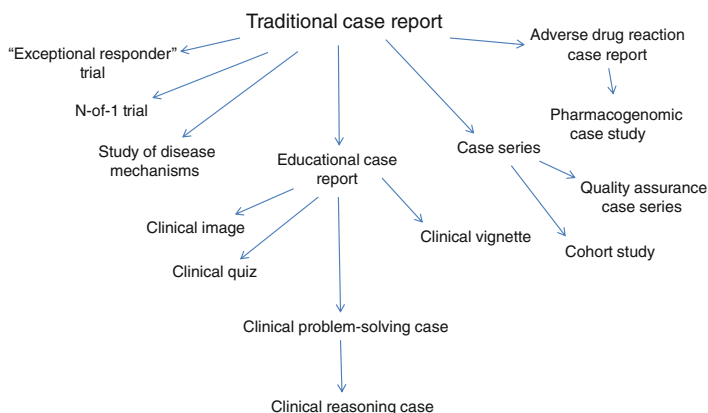


FIGURE 1.1 Taxonomy of the twenty first century case report

specific treatment. Similarly, n-of-1 trials of patients with chronic conditions such as hypertension, sleep apnea, and Parkinson's disease have benefitted from the development of advanced "phenotypic" monitoring devices to assess treatment response. In medical education, the traditional case report has morphed into a variety of forms, including clinical images, videos, quizzes, poster vignettes, and clinical problem-solving cases, all widely available via electronic media. Case series can now be electronically combined and analyzed for purposes of outcome studies, case definition, quality assurance, and multi-institutional registries.

Clearly, we have come a long way from the traditional print journal case reports of 30 years ago. In fact, it can be argued that case reports have changed more in form and function over the past 30 years than in the 2000 years between Hippocrates' *Epidemics* and the first modern case reports. How long can case reports continue to grow and reshape themselves and reach ever-increasing numbers of readers? Will the traditional case report stay relevant, or will it wither away and become a forgotten relic in 30 years? We hope that readers of this book – especially medical students, residents, and early-career physicians – will take these questions to heart and preserve the best that case reports have to offer.

References

1. Packer CD, Packer DM. Beta-blockers, stage fright, and vibrato: a case report. *Med Probl Perform Art.* 2005;20(3):126–30.
2. Packer CD. Chronic hypokalemia due to excessive cola consumption: a case report. *Cases J.* 2008;1:32.
3. Nabokov V. *Lectures on literature.* New York: Harcourt Brace Jovanovich; 1982. p. 6.
4. Agha R. Time for a new approach to case reports. *Int J Surg Case Rep.* 2010;1(1):1–3.
5. Jenicek M. *Clinical case reporting in evidence-based medicine.* Oxford: Butterworth-Heinemann; 1999. p. 5.
6. Vandenbroucke JP. Case reports in an evidence-based world. *J R Soc Med.* 1999;92(4):159–63.

7. Mlakar J, Korva M, Tul N, Popović M, Poljšak-Prijatelj M, Mraz J, et al. Zika virus associated with microcephaly. *N Engl J Med.* 2016;374:951–8.
8. Kreuels B, Wichmann D, Emmerich P, Schmidt-Chanasit J, de Heer G, Kluge S, et al. A case of severe Ebola virus infection complicated by gram-negative septicemia. *N Engl J Med.* 2014;371:2394–401.
9. Tsang KW, Ho PL, Ooi GC, Yee WK, Wang T, Chan-Yeung M, et al. A cluster of cases of Severe Acute Respiratory Syndrome in Hong Kong. *N Engl J Med.* 2003;348:1977–85.
10. Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus ADME, Fouchier RAM. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. *N Engl J Med.* 2012;367:1814–20.
11. Hymes KB, Greene JB, Marcus A, William DC, Cheung T, Prose NS, et al. Kaposi's sarcoma in homosexual men – a report of eight cases. *Lancet.* 1981;2(8247):598–600.
12. Todd J, Fishaut M, Kapral F. Toxic-shock syndrome associated with phage-group-I Staphylococci. *Lancet.* 1978;2(8100):1116–8.
13. Asnis DS, Conetta R, Texeira AA, Waldman G, Sampson BA. The West Nile Virus outbreak of 1999 in New York: the Flushing Hospital experience. *Clin Infect Dis.* 2000;30(3):413–8.
14. Vandenbroucke JP. In defense of case reports and case series. *Ann Intern Med.* 2001;134:330–4.
15. Nissen T, Wynn R. The clinical case report: a review of its merits and limitations. *BMC Res Notes.* 2014;7:264.