Chapter 9
How to Write a Scientific Article Reporting Original Research

Scientific progress depends on journal articles that report original research. In addition, for better or worse, "publish or perish" is still the driving force behind promotion, reputation, and funding for most researchers and many health professionals. Even if you are not required to contribute to the scientific literature, you are required to read it to stay current in your field. Knowing the sections and functions of the scientific article—and their strengths, weaknesses, and variations—is thus an important part of your training, no matter what your position in the life sciences.

I encourage you to write as much of the article as you can before you start the research. If this advice seems strange, remember that the process is exactly what you do when you write a grant proposal. This process will help you plan your research methods and analytic approach. Some data (such as biomedical images; see Chapter 10) acquired during the research cannot be duplicated later, so realizing in advance that you might need them can help. The literature should always be reviewed before you start a study (and again before you submit your manuscript for publication). Finally, and perhaps most importantly, you may be able to establish authorship of the published article in advance. Determining authorship in advance, or at least establishing the criteria for co-authorship and the order of authorship, helps assign responsibility for the research tasks and may avoid later conflicts about authorship. (See Chapter 7.)

In this chapter, I describe how to prepare a manuscript reporting original research for submittal to a scientific journal. I briefly review the sections of the scientific article and describe what each is for, how it can be structured, and ways in which to write it. The submittal and publication processes are described in Chapter 11.

OVERVIEW

Following the journal's instructions for authors is one the most important things you can do when preparing a manuscript for publication. A particularly useful resource for authors in the life sciences is the website of **The Mulford Library of the University of Toledo**, Health Science Campus:

http://mulford.meduohio.edu/instr/.

This site contains links to the instructions for authors for more than 3,500 journals in the health and life sciences. All links are to the publishers and organizations that have editorial responsibilities for the journal, so the information is as reliable as it can be.

The order of the elements of the submitted manuscript is basically the same for all journals: title page, text of the article, acknowledgments references, tables,

figure captions, and figures. Within these elements, however, are some important differences. For example, although the most common organization of a scientific article is the IMRAD format (Introduction, Methods, Results, And Discussion), journals differ in the order in which they present these sections and how they want them labeled. Three common orders are:

Introduction	**Introduction**	**Introduction**
Patients and Methods	**Results**	**Experimental Considerations**
Results	**Discussion**	**Results and Discussion**
Comment (Discussion)	**Conclusions**	**Conclusions**
	Materials and Methods	

If only to determine the order of the sections, you should be sure to read the journal's instructions for authors and to review recent issues of the journal.

PREPARING THE TITLE PAGE

The title page of a submitted manuscript generally contains more than the title because it provides the information that will identify the manuscript as it moves through the journal's publication system. Most journals' instructions for authors require at least the following information on the title page:

- The title of the article (see below)

- The full name, highest academic degree, and institutional affiliation of each author. If authorship is attributed to a group (e.g., Eastern Cooperative Oncology Group), each author must meet the requirements for authorship (see Chapter 7). If authorship is attributed to a writing group (a subset of the larger research group), all members of the writing group must meet the requirements for authorship; other members can be listed in the Acknowledgments.

- A statement that the research has not been presented before, but if so, where. If the research was presented at a conference, give the name of the sponsoring organization and the date and place of the conference. If the abstract was published, cite the proceedings in which it appears. If the substance or a portion of the research has been published elsewhere, explain this fact in your cover letter to the editor.

- A suggested "running" title, often with a character limit, that will identify the article on each page of the published article

- Disclosures of any potential competing interest for the authors, such as having received research funding or speaking fees from the pharmaceutical company the makes the study drug or holding stock in the company that makes the medical device tested in the research. (See Chapter 7.) In addition to providing this

assurance on a specific form, the journal may also specify that this information be included in the cover letter, in the Methods section, or in the Acknowledgments.

- Key words or index terms (sometimes these terms are to follow the abstract. See below.)

- For clinical studies, the trial's registration number. (See Chapter 7.)

- The name and contact information (mailing address, e-mail address, telephone and fax numbers) of the corresponding author who will move the manuscript through the publication process and to whom reprints will be sent, if ordered. This author need not be the first author or the senior author, but it is usually one who is expected to stay at the same address for some time and who will have access to the data if other authors move on.

Many journals specify that the first author's last name and page number appear on each manuscript page, except the title page. (The title page is counted as page 1 but does not show the page number.) Other journals request that all information identifying the authors and their institutions be removed from the submitted manuscript, in the attempt to reduce bias during peer review.

Writing the Title

The title is the most important part of a scientific article. It is the part most often read and often the only part read. As the link between your research and interested readers, its primary purpose is to help readers find and decide whether to read the full article. Nonspecific, inaccurate, or misleading titles can prevent readers from correctly determining whether they need to read the article. A well written title can thus save readers substantial time by indicating, exactly, what the article is about—and what it is *not* about. Because the title is the most important part of your article, it is worth the time to write it well.

Titles are often read apart from the abstract or full article (on printed literature searches and on on-line bibliographic databases, for instance) and so must be understandable without reference to the rest of the article. Keep them accurate and concise, and avoid using all but the most common abbreviations.

Some journals allow or prefer **declarative titles** (or **indicative, headline,** or **sentence titles)** that report the results of the study rather than identify what was studied. For example, *Microbiology* advises: "The title should include topical keywords and allude to the interesting conclusions of the paper. A title that emphasizes the main conclusions, or poses a question, has more impact than one that just describes the nature of the study." In fact, in many basic science studies, the causal chain being investigated is short, the results are consistent, and the clinical implications limited, so declarative titles are not likely to be compromise clinical care and are perhaps more useful to readers:

Lack of Fiber Cell Induction Stops Normal Growth
of Rat Lenses in Organ Culture

Insulin Resistance is an Intrinsic Defect Independent of Fat Mass
in Women with Turner's Syndrome

Other journals do not allow declarative titles, including many clinical journals, where they are regarded as often simplistic, sometimes misleading, and never necessary. If a title states that a drug is effective, the fear is that readers will accept the statement as established truth without reading the article, which may provide important qualifying information. A hypothetical but illustrative example:

The original, declarative title: "Hepatocyte Growth Factor Prevents Renal Fibrosis in Chronic Renal Disease"

The revised, informative title: "Effects of Hepatocyte Growth Factor on DNA Synthesis of Tubular Epithelial Cells in a Mouse Model of Chronic Renal Disease"

Here, the original title says that fibrosis was prevented, although the full article says that what really happened was that DNA synthesis of tubular epithelial cells was 4.4 times as high in the 6 mice receiving hepatocyte growth factor than it was in the 6 that didn't.

Note that unless you are familiar with hepatocyte growth factor and tubular epithelial cells, the revised title may not be easily understood, whereas the original uses words familiar enough to orient most readers to the general topic of the research. Keep in mind, too, that clinical journals are probably read by a much broader audience of nonscientists than are basic science journals, and they more often report research directly relevant to patient care, so the chances of a declarative title being misunderstood are great enough to discourage their use.

Some journals also allow or prefer **interrogative titles**, or titles in the form of questions: "Measurement of colonic polyps by radiologists and endoscopists: Who is most accurate?" Other journals may prefer that titles asking questions be reserved for editorials: "Is it Time to Change the Peer Review System?"

Especially in clinical journals, the title should usually identify the relationship that was studied. Thus, for articles reporting epidemiological or clinical research, try to put as many of the following six elements in the title as you can: intervention, endpoint, patients or species or tissue, comparator group(s), study setting (for clinical studies), and design. These elements can be remembered by the acronym **SPICED** (Setting, Patients, Intervention, Comparator, Endpoint, Design) or in order, by the mnemonic "Ideally, Every Person Can Select Deliberately."

It may not be possible or desirable to include all six elements, and other elements may need to be included in some articles (dates; trial names, such as

GUSTO or CADILLAC; study sponsors, such as the Eastern Cooperative Oncology Group), but they do give you a good place to start.

Original: "A Randomized Trial of Low-Air-Loss Beds for Treatment of Pressure Ulcers" (72 characters and spaces)

Revised: "Low-Air-Loss Beds vs. Foam Mattresses for Treating Pressure Ulcers in Nursing Home Patients: A Randomized Trial" (111 characters and spaces)

The original title has three of the six elements; the revised title has all six. Some journals limit the number of characters and spaces in the title. If so, drop one or more of the elements:

Shorter: "Low-Air-Loss Beds vs. Foam Mattresses for Treating Pressure Ulcers: A Randomized Trial" (86 characters and spaces)

Shorter still: "Low-Air-Loss Beds vs. Foam Mattresses for Treating Pressure Ulcers" (66 characters and spaces)

Some journals do not allow subtitles, but others find them useful to avoid having to place qualifying information in positions of importance earlier in the title:

Without a subtitle: "A Cost-Benefit Analysis of Low-Air-Loss Beds vs. Foam Mattresses for Treating Pressure Ulcers in Nursing Home Patients:"

With a subtitle: "Low-Air-Loss Beds vs. Foam Mattresses for Treating Pressure Ulcers in Nursing Home Patients: A Cost-Benefit Analysis"

I suggest submitting the manuscript with a title that is as complete and as accurate as possible and to let the journal decide whether to shorten it. If the title is concise and effective, it may be accepted, even if it is over the character limit.

Another form of title that you should avoid in clinical journals is the **"Our Experience"** title:

"Outcomes of Heart Transplantation:
The Cleveland Clinic Experience."

Here, the title emphasizes the fact that the study was conducted at the Cleveland Clinic, which assumes that the reader will know the Clinic's reputation, an assumption not always true, especially to researchers in other countries and in other disciplines. Imagine your interest (or lack thereof) in an article with a similar title:

"Outcomes of Heart Transplantation:
The Tinytown Community Hospital Experience."

Here, "Tinytown" represents any town with a community hospital, and it's hard to imagine how its experience in heart transplantation would make the article noteworthy. The more appropriate form of such a title is to indicate the reason the article is important:

"Outcomes of Heart Transplantation:
A Review of 250 Cases with 3-Year Followup."

One also has to wonder about the value of reporting only "experience" in an article, as opposed to addressing a specific research question.

WRITING THE ABSTRACT

The abstract is the second most important part of the scientific article because, after the title, it is the part most often read and often the only other part read or available. Like the title, the purpose of an abstract is to help readers decide whether to read the full article.

Chapter 7 describes abstracts in detail, so here I will say only that the instructions for authors usually specify the length of the abstract and whether it should be a single paragraph or structured with a series of headings. A few journals also require a second, shorter summary statement that will appear in the journal's table of contents to attract readers.

Writing abstracts is challenging because you have to select carefully both your facts and your words. Try to avoid using abbreviations but define them if you use them. Do not cite references or refer to the full article; abstracts are often separated from the full article and so must be understandable without reference to it.

One of the most common errors in scientific publishing is an abstract that contains information missing from or inconsistent with the rest of the article. In particular, the conclusions given in the abstract should match those given in the article. Other common problems occur when the problem statement is not distinct from the details of the background or when a background or a problem statement is omitted entirely.

Key Words and Abbreviations

Many journals ask you to provide 3 to 6 **index terms** or **key words** about your research. The journal may direct you to a source of standard terms, such as the Medical Index Subject Headings (MeSH) used by MEDLINE, ask you to select from a list on its website, or let you use your own judgment (in which case, use MeSH terms). Do your best to choose the most appropriate words but know that a professional indexer will review your choices and make the final assignments. Indexing is too important to be left to amateurs.(!)

Sometimes journals request that **abbreviations** used in the article be listed on a separate page, either after the title page or after the abstract. Abbreviations should be standard, used often enough to be useful (some journals allow them only if used 5 or more times), and sparingly. Spell the full term out at first mention, followed by the abbreviation in parentheses, then use the abbreviation from then on.

Writing the Introduction

The introduction is probably the least-appreciated section of the scientific article. A good introduction can be enormously useful to readers, but so few authors ever learn how to write good ones that their value is largely ignored.

The purpose of the introduction is to prepare readers to understand your paper; to orient them to your research by establishing the need and importance of the study, indicating in general how you addressed the need, and by telling readers what to expect from your article. To accomplish this purpose, I suggest writing a four-part introduction consisting of:

1. A **background statement** that provides the context for understanding the problem and your approach to it

2. A **problem statement** that describes the nature, scope, severity, or importance of the problem that stimulated your research

3. A **task statement** that indicates the research question, hypothesis, approach, or activities that you undertook to investigate the problem

4. A **forecasting statement** that tells readers what they will find if they continue to read the article.

An abbreviated example:

[Part 1: Background Statement] In patients with atherosclerotic vascular disease, aspirin is widely recommended to prevent myocardial infarction, graft occlusion after coronary artery bypass surgery, and stroke. [**Part 2: Problem Statement]** However, aspirin is also associated with prolonged bleeding. Patients are often asked to stop taking aspirin for several days

> before undergoing bronchoscopy, to reduce the presumed risk of bleeding. The effectiveness of this practice has never been tested, but it does mean that patients must, for a short while, stop taking a medication with proven benefits, and it can also delay the planned bronchoscopy if aspirin use is not stopped soon enough. [**Part 3: Task Statement]** Thus, we sought to determine whether aspirin really does increase the risk of bleeding after bronchoscopy. [**Part 4: forecasting Statement]** In this article, we describe a prospective trial of 138 consecutive patients undergoing bronchoscopy in which we compared the number and severity of bleeding events in those taking aspirin with those who were not.

Weak background and problem statements are the most common shortcomings of introductions. Many authors assume, incorrectly, that readers will know what the problem is and why their research is important. Others begin the introduction with a task statement because it describes their first step in actually conducting the research. They forget the steps that precede research activities: finding and characterizing a problem and justifying the time and resources needed to address the problem.

Journals using the *AMA Manual of Style* usually specify that conclusions not be indicated in the introduction, but a case can be made that they should be, and the practice is common in basic science journals. The purpose is not to eliminate the need to read the full article but rather to give readers some idea of where the article is going so that they can immediately begin to evaluate the methods and analysis in light of the indicated results and conclusions. The above example could be extended by adding the text indicated by italics:

> In this article, we describe a prospective trial of 138 consecutive patients undergoing bronchoscopy in which we compared the number and severity of bleeding events in those taking aspirin with those who were not *and determined that aspirin does not increase the risk of bleeding*.

Social science and some nursing journals include the full literature review in the introduction; clinical and basic science journals almost always include it in the discussion. The introductions in health science journals usually should include only information pertaining to the study at hand. Cite only those references needed to establish the rationale and the approach to the research. Introductions in basic science articles may also be much longer than those in clinical journals because the research may consist of several separate experiments, making the background, justification, and approach more complex. The introduction may also introduce and define some of the terms and abbreviations used throughout the article.

Writing the Methods Section

Also called "Materials and Methods," "Experimental Section," or "Patients and Methods," depending on the nature of the research and the journal, the purpose of this section is to permit readers to judge the validity of your study methods. The

thought that a good methods section would allow someone to replicate the experiment is laudable but often not realistic, given the complexity of most research. A more reasonable goal is to provide enough information to establish the adequacy of the methods to address the problem and, in so doing, your credibility as a careful and thorough researcher.

GENERAL INFORMATION

The organization of the methods section varies greatly by field of science. Below are some general guidelines and some specific suggestions for reporting methods in either basic science or clinical research.

- **If the study involved humans, you must provide assurance that the study was reviewed by the appropriate institutional review board (IRB). If it involved animals, it should have been approved by the Institutional Animal Care and Use Committee (IACUC).** In addition, confirm that written informed consent was obtained from all study participants, that experimental animals were treated according to accepted and ethical guidelines, and disclose any financial conflicts of interest for each author. These assurances often appear in the first paragraph of the methods, but other placements are common. (See Chapter 7.)

- **Tell how the sample was selected and, if applicable, how sample size was determined.** In basic research, it may be necessary to explain why which species was selected, how tissue was obtained, or how the number of animals was determined. In clinical studies, it may be necessary to report how patients were recruited; whether the sample was probabilistic (drawn by random selection), a convenience sample, or consecutive patients; and the details of a power calculation that determined the targeted sample size.

- **Identify the materials used in the research as well as the suppliers' or manufacturers' location.** Materials include experimental animals, drugs, reagents, laboratory and surgical equipment, cell lines, measuring instruments, computer programs, and so on.

- **Avoid leaving gaps in the logic of the methods.** A statement like "We used Colin's method, with modifications" means that the author's didn't use Colin's method. They modified it in some way and so need to describe or reference the modifications. Complex methods can sometimes be described in an appendix to the article or in supplemental information available on the journal's website.

- **Use as many subheadings as reasonable to organize this section and to help readers find information.**

MEASUREMENTS

Science is measurement. We can't study anything scientifically unless and until we can measure it. Thus, the methods section should report the who, what, when, where, why, and how of the measurement and data collection efforts. In particular, you may need to report:

- The **environmental or experimental conditions** under which the measurements were made.

- The **unit of measurement** or **unit of observation.** Did you study mouse litters, individual mice, mouse kidneys, or mouse kidney cells? Did you study *people* with heart attacks or *heart attacks* among people who may have had more than one?

- Any **indicators**, **biomarkers,** or **surrogate endpoints** that were measured instead of the underlying biological or clinical event of interest. For example, an elevated antibody titer may be used a marker for infection, which is not measured directly.

- **Operational definitions.** Operational definitions consist of objective criteria that define concepts clearly enough to allow unambiguous measurement. An acidic environment can be operationally defined as one that has a pH of less than 7.0. Depression can be operationally defined as a score above 17 on the Beck Depression Inventory. How well the operational definition measures the concept may be questioned, but the clarity of the definition should not be.

- The **level of measurement** of key variables. Variables measured at the **nominal level** consist of categories with no inherent order (blood type: O, A, B, or AB); those at the **ordinal level** consist of ranked categories (age groups: birth to 15 years; 16 to 35 years; 36 years and older); and those at the **continuous level** are measured on scales with equal intervals and that can include fractions (height measured in centimeters; time measured in seconds). Many variables can be measured at any of these levels, so indicating which level was chosen may be important.

- The **characteristics and qualification of judges** whose decisions are data for the study. How long has the pathologist worked in the area? Is she board-certified? What additional training might she have had that would affect her skill in identifying cancerous cells? A related issue may be the certifications of laboratories to perform certain tests.

- The **precision of the measurements**. Precision is the degree of **accuracy** (sometimes called **analytic sensitivity**) with which a measurement is made. Measurements to the nearest nanometer are more precise than those to the nearest millimeter, for example. Related concepts are **diagnostic sensitivity** and **diagnostic specificity**, or how well a diagnostic test correctly detects the presence or absence of disease.

- The **calibration** and **settings of equipment**. Many instruments must be calibrated before use to assure accurate measurements, and many have any number of settings that may need to be reported, such as degree of magnification, duration of exposure, flow rates, temperature, and so on. Such information is often included in tables or figure captions.

- The **validity of the measurements**. A valid measurement is one that measures what it is intended to measure. Validity is assessed by comparing a new method of measurement to those made with a reference (or "gold") standard, which may also need to be identified.

- The **reliability of the measurements**. A reliable measurement is one that returns the same value under the same conditions. Reliability is assessed by determining the degree of agreement among repeated measurements or among the observations of two or more judges.

FEATURES OF BASIC RESEARCH ARTICLES [Deleted from this handout]

FEATURES OF CLINICAL RESEARCH ARTICLES

Clinical research studies generally follow similar patterns and have similar components. Common subheadings in the methods section include:

∑ Study Design (e.g., cohort, case-control)
∑ Patient Selection (sampling or recruitment, eligibility criteria)
∑ Patient Assignment (how the experimental groups were formed, e.g., case definitions, random assignment procedures)
∑ Interventions (drugs, therapeutic procedures, exposures)
∑ Measurements
∑ Endpoints
∑ Statistical Methods (statistical analyses, sample size calculation)

How To Report Statistics in Medicine contains comprehensive, annotated guidelines for documenting research designs and activities for randomized controlled trials, cohort and longitudinal studies, case-control studies, surveys and cross-sectional studies, systematic reviews and meta-analyses, diagnostic test characteristics, time-to-event (survival) analyses, economic evaluations (e.g., cost-effectiveness analyses); decision analyses, and clinical practice guidelines.

In addition, several shorter checklists have been developed for reporting specific types of research, including the CONSORT Statement for reporting randomized controlled trials; the QUOROM (PRISMA) and MOOSE Statements for reporting systematic reviews and meta-analyses of randomized trials and observational studies, respectively; the STROBE and TREND Statements for reporting observational studies, and the STARD checklist for reporting diagnostic test development. These checklists can be accessed through the Mulford Library website cited above or from the EQUATOR WebSite.

Statistical Methods

Almost all methods sections include a subsection on statistical methods, which usually ends the section. In studies that use statistics, the details below may need to be reported. (For more detailed information on reporting statistical methods and results, see *How to Report Statistics in Medicine*.)

- How the data will be reported, such as medians and ranges for continuous data, counts and percentages for nominal and ordinal data, and estimates and confidence intervals for outcome variables

- The primary statistical comparisons to be made and the methods used to make them

- The details of the statistical power calculation used to determine the sample size

- Details of group assignment, such as the details of allocation concealment, random assignment, or "blocking and stratification" of the sample

- For randomized trials, whether the analysis was by intention-to-treat, per-protocol, or both

- The alpha level that defines the threshold of statistical significance, such as 0.05 or 0.01

- The statistical software package used in the analysis.

Lack of adequate statistical support is a common and major problem in many research efforts. *If possible, consult with a biostatistician before you begin your research*, don't simply give him your data and ask him to tell you what you found. Statisticians can help design your research and thus help you collect the right data in the right way and to control for potential error, confounding, and bias. They can suggest or perform statistical analyses, help write the statistical methods section, and help interpret the results. Statisticians who contribute substantively to the research by performing any of the above tasks should be listed as authors. The belief that statisticians do not deserve authorship because they are paid to analyze data is nonsense.

Writing the Results Section

The purpose of the results section is to tell what happened during the study (e.g., protocol deviations, substitution of reagents, unexpected data losses), as well as to report the findings of the study.

Report the results in figures or tables when possible, and do not duplicate too much of this information in the text. Rather, in the text, call attention to the data given in the tables and figures. When doing so, describe the results rather than the figure (or

table): instead of: "Figure 2 shows the decline in blood values," say: "Blood values declined (Figure 2)."

Report data with the appropriate descriptive statistics. The standard error of the mean (SEM) is not a descriptive statistic; it is not a measure of dispersion for a distribution of measurements. Instead, report the standard deviation (SD) for normally distributed data or the range or an interpercentile range for skewed data. Measurements may also need to be presented in (and converted to) *Systems Internationale* (SI) units if required by the journal.

In basic science journals that allow a separate discussion section, avoid including too many conclusions in the results. A summary sentence at the end of every section is not necessary. In particular, do not restate results as conclusions: "Treatment X increased Y, therefore, Y is higher after treatment X." When describing sequential experiments, you can refer to previous results: "Because we found A, we further examined the effect in system B…")

In clinical articles, the descriptive, baseline characteristics of the sample are usually presented first because they are the results of the sample-selection process. Report the study results of the primary comparisons first and other results of interest later. A common error that can call your integrity into question is to report only statistically significant results or to report statistically significant results first, even if they came from secondary or unplanned analyses. Exact *P* values are preferred to threshold values (that is, $P = 0.02$ vs $P < 0.05$), and the smallest P value that need be reported is $P < 0.001$. However, many journals now request 95% confidence intervals rather than, or in addition, to *P* values.

Report the actual (absolute) change or difference between groups (the "estimated treatment effect" in clinical articles) and a 95% confidence interval for each estimate (NOT the SEM, which is about a 68% confidence interval). Be careful when reporting percentages; in small samples, small numbers can appear larger when expressed as percentages. ("In all, 33% of the rats lived, 33% died, and the last one got away.") The numerators and denominators of all percentages should be readily identifiable. Reserve the terms "significant" and "significantly" for their statistical meaning. Clinical or biological importance can be indicated instead by phrases such as "substantial improvement" or "markedly reduced."

Other details that may need to be reported in the results include:

_ The dates or time periods of data collection
_ Any unplanned or unanticipated events that could affect the results
_ Any adverse events and their timing with respect to the treatment protocol
_ A complete accounting of all subjects or observations and explanations for any missing data or lost patients
_ The names of specific statistical tests or procedures used in the analysis
_ Assurance that the assumptions of the statistical analyses were met by the data

_ Justification for any unplanned secondary, subgroup, or exploratory analyses conducted after the results were analyzed as planned or after they were known.

Discrepancies in information presented in the methods, results, and discussion are a common problem in reporting research. Make sure that all the data described in methods section are reported in the results and addressed in the discussion and that method of data collection is described for all the data reported in the results.

Writing the Discussion Section

In the discussion, discuss your research! Place your research in context, interpret your results, and explain their implications and, hopefully, their importance. In other words, you have to answer the same two questions journal editors will ask: "So what?" (Is this research new, true, and important?) and "Who cares?" (Who needs to know about it?)

Especially during training, you may be required to conduct publishable research. Without adequate money, experience, or supervision, however, you may have to investigate something that you *can* study with limited resources rather than something that *needs* to be studied. This unfortunate situation may not be apparent until you begin to write the discussion section and realize that the rationale for the study was weak and that the results are thus unremarkable. (See Appendix 1 for an alternative.) You may struggle to justify your research and end up more or less repeating the results in the discussion; a common problem with discussions. A *very* common problem.

Consider the following organization for the discussion:

1. **Briefly summarize the study and the main results in a paragraph or two.** *Be sure you answer the research question you posed in the introduction*.

2. **Interpret the results and suggest an explanation for them.** What do they mean? Do they support your hypothesis? Can you attribute them to a specific biological mechanism?

3. **Describe how the results compare with what else is known about the problem**; **review the literature and put the results in context.** Rather than summarizing the literature in one portion of this section and interpreting your research in another portion, address each point in your research one at a time. Introduce your point and then tell what other researchers have found that is relevant to this point.

4. **Suggest how the results might be generalized.** Would they apply to other types of cells? Other diseases? Different populations?

5. **Discuss the implication of the results.** Will they change patient care? Do they suggest another hypothesis or follow-up experiments? How should your results be used? Could they lead to the development of a new therapy?

6. **Under a separate subheading, state the** limitations of the study**, their possible effects on the results, and, if possible, the steps taken to minimize their effects.** All studies—even yours—have limitations. Authors who acknowledge limitations tend to be seen as honest, careful researchers. Readers who find unacknowledged limitations may conclude that the author was at best careless and a worst, deceptive.

7. **Under a separate subheading, *list* your conclusions**. Describing each conclusion individually will force you to be more specific and will aid readers in understanding your research.

The most common problems in the discussion are:

1) Not answering the research question that was posed in the introduction

2) Repeating the results rather than discussing their implications

3) Confusing statistical significance with biological or clinical importance

4) Not distinguishing between supported conclusions and speculation.

Writing the Acknowledgments

The purpose of the acknowledgments is to identify and thank contributors who do not qualify as authors. Some journals allow only people who provide scientific support to be acknowledged, not those who provide editorial or clerical support. Most require written approval from those acknowledged to allow those who do not wish to be associated with the research the opportunity to decline being acknowledged and to prevent famous people from being acknowledged without their permission in the attempt to indicate endorsement.

Citing and Preparing the References

WHAT AND WHERE TO CITE REFERENCES IN THE TEXT

The purpose of citing references is to allow readers to verify the claims and arguments that establish the rationale of your research, document the adequacy of your methods, and support the interpretation of your results and conclusions, as well as to give credit to others whose work has influenced your own. In an article reporting original research, you are making the case that your results are true and that your interpretation is reasonable. In science, making such a case means proposing a logical argument based on facts and sound reasoning. References help establish that your facts are true and that the evidence supports your reasoning.

Thus, be sure to review the logic of your finished manuscript and to cite references wherever necessary throughout your reasoning process.

Before you submit your manuscript, be sure your literature review is comprehensive and current. A reference list that does not include key articles in the field or that cites outdated articles is grounds for rejecting your manuscript.

The general rule is that only easily and publicly available references should be cited. Thus, personal communications, unpublished observations, oral presentations, and manuscripts submitted but not yet accepted for publication are not usually acceptable in reference lists. Instead, they can be cited in parentheses in the text. Abstracts and conference presentations are also often excluded from reference lists because they do not contain enough information about the research to judge its validity. They, too, can be cited in parentheses in the text.

Cite only references you have read, and read in their entirety. If you write your literature review having only read abstracts, you will quite likely have incorrect information and will miss important qualifying information, both of which can seriously mislead you and your readers. (See Chapter 8.) Also, citing (and reading) original sources is preferred to citing (and reading) secondary sources that cite original articles. Don't rely on the author of the secondary publication to get things right. The exception to this advice is the definitive review article published in a top peer-reviewed journal that can be cited with confidence.

Avoid citing unnecessary references and do not cite references unnecessarily. Unless you are writing a comprehensive or a systematic review, and depending on the circumstances, one or two references to high-quality studies may be enough to establish the validity of a fact. For general statements (e.g., "The estrogen receptor is important for female hormone regulation and signaling"), citing a quality review article may be sufficient.

PREPARING THE REFERENCE LIST

Many journals in the life sciences cite references in the text with sequential numbers, either in brackets or as superscripts, and before commas, colons, and semi-colons but after periods at the end of sentences. The citations are then listed sequentially in the reference list. An alternative often used in social sciences, nursing, and in some basic science journals is the name-date or Harvard method, in which the first one or two authors' last names and the date of the publication are given in parentheses in the text. The citations are then listed alphabetically in the reference list. A third way to organize references is to list them in alphabetical order by the first author's last name, number them in that order, and then cite the reference by this number in the text.

Unless you are using reference management software that automatically renumbers citations when you add references in the middle or cut and paste text (see below), use the name-date system until the manuscript is in final form; you don't

want to have to keep renumbering the references to keep track of them during the revision process.

The journal's instructions for authors will tell you how to format the references. If you are reporting clinical research, hope that the journal uses the Vancouver Style as presented in the *Uniform Requirements for Manuscripts Submitted to Biomedical Journals*, which is not only an efficient style but also widely accepted among clinical journals. Otherwise, you may be directed to use any of a large number of style manuals, such as those of the Council of Science Editors (CSE), the American Medical Association (AMA), the American Psychological Association (APA),the American Chemical Society (ACS), the American Institute of Physics (AIP), or the Modern Language Association (MLA).

Most styles require the same information for each reference, but the order and formatting of this information differs greatly. Some styles omit the titles of articles, for example, and some require listing the names of all authors whereas others list only the first 3 or the first 6 authors before using et al. (a Latin abbreviation, "*et alia*," meaning "and others." When used, the period follows the "al.," which is abbreviated, not the "et," which is not).

When journal titles are abbreviated, the abbreviations are almost always those used by the National Library of Medicine (NLM); see:

www.nlm.nih.gov/tsd/serials/lji.html.

Journals with a single word as a title (*Cell*, *Gut*, or *Memory*, for example) are not abbreviated. Longer titles are shortened sensibly: *Ann Intern Med*, for *Annals of Internal Medicine*; *J Clin Invest* for *Journal of Clinical Investigation*; and *Arch Toxicol* for *Archives of Toxicology*.

For more information on citing references in any media, see the National Library of Medicine guide titled *Citing Medicine: the NLM Style Guide for Authors, Editors, and Publishers*, which is available free on the NCBI Bookshelf:

www.ncbi.nlm.nih.gov/sites/entrez?db=Books&itool=toolbar.

Whatever the journal's reference style, FOLLOW IT EXACTLY. Also, in any given published article, the references will contain more errors than any other section of the article. (See references 26, 27, and 28 for illustrative studies on error rates in reference lists.) So, as tedious as it can be, verify the accuracy of each reference citation. Some authors maintain a file box for each article they write and keep paper copies of all reference cited in the article, a practice I recommend highly. There is no substitute for having the full reference at hand both before and after publication. You can also check each citation electronically on NLM's MEDLINE database, PubMed: www.ncbi.nlm.nih.gov/sites/entrez.

Many on-line references have a unique **digital object identifier (DOI)** that allows them to be found on the Internet, no matter where they are archived electronically. In general, if a reference has a DOI, it should also be included at the end of the reference. Citations to online publications and websites should include the date of access.

Reference Management Software

Several software programs will keep track of your references within and between manuscripts and will automatically reformat them for most major reference styles. They can save you *lots* of time. These programs include: EndNote, ProCite, Reference Manager, RefViz, the web-based RefWorks, and sciPROOF. Once you enter the bibliographic information for references into the program, either by hand, by downloading them from MEDLINE, or by importing them from existing files, you can add a citation into your manuscript that will be linked to the reference. Should you rearrange your text, the software will keep track of the changes and reorder the references automatically. The journal may require that you convert the field codes used by the software to plain text before submitting the manuscript, or you may need to do so to avoid software conflicts. If you do, keep a copy with the field codes to facilitate revisions.

Different journals use different reference styles, which is another reason you need to read the journal's instructions for authors. Look for differences in the number and order of the authors' names, punctuation, locations of publication dates, the presence or absence of titles, and how journals are identified.

Reference Style	Example of a Reference to a Journal Article
Uniform Requirements for Manuscripts Submitted to Biomedical Journals (Vancouver Style)	Lau J, Ioannidis JP, Balk E, Milch C, Terrin N, Chew P, et al. Evaluation of technologies for identifying acute cardiac ischemia in emergency departments. Ann Emerg Med. 2001;37(5):453-60. Review.
American Chemical Society	Lau, J.; Ioannidis, J.P.; Balk, E.; Milch, C.; Terrin, N.; Chew, P.; et al. *Ann. Emerg. Med*. **2001**, 37, 453-60.
American Psychological Association	Lau, J., Ioannidis, J. P., Balk, E., Milch, C., Terrin, N., Chew, P., & Salem, D. (2001). Evaluation of technologies for identifying acute cardiac ischemia in emergency departments. Annals of Emergency Medicine, 37:453-460.
American Institute of Physics	Joseph Lau, John P. Ioannidis, Ethan Balk, Cathy Milch, Phyllis Chew, and D. Salem. Ann Emerg Med **37**, 453 (2001)
Institute of Electrical and Electronics Engineers (IEEE)	J. Lau, J.P. Ioannidis, E. Balk, C. Milch, N. Terrin, P. Chew, D. Salem, "Evaluation of technologies for identifying acute cardiac ischemia in emergency departments," *Annals of Emergency Medicine*, vol. 37, pp. 453-460, 2001.
Chicago Manual of Style	Lau, Joseph, John P. Ioannidis, Ethan Balk, Cathy Milch, Phyllis Chew, and Deeb Salem. 2001. Evaluation of technologies for identifying acute cardiac ischemia in emergency departments. *Ann Emerg Med* 37: 453-60.