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Hubris in Science?

Lewis Thomas

Everyone says that the root cause of society's diminishing confidence in science is the failure of scientists to explain what they do with their lives, and I agree with this. But I do not see this as an easy problem to solve, not so much because of any inarticulateness on the part of the scientists, and not so much because of deficiencies on the part of the professional journalists who devote their careers to science, but because of the sheer, overwhelming enormity of the field. The enterprise of biomedical research in the United States has expanded in scale and scope so greatly in the past 30 years that no one can begin to keep up with the reading of it. It used to be that a working immunologist could keep abreast of his field by covering three or four professional journals, plus *Nature* and *Science* for the first accounts of new observations. Now there are ten times that number of journals, each containing papers on immunology that cannot be overlooked, plus any number of monographs, review volumes, national and international symposium reports, and even a few newsletters. The journals are themselves five times their former size, with briefer articles and smaller print.

It is the same for all the other fields of biology and medicine. The literature has become too vast to be comprehended. And, to make matters even more difficult, most of the published work is good. The papers that one ought to be reading are important and interesting. The quality of the science, despite its enormous bulk, is really better today than at any time in the past. It is intricate and complicated, and much of it is difficult to grasp even for the workers in closely neighboring fields, but it is filled with meaning.

So, communication has become a serious problem not only between the scientists and the public, but among the scientists themselves. How do the investigators cope with the problem? Not, I think, by relying on computerized library services, although increasingly clever systems for retrieving more or less current information have come into existence in recent years. Nor are the journals themselves used as extensively as they used to be as sources of new information.

What is happening is that there is much more reliance on word of mouth for the transmission of scientific data than ever before in my memory. And, despite the literature problems that I have just been citing, I have the impression that the people doing the work are really better informed about what is going on in other laboratories than ever before. There is a new system at work, which I do not understand. I have the impression that a great body of information is getting around by a mechanism that can only be termed gossip.

The telephone has become an indispensable scientific instrument. Laboratories in New York are in touch with Dallas, La Jolla, Boston, and Paris, all on the same day. By the time papers are published in the *Journal of Experimental Medicine*, most of the people working in that particular field are already familiar with the general drift of the work. If a group in Edinburgh is getting close to solving a special problem, the other laboratories all around the world seem to know about it, and in fine detail. And the information travels almost with the speed of light. A corridor conversation in a research institute in Cambridge will be reported almost instantaneously in Pasadena.

The most surprising thing about the system is that it seems to be functioning with considerable accuracy and reliability. It is also surprising that there is so much openness and candor. It used to be thought that scientists tend to be rather secretive, hiding their data away from each other in order to be sure of priority for the published manuscripts; but these

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days it seems as though they are all telling each other everything they know, by telephone, and as soon as they know it.

Also, and perhaps as the result of the new method of passing around bursts of information by word of mouth, there is a great deal more collaboration going on, often between laboratories set at great distances from each other. Some of the American and European laboratories are working together as closely as if they were located on the same corridor.

It is a new phenomenon for science, and, I should think, a highly encouraging one. There is always the risk that news passed around so rapidly and in so informal a manner may become degraded in the process, altered as in the repeated telling of the same joke, but this does not seem to be happening. The bits of information that one picks up over lunch, or out in the lobbies of the meeting places of the international congresses, are amazing for their accuracy. Moreover, although you might think it would be disheartening to keep hearing, in this kind of gossip, that someone else's laboratory is closing in on your problem faster than you are, and that you are about to be scooped, this does not seem so much of a discomfort. On the contrary, the excitement among the workers seems to be enhanced by the process, and the pace of the work is speeded up by it.

This change has come about, in part anyway, from the realization by so many that there is so much still to be learned. The young investigators, even the youngest ones looking around desperately for grants, are not quite as oppressed as their predecessors were by the anxiety that someone else might run away with the project and thus bring all of science to a conclusive standstill. There is so much more to be done, and so many good, answerable questions to be raised, that there can never be enough researchers. Everyone is becoming conscious of this, and it makes the atmosphere lighter, in spite of the shortage of funds.

And yet, the public hears very little about what is really happening in the laboratories. You might think, to read the papers on some days, that the scientists are ready and eager to take the world over and run it to their liking, filled with hubris, knowing everything about everything.

The truth is, of course, that we have not reached the end of knowledge; we have only just begun, we are just at the edge. But already, here at the edge, it has become a very big area, with much more to come.

It is true that the nucleus of a frog's cell or a plant cell contains all the nucleic acid needed for coding out a whole new identical frog, or a whole new plant. It is also true that a technology for proving this point exists today. You can clone a frog, at least partway toward a new frog, and you can clone certain plants. Therefore, it has become theoretically possible that cloning is possible for other forms of life, if the technology could be developed. But to leap from this level of information to the conclusion that biomedical scientists are on the verge of cloning human beings is the wildest, craziest sort of extrapolation. Leave aside the question of whether there is a competent cell biologist anywhere who would be interested in doing such a thing. Forget about the money, although the high technology involved in such a project would surely consume a large portion of any country's gross national product. Think only of the time that it would take, and what the final outcome, in real life, would be. Unless all our ideas about the development of a human personality are totally wrong, the newly cloned individual could not be similar to the uniparent in any significant aspect, beyond a physical resemblance, unless you took pains to clone, at the same time, the father and mother, sisters and brothers and cousins, friends and acquaintances, the whole neighborhood. You need an environment to mold a personality, for better or worse, and the environment means people. Really, if you wanted to clone a single human being and come away with anything like the "clonee," you would have to drop everything else and clone the whole world. Moreover, you would need a superhuman amount of patience. There could be no bypassing or speeding up the 9 months of fetal development, or all those difficult years of childhood and adolescence, duplicating precisely every educational experience, every human contact. It would be an impossible experiment and a truly unimaginable technology.

Still, there it is. This is one of the most talked-about hazards of science, especially in social science circles.

Recombinant DNA is another. Here the danger is said to be embodied in the creation, accidentally or on purpose, of new pathogens by inserting strips of foreign DNA into the plasmids of *Escherichia coli*. We seem to have come full circle, and the making of hybrids, like the Roman wild boar offspring, is hubris. And here, as in the case of cloning, there is a certain hubris in the claim that such things can be done. We do not have a clear understanding of pathogenicity, but what we do know is that it is enormously complex. Considering the vast number of microbial species on this planet, the property of causing disease by infection is excessively rare, almost freakish. Most of the bacteria and fungi make their living by browsing, reducing dead matter to reusable organic forms. The few microbes that have evolved as infectious agents have only done so after millions of years of adaptation and interliving. Most of them are equipped with elaborate signaling systems, special markers at their membranes, and bizarre products that imitate enzyme reactants in certain cells of their hosts. Organisms like these have to have multiple guidance mechanisms before they can even approach the tissues of a host. Pathogenicity is a highly skilled trade. It takes a kind of arrogance to assert that microbiologists can manufacture complicated creatures like these, by choice or by chance.

On the other hand, the pure research potential of the recombinant DNA technique is simply tremendous. It does not exaggerate the case to say that this may be the greatest scientific opportunity for biology in this century. Deep questions can now be asked about chromosomes and genes and about the most fundamental processes of living cells, questions which were unthinkable just a few years back. The possibilities for benefit are incalculable. Our greatest handicap in coping with human disease has always been our ignorance of how the organism really works. We need this new approach, not only for biology but for medicine itself.

And yet, here we are, caught up in a public controversy in which the only issue being talked about seems to be the invention of monsters for their own sake, mini-Frankensteins, and it is even being made to seem as though this is really how the investigators engaged in work of this kind obtain their pleasure, like the mad scientists in their basement laboratories in grade B movies.

But the fundamental misunderstanding in this case is around the issue of the power of science. Somehow, the myth has grown up, and has been allowed to flourish, that science already knows too much and can manipulate living matter with such command that new technologies for altering all of nature are just around the corner. It is not like that at all. The recombinant DNA technique is a way of exploring important territory that is now totally bewildering, about which we possess only the most primitive level of hard information. The workers in this field are not about to manufacture hybrid beings. They are trying to find out how things work.

Because of the concern raised about the imagined hazards of recombinant DNA, there is now talk in political circles of the need for a new agency in government, for taking a look at science before it is done, in order to ward off the risks of new knowledge. It is a fundamental misunderstanding of the scientific process. It is as though we had decided, at the time of Koch's discovery of the tubercle bacillus, to put a stop to such work lest we all catch something. There is simply no way of deciding in advance where a basic scientific exploration will come out, or what the risks and benefits will be. If such things could be forecast with any accuracy at all, there would be no point in doing the research, for the answer would already be in hand. Biomedical science is an inquiry into the unknown, and the extent and scale of unknown territory is far greater than the public has imagined.

I suppose the scientific community is mostly to blame for the dilemma. We have often made it seem as if we are almost there, and, with just a bit more effort and more funding, we will be home and dry, knowing everything. Also, we have made too many promises, too explicitly and of too short a term. In my own field of interest, cancer, it is reasonable and honorable to say aloud that cancer has become both an approachable and an ultimately solvable biological problem, and today's massive research program will turn out to be both useful and, one day, successful; but it is not possible to say when. Nor is it possible to forecast, at this stage of our understanding, which of the many avenues now open for approaching the fundamental problem of cancer is the best one, or the likeliest to produce decisive answers. We do not know enough. It is absolutely essential that a very wide net be cast, that research be conducted along many different lines. It is even necessary that there be some duplication of effort, with different laboratories studying essentially the same process, for one investigator may notice something overlooked by all the others.

It is sometimes made to seem as if basic research might be improved into a more orderly, predictable business, by more systematic management, in which predictions could be made solidly on the basis of reliable facts now at hand, and then simply confirmed by testing. This is, indeed, the way good applied science is done, but basic research is something quite different; and it is useful to make the distinction based on the single issue of certainty. It is especially useful for making science policy, since the methods used for the two kinds of science are fundamentally different. In the creation of the polio vaccine, for example, once it was known with certainty from basic research, that there were three antigenic types of poliovirus and only three, and that they could be grown to abundance in tissue culture cells, it became an absolute certainty that a polio vaccine could be made; the sole question was how best to do the job. As soon as there was agreement all around on the certainty of these essential facts, committees were formed for the purpose of laying out the most detailed kinds of protocols, and all members of the teams of investigators agreed in advance to follow the protocols in scrupulous detail. The outcome, under the leadership of Jonas Salk, was a masterpiece of beautifully organized and executed applied science.

In basic science, things are just the opposite. To begin with, committees cannot formulate the ideas or lay out the plans; this is work that can only be done in the mind of the investigator himself. The plans must be flexible and changeable. The work has to proceed in an atmosphere of high uncertainty. The basic facts at hand can only be solid and suggestive enough to allow for imagining and guessing. Hypotheses must be set up for testing, but it is understood all around that these are likely to be wrong. Sometimes an idea emerges from what can only be called intuition, and when the mind producing the idea is very imaginative, and very lucky, the whole field moves forward in a quantum jump.

This kind of work can be extremely frustrating and tedious, and the odds against success are always very high. Nevertheless, the experience of being right in making a guess about nature is such a splendid excitement that the people who do such work lead, by and large, enviable lives. The territory is always open, and the frontier is immense ground, all unknown. It is exploring, in the classical meaning of that excellent word: to cry aloud on finding. To see something never seen before, to understand a mechanism never before comprehended by anyone, is the purest kind of fun. It is a curious fact that some of the most important discoveries seem enormously funny to the explorers, when they are first made. A sudden burst of unbelieving laughter in a laboratory is one of the surest signs that the work is going well. Some of the shrewdest insights into natural processes have been greeted at the outset by the exclamation, "But that's ridiculous!"

It is important to understand that there is a single driving ambition in basic science, and it is quite different from the motivation that pushes applied science and the development of technology. Basic science is done to find out how things work in nature. It is, essentially, a search for mechanisms. The cell biologist is not trying to clone a human being; he is interested in how the individual cells of an organism are switched into different forms during the miraculous process of embryologic differentiation. The neurobiologist is not hankering to learn how to control behavior; he is out to learn how the brain works.

Basic science cannot be regulated, nor is there any reason to try doing so in my opinion. Technology is, of course, quite a different matter, and we ought to have better political mechanisms for deciding, beforehand, what kinds of applied science should be pursued with public funds. The public regulation of technology development is in no sense an intrusion on scientific freedom and should be welcomed by the scientific community.

I can imagine all sorts of problems for a public agency, or a commission, if it were set up to regulate or censor basic science, especially if charged with decisions about what kinds of new knowledge we are all better off not having. There are, after all, all sorts of scientific inquiry that are not much liked by one constituency or another, and we would soon find ourselves with crowded rosters, panels, standing committees, set up in Washington for the appraisal, and then the regulation, of research. Not on grounds of the possible value and usefulness of the new knowledge, mind you, but for guarding society against scientific hubris, against the kinds of knowledge we are better off without.

It would be irresistible as a way of spending time, and people would form long queues for membership. Almost anything would be fair game, certainly anything to do with genetics, anything relating to population control, or, on the other side, research on aging. Very few fields would get by.

The research areas in the greatest trouble would be those already providing a sense of bewilderment and surprise, with discernible prospects of upheaving present dogmas. I can think of several of these, one from the remote past of 40 years ago.

First, the older one. Suppose this were the mid-1930's, and there were a Commission on Scientific Hubris sitting in Washington, going over a staff report on the progress of work in the laboratory of O. T. Avery at the Rockefeller Institute in New York. Suppose, as well, that there were people on the commission who understood what Avery was up to and believed his work. This takes an excess of imagining, since there were vanishingly few such people around in the 1930's, and also Avery did not publish a single word until he had the entire thing settled and wrapped up 10 years later. But anyway, suppose it. Surely, someone would have pointed out that Avery's discovery of a bacterial extract which could change pneumococci from one genetic type to another, with the transformed organisms now doomed to breed true as the changed type, was nothing less than the discovery of a gene; moreover, Avery's early conviction that the stuff was DNA might turn out to be correct, and what then? To this day, the members of such a committee might well have been felicitating each other on having nipped something so dangerous in the very bud.

Here is an example from today's research on the brain, which would do very well on the agenda of a hubris commission. It is the work now going on in several laboratories here and abroad dealing with the endorphins, a class of small polypeptides also referred to as the endogenous opiates. It is rather a surprise that someone has not already objected to this research, since the implications of what has already been found are considerably more explosive, and far more unsettling, than anything in the recombinant DNA line of work. There are certain cells in the brain which possess at their surfaces specific receptors for morphine and heroin, but this is just a biological accident; the real drugs, with the same properties as morphine, are the peptide hormones produced by the brain itself. Perhaps they are switched on as analgesics at times of trauma or illness; perhaps they even serve for the organization and modulation of the physiological process of dying when the time for dying comes.

These things are not yet known, but such questions can now be asked. It is not even known whether an injection of such pentapeptides into a human being will produce a heroin-like reaction, but that kind of question will also be up for asking, and probably quite soon since the same peptides can be synthesized with relative ease. What should be done about this line of research—or rather, what should have been done about it 2 or 3 years ago when it was just being launched? Is this the sort of thing we are better off not knowing? I know some people who might think so. But if something "prudent" and cautious had been done, turning off such investigations at an early stage, we would not have glimpsed the possible clues to the possible mechanism of schizophrenia which are now beginning to emerge from this research.

This is characteristic of the enterprise. If the things to be found are actually new, they are by definition unknown in advance, and there is no way of foretelling where a genuinely new line of inquiry will lead. You cannot make choices in this matter, selecting things you think you're going to like and shutting off the lines that make for discomfort. You either have science, or you do not, and if you have it you are obliged to accept the surprising and disturbing pieces of information, even the overwhelming and upheaving ones, along with the neat and promptly useful bits.

The solidest piece of scientific truth I know of, the one thing about which I feel totally confident, is that we are profoundly ignorant about nature. Indeed, I regard this as the major discovery of the past 100 years of biology. It is, in its way, an illuminating piece of news. It would have amazed the brightest minds of the 18th-century enlightenment to be told by any of us how little we know, and how bewildering seems the way ahead. It is this sudden confrontation with the depth and scope of ignorance that represents the most significant contribution of 20th-century science to the human intellect. We are, at last, facing up to it. In earlier times, we either pretended to understand how things worked or ignored the problem, or simply made up stories to fill the gaps. Now that we have begun exploring in earnest, doing serious science, we are getting glimpses of how huge the questions are, and how far they are from being answered. Because of this, these are hard times for the human mind, and it is no wonder that we are depressed. It is not so bad being ignorant if you are totally ignorant; the hard thing is knowing in some detail the reality of ignorance.

But we are making a beginning, and there ought to be some satisfaction in that. The method works. We obtained the techniques of immunization and all the antibiotics as the direct result of a half-century of difficult, painstaking basic research in the fields of bacteriology and immunology. We will solve the problems of heart disease, cancer, stroke, arthritis, schizophrenia, senile dementia, and all the rest if we can just keep learning. Ultimately we can become a relatively healthy species, as healthy as we now expect our domestic animals and plants to be. We can look forward, one day, to natural death, dying by the clock in the fashion of Oliver Wendell Holmes' "one-hoss shay." There are probably no questions we can think up that cannot be answered, sooner or later, including even the matter of consciousness. To be sure, there may well be questions we cannot think up, ever, and therefore limits to the reach of human intellect which we will never know about; but that is another matter. Within our limits, we should be able to work our way through to all our answers, if we keep at it long enough, and pay attention.

I am putting it this way, with all the presumption and confidence that I can summon, in order to raise another, last question. Is this hubris? Is there something fundamentally unnatural, or intrinsically wrong, or hazardous for the species, in the ambition that drives us all to reach a comprehensive understanding of nature, including ourselves? I cannot believe it. It would seem to me a more unnatural thing, and more of an offense against nature, for us to come on the same scene endowed as all human beings are with curiosity, filled to overbrimming as we are with questions, naturally talented as we are for the asking of clear questions, and then for us to do nothing about it, or, worse, to try to suppress the questions. This is the greater danger for our species, to try to pretend that we are another kind of animal, that we do not need to satisfy our curiosity, that we can get along somehow without inquiry and exploration, and experimentation, and that the human mind can rise above its ignorance by simply asserting that there are things it has no need to know. This, to my way of thinking, is the real hubris, and it carries danger for us all.