Clinical Chemistry

A Critique of the Hypothesis, and a Defense of the Question, as a Framework for Experimentation

Host: This is the podcast from *Clinical Chemistry*. I am Bob Barrett.

The July issue of *Clinical Chemistry* published an opinion piece by Dr. David Glass, that critiqued the use of hypothesis within scientific research and defended the use of questions as a framework for experimentation.

Dr. Glass teaches a course on Experimental Design for Biologists at Harvard Medical School and has written a book by that title, published by Cold Spring Harbor Laboratory Press.

He continues the valuation of hypothesis-driven research in this podcast.

So tell us Dr. Glass, why are you supporting questions as a framework for experimentation? Why do you feel that this subject is so important that you wrote the paper?

Dr. David Glass: Well, I noticed to my surprise that experimental design isn't being taught currently in graduate schools. So we got some scientists who came into the lab and we started just chatting about how to do experiments and what they thought about different authors. And they told me that they really didn't know about those authors, like people who are pretty well-known, like Francis Bacon and Descartes and Hume all those.

And of course nowadays philosophy is so divorced from science often education, that people use terminologies without really knowing the roots of them. So I thought it would be useful to write the paper.

And as for why advocating any questions, this really can be traced back to Francis Bacon and to Isaac Newton who said that, hypothesis have no place in experimental science. And the reason he said that was that, hypothesis is a guess, a statement as to how one thinks things work before you actually do the experiment. And their view was that you should first do the experiment and in response to your data sort of develop from the ground up a model or rule as to how things work, rather than starting with a preconceived notion as to how things may work or should work and then try and prove that thing true or false.

Nowadays people talk about falsification of hypotheses that they are just trying to falsify them. But if you actually look at the literature, you will see that what really people are trying to do is to verify their hypothesis, and that's where you get into trouble.

Host: Well, now, if there is such a problem in requiring scientists to have a hypothesis, then how has hypothesis-driven research become so successful?

Dr. David Glass: Well, the use of hypothesis was in response to a real problem which was isolated by Hume, which was that, just because something may have worked in the past doesn't mean it's going to work in the future. That was his complaint. And that's why he rejected something that's called Inductive Reasoning, which is using past results to make assumptions about the future.

But between then and now we have developed statistics and more and more comfort in the idea of probability, that if you do an experiment enough times, with a broad enough number of people or subjects, you can with confidence to a probability say how something is going to work.

But it was in response to this problem that this philosopher called Popper advocated falsification of hypotheses and that's really the dominant theory right now of experimentation.

And that's been adopted by the NIH and by other funding societies. Once a funding organization adopts it, that's why it's so successful, because people basically have to follow that otherwise they don't get their grant, and there is no shortage of grant applications that have been returned to the applicant, because there is not a hypothesis.

And the argument that is made in these papers is that that's really a mistake to impose that on scientists, because there is even some types of science where hypothesis really isn't appropriate, like the newer kinds of scientific experiment such as Systems Biology, where you are surveying whole genomes or every protein in the body, you can't really have a hypothesis as to what's going to change in response to a stimulus.

So this has been a real problem, because Systems Biologists can't give a coherent hypothesis there. They are not in a position to guess when it's so complicated and so their grants might be refused or rejected. Whereas the question just simply asking, what will change in response to a stimulus or what is the effect of doing something on a particular system, like a human for example, you can ask a question and that's a perfectly reasonable way to frame such an experiment.

Host: Well, in your opinion, what's the biggest problem with hypothesis-driven research?

Dr. David Glass: I think the biggest problem is probably that it creates a bias in advance of the experiment. Once you have the hypothesis in place that something causes something else, or that if you give a particular agent, a particular result will happen, the entirety of your experimental design is organized around testing that thing.

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This is not to say the scientists may be intentionally biased, but just by nature of meeting the demands of measuring the thing within the hypothesis, the design becomes skewed. As opposed to a question, where if you don't know the answer, if you are asking sort of an open-ended question to start things, then you are forced to measure many possibilities and cast a broad net to start without bias. Then once you have that data, then you can start constructing a model and test that model.

And the difference between testing a model and testing hypothesis is that the model is based on your actual data, your actual research results as opposed to a guess. And the model can be changed or altered based on your results. You don't just have to abandon it, but if you have a model of how something works and then your data contradicts it, it's perfectly fine to then alter your model going forward, refine it going forward, because the model is an instrument of inductive reasoning. You are trying to verify your model as opposed to falsify your hypothesis. That's why asking questions and developing a model seems to be a much more fruitful way to go forward with the experimentation.

Host: Well, with that in mind, could you explain your alternative to hypothesis-driven research?

Dr. David Glass: Well, it really is the question and the model. So I guess if you don't have any data, when you are just starting a new project, then instead of hypothesis, the suggestion is to simply ask a question. In other words, let's say you want to know what the effect of caffeine is on blood pressure? So rather than having hypothesis that says, caffeine will increase blood pressure, you just ask a question, what is the effect? And you already see there is a difference, because the hypothesis demands you only look for increases, where the questions, you can look for increases, decreases, or no effect.

And then once you get data in response to the question, then that data set becomes a model as to how caffeine behaves in terms of perturbing blood pressure. And then you can refine that model by doing more and more experiments; giving more caffeine, giving it more time,

giving it to different sorts of people, following it according to different markers. That alternative seems to be really how we are actually doing science, although, again, we seem to be forced by convention to reconfigure that all into hypothesis for the purpose of getting funding.

Host: Dr. David Glass teaches a course on Experimental Design for Biologists at Harvard Medical School. He has been our guest in this podcast from *Clinical Chemistry*.

I am Bob Barrett. Thanks for listening.

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