

REVIEW

How to Conduct a Pleural Research: Master's Advice

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I have been doing medical research for nearly 50 years and most of it has dealt with pleural disease. While doing research during these years, I have also mentored many young researchers. This article summarizes what I have learned during this time.

Why Do Research? There are several reasons that one might want to do research and the reason will vary from person to person. First, one might do research to get **rich**, but the great majority of researchers do not get rich. Second, one might do research to get **famous**, but only a rare researcher gets famous. Third, one might do research to earn a **free trip**. Certainly, if you perform research and your abstract is accepted for presentation, you might get a free trip to an interesting place. Fourth, one might do research to get a **good professional position**. It is unequivocal that the more publications one has, the more opportunities there are professionally. Fifth, one might want to **answer a question** about the diagnosis or treatment of a disease. This is a very rationale reason to perform research. Lastly, one might want to **discover something that is unknown**. The last two reasons are the reasons that I have done most of my research.

What is necessary to perform research? There are many things that some think are necessary to perform research including a genius level of IQ, a lot of money, an inquisitive mind, dedication, persistence and organization. In my opinion, the most important element is **persistence**. I have worked with many individuals who start a project but never complete it. They most commonly stop after the research is completed, but before the paper is written. They may also stop while they are writing the protocol, doing the research or writing the paper. To be a successful researcher, one must be persistent. The second most important element is **organization**. By organization, I mean arranging one's life so time is not wasted. Do not waste time complaining about things. I keep a list of things that I need to do on my computer. When I have a number of minutes free I look at the list and see what I can accomplish in that number of minutes. If one is organized, one will not spend an hour looking for a paper. If one has their life organized, then they will have time for those things outside of research that gives them enjoyment. The third most important element is **dedication**. If you watch sporting events or go to movies rather than work on your research, you will be less likely to be successful. The fourth most important element is to have adequate **money**. Obviously, your research will fail if you do not have adequate funding. However, it should be noted that much research is completed with no funding. When I wrote the paper on Light's criteria, I had no funding for the project. The fifth most important element is to have an **inquisitive mind**. This element is important to aid the researcher in formulation the research and analyzing the data. The least important of the elements is a **genius level of IQ**. It certainly helps to be smarter than the average person, but a genius level of IQ is not necessary.

What are the different types of research? The types of research include case reports, reviews of the literature, retrospective reviews of case series, prospective reviews of case series, evaluation of new diagnostic tests, evaluation of new therapies, evaluation of new medical devices, and papers on basic science. **Case reports** are frequently the type of research that one starts with. However it is difficult to get case reports published in first rate journals because the publication of case reports decreases the impact factor of that journal. However, there are several pulmonary journals that are on Medline that now publish only case reports. **Reviews of the literature** are worthwhile but again are hard to



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get published unless one is invited to write the review. **Retrospective reviews of case series** are certainly useful and generally do not cost any money. However, with retrospective reviews, often some of the data points are missing. **Prospective reviews of case series** again do not cost any money and if they are organized, missing data should not be a problem. However, it may take years to accumulate the appropriate number of patients. **Evaluation of new diagnostic tests** is very important in advancing the practice of medicine. When a new diagnostic test is evaluated, it is important to compare the results with the new test with a test that has previously been used as the gold standard. **Evaluation of new therapies** is one of the most commonly performed types of research. Ideally evaluation of new therapies should be done with randomized double-blind controlled studies. If the study is not blinded, the researcher probably believes in his new therapy and will be biased in evaluating the results. **Evaluation of new medical devices** is also important in advancing medical science. Again it is best to do randomized controlled studies but frequently with medical device studies it is difficult to design the study so that it is blind. Lastly, a large percentage of medical research has to do with **basic science**. I did no basic science or animal studies until after I had been doing research for 20 years. I rapidly discovered that animals were much easier to recruit than patients. However, basic science research requires more resources than do many types of human research.

How do you get started to do research? The first thing you need to do is to **develop an idea**. How do you develop the idea? It can be a question raised when taking care of a patient. It can be a question raised by an associate, an attending or a subordinate. It can be a question raised while attending a lecture or while reading the medical literature. It can also be a question raised while dreaming or even while drinking.

Once you have the idea, then you need to **develop a hypothesis**. For example, this treatment is better than that treatment. Once you have your question and your hypothesis, you should review the literature. PubMed is a good place to start. You should narrow your search as far as is practical. One should obtain a copy or download to your computer all pertinent reference papers. Do not rely on review papers. Do not use Wikipedia.

It is important to organize the pertinent references. I recommend transferring all abstracts to your computer. Keep them organized by putting them in alphabetical order by the first author's last name. Make notes on the abstracts as pertinent. Make an outline of what you have found in your review.

Once you have your idea formulated and have the literature reviewed, then discuss the proposal with your associates. Carefully consider their comments, but you do not have to accept them all. At this time you should also evaluate the resources necessary to complete your project. How many

patients will be needed to answer your question? How much money will it take to conduct the study? Take into account personnel, Elisa kits, animals, pharmaceuticals, pipettes, etc. What space is necessary including office space, freezer space, and laboratory space? Estimate how long it will take to complete the study. In general it is a good idea to multiply your estimate by at least a factor of two.

Is the research ethical? It is important to make certain that the research is ethical. For human subjects, the question I ask myself is as follows: Would I volunteer for this project if I qualified to participate. If the answer to this question is no, then the research should not be performed.

Writing the protocol. Before the research can be conducted, a research protocol needs to be written. You should start with the specific objectives and hypothesis. Then you should set the stage for your protocol by writing the background information which is essentially a review of the literature in the context of your research. Then describe the actual research protocol. Make this very detailed. Do not leave anything open to question. Include the statistical method of analysis in the protocol and perform a power analysis. Include references in the protocol.

Necessary Approvals Before Research Can Begin. If the project involves humans, approval must be obtained from the Institutional Review Board (IRB) before the study can be started. IRB approval is necessary even if you are doing a chart review but this does not require a written informed consent. IRB approval is also necessary if blood or tissue is obtained for use in present or future studies. Most journals will not accept a paper for publication if the project has not been approved by an IRB. If animals are being studied, the animal studies committee must approve the project. If radioisotopes are used in the study, the radioisotope committee must approve the project. If biohazards are involved, e.g. Staph.aureus or asbestos, the biohazard committee must approve the project. If you are studying a new drug or an old drug for a new indication, your proposal must be submitted to the National Health Service (NIH in the United States).

Eliciting Cooperation of Collaborators. One needs to create a WIN WIN situation in order to elicit the cooperation of collaborators. By this I mean that you need to create a situation in which you win (your project gets done) but the collaborator also needs to benefit. This at times can be troublesome. This can be in the form of a co-authorship on the manuscript, saving the collaborator work, a dinner, a book or money. It is important to avoid the following. It is unethical to provide direct payment of patient referral. Also avoid competition for patients that the collaborator wants to study, do not make extra work for the collaborator where he/she gets nothing in return.

Performing the Research. It is important to have everything organized before you actually start the research. Effort is

wasted if everything is not done on the first patients. It is best to develop forms for all the data which will be collected. The forms should be such that the data is easily transferred to a computer. The responsibilities of all co-investigators and collaborators should be well defined. Once the research is started, one should be patient, persistent and compulsive. If the research is going poorly and the chances for success appear minimal, the research project should be stopped.

Reasons for Failure of Research Projects. The most common causes for failure of a research project are a lack of organization or a lack of persistence. Other reasons for failure include the following: Inadequate literature review – after the research has been started it becomes apparent that the study has already been done or that the hypothesis is completely different from what is accepted in the medical literature. It is also possible that someone completes an identical project before you project is completed, but this is uncommon. Inadequate numbers of patients can lead to failure of a project as can lack of the required cooperation. In some instances, there is just not enough time to complete the project. This is particularly likely to happen when residents, fellows or visiting researchers are primarily responsible for the project. And lastly and most importantly, the research is done but the paper never gets written. This has happened to me numerous times in my career.

Analyzing the Data. After the research is completed, it is time to analyze the data. Many individuals are frightened by statistics. However, data analysis is easy if the data is organized. The actual statistical analysis will depend upon the design of the project. In general one desires to discover whether the results in two groups differ significantly. Basic terms in statistics are the mean (the average value), the median (the value with an equal number of results above and below) and the variance which is a measure of the variability of the results in one group.

Minimize the Variance. The formula for the variance is shown in the following equation

$$\text{Variance} = \text{Sum}(x_i - x_{\text{mean}})^2 / (n-1)$$

Where x_i is the value of the i th observation, x_{mean} is the average of all the observations and n is the total number of observations in the group. The standard deviation (SD) is the square root of the variance. The standard error of the mean (SEM) is the SD divided by the square root of n . In order for two means to be different with a probability (p) value less than 0.05, the two means need to be separated by at least 2 SEMs. From the above discussion, it is apparent that if the variance is minimized, the two means are more likely to differ significantly. In performing research, it is important to make every effort to minimize the variance. This can be achieved by paying careful attention to the details to decrease the randomness of the results.

Writing the Manuscript. The main sections of the manuscript are the abstract (summary), the introduction

(why?), the materials and methods (how?), the results (what you found) and the discussion (so what). When I write a manuscript, I write the sections in the following order. First I write the material and methods section. This section is the easiest to write - just cut and paste from the protocol (remember to change tenses from future to past). I then write the results with the liberal use of tables and graphs. I then write the introduction again relying heavily on the protocol. I do not write the introduction initially because the results of the study may alter the introduction somewhat. I then write the discussion. Lastly I write the abstract. I write the abstract last so that it will be consistent with the remainder of the paper.

Writing the discussion. The discussion without a doubt is the most difficult part of the paper to write. Before I start writing the discussion, I always make an outline of what I want to include in the discussion. In the outline, the first entry is a brief summary of the results of the study and the last entry is the conclusion of the study. The other entries in the discussion should compare the results of the present study with those reported previously, the clinical implications of the study, and the limitations of the study.

Tips on Writing. Write in a simple manner. Keep the sentences short. The first sentence in each paragraph should say what that paragraph is going to say. This makes it easy for the reader to speed read the paper. If the reader agrees with and knows about what is said in the first sentence, he/she can skip the rest of the paragraph. If you have difficulty writing on paragraph, go to a different paragraph. Writing the manuscript is a big task. Count your successes as paragraphs, not entire papers. If you write one paragraph per day, you will have at least 12 manuscripts a year.

Submitting the Paper. Before you submit the manuscript, have someone whose first language is English (if you are submitting to an English journal) review the manuscript and edit it. The more people you have review the manuscript before submission the better. Next you need to choose the journal for submission of your paper. One should look at previous editions of the journal to see if they have accepted similar papers on similar subjects. It is best to select a journal with a high impact factor. After the journal is selected, read the instruction to the authors carefully and follow the instructions. If the instruction state that the upper limit of words is 3000, do not submit a manuscript with 4000 words. If you do not follow the directions, the reviewers will think that you are not a careful researcher.

When the Paper is Accepted Provided Revisions Are Done. Rarely is a paper accepted without some revisions being requested. The goal of revising the paper is to get it accepted for publication. A rebuttal letter should be written where the critiques of each of the reviewers is addressed. List each criticism by a reviewer and then formulate a response. It is best to use different fonts when listing criticisms and making responses. When the reviewer requests an explanation of

something, he wants it explained in the manuscript-not only in the rebuttal letter. Make simple requested changes without argument. Remember the reviewer is trying to make the paper better. Thank the reviewers for their constructive criticisms whether or not you like them.

When the Paper is Rejected. If the paper is rejected, do not give up but rather plan on resubmitting. Remember that submitting a paper is a little like playing the lottery – sometimes you get favorable reviewers and sometimes you get unfavorable reviewers. Remember the reviewers frequently do not agree-maybe you were just unlucky or alternatively maybe the paper is really bad. There are many

medical journals and some have higher standards than others. Before you submit to another journal, look carefully at the criticisms and answer as many as possible. You may get the same reviewer again and nothing irritates a reviewer more than seeing the same paper again without any changes.

Conclusions. The most important factors for successful research are persistence and organization. Before the research is started, review the literature and write a detailed protocol. Create win win situations to elicit the cooperation of collaborators. Write the paper one paragraph at a time. Respond to reviewers and change the paper as suggested.