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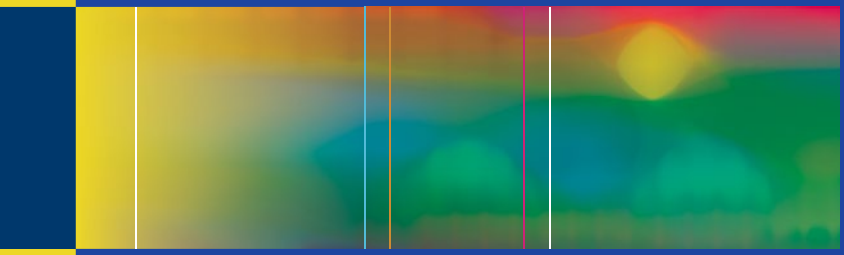

Writing Case Reports

A Practical Guide from Conception through Publication

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CDP dedicates this book to his wife, Marie Sullivan.

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GB dedicates this book to all the students and residents who inspire her to "just write it up!"

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SM dedicates this book to his best friend, Leah Smith.

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Preface

Why write a book about writing case reports? One very practical reason is to bridge the gap between aspiration ("we ought to write this up") and publication. Despite the increasing numbers of case reports published each year, we suspect that this gap remains wide, especially for medical trainees and physicians practicing in the community. Consequently, interesting and potentially important cases that ought to be in circulation are going unpublished. Second, although there are many fine articles on how to write case reports, and one excellent book – Milos Jenicek's *Clinical Case Reporting in Evidence-Based Medicine* – we think that prospective case report authors need a practical, single-source guide to the whole process, from case selection through publication. In the twenty-first century, this guide must go beyond the traditional case report to instruct potential authors on its many modern variants: clinical vignette abstracts, case series, clinical images, clinical quizzes, adverse drug reaction case reports, n-of-1 trials, and clinical problem-solving cases. Today's case report author needs to be versatile; that classic case of Mirizzi syndrome may not work as a straight case report, but it could be a superb clinical image or clinical reasoning case. Our aim is to help authors navigate these many options, select the form and venue that works best for their case, and then write it up in a concise, informative, and publishable style.

But perhaps the best reason for writing this book is simply that case reports are fun to write, fun to read, great for teaching, and useful in our clinical practices. I am extremely lucky to have found two co-authors, Gabrielle N. Berger and

Somnath Mookherjee, who not only feel the same way about case reports but have been willing to devote considerable time and energy to writing about them.

Over the course of our collaboration, what started out as a simple case reporting handbook has evolved into something more – a handbook with supplemental essays on the history, educational value, career enhancements, scholarly opportunities, social media aspects, and future prospects of the case report. A major goal of any case report is to put the case in context; our parallel goal is to put the art and science of case reporting in context for our readers. Case report authors should understand that they are part of a great historical tradition, that case reports can be powerful educational tools, and that writing case reports can lead to exciting scholarly opportunities, new collaborations, and useful clinical insights. Writing case reports, in other words, can help to make us better teachers and physicians.

If even a few medical students, residents, and practicing physicians publish their first case reports with the help of this book, it will have served its purpose.

Cleveland, OH, USA — Clifford D. Packer, MD
May 8, 2016

Contents

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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

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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 sociocultural 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

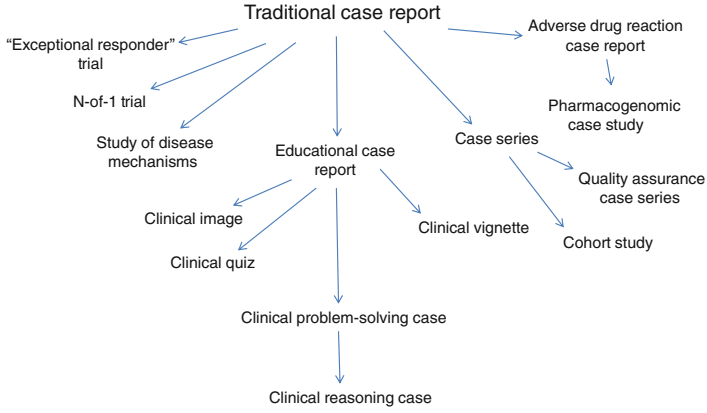

Figure 1.1 Taxonomy of the twenty first century case report

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.

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Chapter 2
The Historical Tradition of Case Reporting

Clifford D. Packer

The Case Report in Ancient and Medieval Times

The medical case report as we know it today is not a static form of medical communication. It has evolved over almost 4000 years, and the format, content, and uses of case reports have undergone remarkable changes according to the shifting historical, technological, and cultural contexts. While the tradition of case reporting is ancient, our current way of writing a case report is a relatively recent development.

The first known medical case reports, circa 1600 BC, were written and preserved on an Egyptian papyrus. They comprise a series of 48 cases which discuss injuries and disorders of the head and upper torso, and include an accurate description of a maneuver to reduce a jaw dislocation [1]. Another ancient Egyptian medical treatise, the Ebers papyrus (1552 BC), is a 110-page scroll which contains folk remedies, magical potions, and descriptions of a wide variety of diseases, including a disorder of frequent urination that is probably the first report of diabetes mellitus (although an ancient Hindu text from the same period noted that ants were attracted to the urine of people with a mysterious wasting disease) [2]. Egyptian medicine was practiced by physician-priests, and treatment, though often practical and occasionally useful, was inextricably

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entwined with magic [3]. In contrast, the Hippocratic case histories from the Greek classical era (ca. 400 BC) show no belief in supernatural origins of disease, and are characterized by objective and detailed descriptions of the findings and courses of various illnesses [1]. The physician-narrator was generally an observer, and did not intervene or otherwise participate in the case [4]. This case history from the *Epidemics*, of a patient with what sounds like a foot infection complicated by cellulitis and overwhelming sepsis, is typical:

> Criton, in Thasus, while still on foot, and going about, was seized with a violent pain in the great toe; he took to bed the same day, had rigors and nausea, recovered his heat slightly, at night was delirious. On the second, swelling of the whole foot, and about the ankle erythema, with distention, and small bullae (phlyctaenae); acute fever; he became furiously deranged; alvine discharges bilious, unmixed, and rather frequent. He died on the second day from the commencement. [5]

Hippocrates' crowning achievement was the *Aphorisms*, a collection of 412 short, pithy maxims which conveyed the collected "teaching points" of his case histories. Aphorisms lend themselves to oral transmission – they live in speech, not on the page – and the best and most memorable of them are like poetry, the haiku of medicine. "It is the oral-poetic nature of a good aphorism," writes Quentin Shaw, "that flash-welds it into the memory" [6]. The aphorism has persisted as a teaching tool; consider three Hippocratic aphorisms [7], followed by three that I memorized from my own medical training:

> Dysentery, if it commence with black bile, is mortal.
> In dropsical persons, ulcers forming on the body are not easily healed.
> In acute diseases, coldness of the extremities is bad.
> The pain of biliary colic radiates to a point just below the right scapula.
> The sun should never set on an empyema.
> Chest pain that is substernal, exertional, and relieved by nitroglycerine is angina pectoris.

In the modern case report, it is still customary to conclude the discussion with an aphoristic teaching point. As we sum up the case, we invoke the authority of Hippocrates.