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HEGEMONY OF MEDIOCRITY IN CONTEMPORARY SCIENCES, PARTICULARLY IN IMMUNOLOGY

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The controversial article which follows, grapples with the "business of doing science." As a criticism of research generally and immunology in particular, it bears directly on lymphology as an investigative discipline. As an indictment of modern scientific research the author cuts a braod swathe and paints a grim if not grimy picture of academia and the research enterprise. If this eminent immunologist's highly critical thesis strikes a responsive chord, then not only is wide dissemination of his message justified, but along with it honest reappraisal and remediation of harmful trends in medical research and scientific communication as currently practiced world-wide (CLW).

Like body size, human intelligence is distributed over a wide spectrum. There are some very stupid, some very smart, and a lot of mediocre people; only some very stupid people deny this fact. It is true that we do not have an intelligence test on which we can all agree, but no matter what intelligence test we use, the result is always the same: normal distribution of intelligence. And it cannot be otherwise. Intelligence is a quantitative trait and quantitative traits are distributed along a normal distribution curve.

Because it takes some intelligence to do science, we scientists, of course, believe that we have been selected from the right arm of the normal distribution curve.

If we accept as a measure of intelligence an IQ test then this statement might even be true. After all, before we become scientists, we have to go through all kinds of schools, take all kinds of courses, and pass many examinations and tests. Only when we perform well on these tests, are we allowed to become scientists. Since all the examinations are based on the same principle as the IQ test, we are basically selected for higher than average IQ values.

But what does the IQ test measure?

I am aware of the fact that answers to this question are controversial and I, by no means, want to contribute to this controversy. However, perhaps, we can agree on a general answer which is that the IQ test *measures the ability to solve problems* and that these problems are selected by people with a certain cultural heritage, a certain way of thinking, and certain logic — in short, a certain form of intelligence.

The popular idea of science is that it is a problem-solving activity. According to this view, all we scientists do is answer questions, solve puzzles, solve problems, and the better we are at it, the more successful scientists we are.

Thus everything seems to be in best order: science requires the ability to solve problems and scientists are selected for their ability to solve problems. We should therefore be happy about how well we have arranged things.

Unfortunately, solving problems is not all there is to the scientific endeavor. Even more important than solving problems is *finding relevant* problems — formulating questions that really matter. The world offers us an infinite number of problems to solve, of which we select some and disregard others. Much of the art of doing science is then deciding which problems to concentrate on and which to ignore. We, of course, want to select the most important problems and not waste time

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on trivial ones. To decide which problem is important and which is trivial is an ability that, undoubtedly, we all do not possess in equal amounts. Undoubtedly, it is a quantitative trait and as such has a normal distribution in the human population.

I would like to claim that for this ability we, scientists, *are not selected.* Our educational system does not foster this ability and it does not test for it. All we are required to do, when we want to pass through the system, is to show that we can *solve* problems which somebody else has formulated for us; we are not required to demonstrate that we can *select* from an infinite number of problems those worth studying.

One might argue that there is a linkage between the ability to solve problems and the ability to identify problems worthy of our attention and that by being selected for the former, we are also selected for the latter. However, I don't believe that such a linkage exists because the two abilities are based on totally different requirements. The ability to solve problems requires logical thinking, and hence a rational mind, whereas the ability to identify consequential problems is only in part based on logic; mostly it is based on instinct, intuition, subconscious perception, a sixth sense, inborn proclivity, talent, irrational impulse or whatever you might want to call it.

There is plenty of evidence from the history of science for an independent assortment of these two traits. I will give only one example, namely that of Johann Gregor Mendel, the founder of genetics, who died 100 years ago. As most of you probably know, in 1850, Mendel had to take a teacher's qualifying examination in natural sciences, and this examination he failed. Later he probably made a second attempt and failed again so that he had to remain a mere substitute teacher for the rest of his teaching career. The examination papers have been preserved and so we know that he was not flunked by an examiner who did not like him. When one reads the papers, one has to admit that in all fairness no examiner could have let Mendel pass the examination. For example, in one of the questions he was asked to classify mammals and to state some of their uses to man. Mendel answered this question thus:

"Order I: Quadrumana. Order II: Quadrupeds. Among the animals notable for their utility to man may be mentioned: 1. the kangaroo which lives in New Holland in a wild state and whose flesh is greatly esteemed by the natives; 2. the hare; 3. the beaver. Order III: Plantigrades. Order IV: Clawed Ungulates: 1. the dog, 2. the wolf; 3. the cat, a useful animal because it exterminates mice, and because its soft and beautiful fur can be dressed by furriers; 4. the civet, whose anal glands secrete an aromatic substance which is an article of commerce. Order V: Hoofed Ungulates; among the animals belonging to this order especially useful to man are: 1. the horse; 2. the ass; 3. the ox (sic); 4. the sheep; 5. the goat; 6. the chamois, the deer, and the stag; 7. the llama, much used in Mexico as a beast of burden carrying light loads up to one or two hundred weight; 8. the musk ox; 9. the reindeer; what the reindeer is for north, the camel is for the hot steppes; 11. the pig; 12. the elephant is a splendid beast of burden. Order IV: Web-footed animals; etc."

As Mendel's biographer, Hugo Iltis, who certainly cannot be suspected of trying to denigrate his subject, comments:

"One cannot but realize that the most kindly of examiners would have been compelled to withhold his approval from the candidate..."

Hence to the examiners, Mendel appeared to be a rather unintelligent fellow. Yet among his contemporaries, whose intelligence was certified by university diplomas and who included such luminaries as Gartner, Prinsheim, Naudin, Darwin, Galton, Focke, Weismann, Beijerinck, and Nageli, Mendel was the only one who could ask the right question.

Nageli, with all his certified intelligence, did not grasp the significance of this question even when Mendel presented it to him with the answer. Judged by his ability to ask the right question and to choose the right approach to answering it, Mendel was a genius. Anyone who considers this statement an exaggeration should read Mendel's paper. It is absolutely brilliant.

I could give many other examples

documenting my thesis: Peter Gorer was considered slightly retarded by his teachers, whereas his contemporary, J.B.J. Haldane was regarded by all as a genius. Yet it was Gorer, who discovered mixed histocompatibility complex (Mhc), whereas Haldane did a little of everything but nothing really great. Jon van Rood, the co-discoverer of the HLA system, failed the final examination in a discipline to which he was to make his most significant contribution — internal medicine.

The mathematician Evariste Galois failed the entrance examination to the Ecole Polytechnique — in mathematics!

I conclude, therefore, that in terms of aptness to carry out research, we scientists, are an unselected population, and that with regard to this trait we are distributed along the entire range of the normal distribution curve.

To come to my main thesis, I start with a picture of a pyramid as a symbol of the most common structural element in the organization of human society. The society of scientists is also organized in a pyramidal fashion. We don't have a single leader on the apex of the science pyramid but we do have an oligarchy, a few leaders at the top of the pyramid and then a hierarchy of researchers whose influence decreases with the distance from the top. At the base of the pyramid we then have the common plebs. The leaders possess considerable power because they control the press, the money, and the positions. Hence, they influence what kind of research is done and what kind of people do research.

In this sense, the quality of research reflects the competence of the oligarchy. Bad research suggests a society ruled by an incompetent oligarchy; good research a society ruled by a good oligarchy.

Now, let us ask the question: From which part of the normal distribution curve is the oligarchy recruited? Is it from the lower range, the high range, or the middle range? My contention is that it is drawn from the middle range, the range that contains most members. In this respect, our society of scientists is democratic. It draws its representatives from the majority.

Unfortunately, this kind of democracy is not good for science. It does not lead to bad science; but it does not produce a very good science either. It produces mediocre science. I wish to claim that much of immunology research done today is not bad or good; it is mediocre and that this is so largely because we have a mediocre oligarchy governing us. We have a hegemony of *mediocrity.*

To document this hypothesis I enumerate the signs of mediocrity in contemporary immunology and give examples of their manifestation.

The most conspicuous sign of mediocrity is *asking trivial questions.* As I said earlier, finding an answer to a question is only one part of successful research. The other part is *asking* the right question — and I would like to maintain that most of the questions asked by immunologists today are trivial. Here are some examples.

I have in my files 529 papers dealing with tissue distribution of major histocompatibility complexes (Mhc), but I am sure that my files are incomplete, and that in actual fact many more papers have been published on this topic. The true figure might be double or triple of what I have accumulated. Now, why would someone want to know what tissues do and what tissues do not express Mhc molecules? If we did not know the function of the Mhc molecules, we might presume that the tissue distribution would give us a clue. But we *do* know the function of the Mhc molecules, so this could not be the reason for such a study. We could then argue that the surgeons need to know what tissues express what antigens so that they know what to expect when they transplant organs. But the fact is that the surgeons couldn't care less about such studies, relying instead on simple logic that if the transplants are rejected, they must express antigens. We should then try to find still another justification:the expression of Mhc molecules might serve as a marker for different types of tumors. But why then study the distribution in normal tissues? Finally, we could simply say: we study this question because we want to know the answer — and that's that! Nobody can argue with such a motivation, of course, but we should remind ourselves occasionally that we are, after all, paid for what we are doing and therefore should not do research just for our private

pleasure.

In trying to find the answer to the question why researchers study the tissue distribution of Mhc molecules, I read the papers in my collection. But I did not become wiser. Most of the papers do not give any reason at all. Some say:

"We have produced this new monoclonal antibody and we thought it could be used ..."

Or:

"We have developed this new method of separating cells, staining tissues, or killing cells and wanted to know ..."

Or:

"We have acquired this new fancy gadget (for example, cell sorter) and decided to retest some claims ..." etc.

Some papers, particularly those dealing with human cells, suggest clinical relevance of the type I mentioned — markers for leukemias, inducers of autoimmunity, stimulators of graft rejection — without actually ever demonstrating such relevance.

We often make fun of 19th century entomologists who spent their lives counting bristles on beetles' feet. But we do something much worse — we count bristles without knowing how to count. For if you were to read the 500 or so papers, which, of course, nobody does, you would still not know whether, for example, T lymphocytes do or do not express class II Mhc molecules. Some of the papers in my collection claim that they do and others that they do not, and the only way to get an answer is either to believe some reports and ignore others, or to be democratic and accept the claim of the majority. Either way is not very scientific. So, as a consequence, we know how many bristles a particular beetle has on its feet but we still do not know whether T cells express class II Mhc molecules.

The fact that over 1000 papers have been published on tissue distribution of Mhc molecules indicates not only that the 800 or so investigators who authored these studies have not realized how trivial the question was, but also that the reviewers of these papers and the editors of the journals in which the papers were published have not realized this either.

In what kind of journals have these papers been published? Here is a breakdown of the papers in my file. High on the list are the Journal of Experimental Medicine, Proceedings of the National Academy of Sciences and Nature. Now you know as well as I that it is very difficult to get a manuscript accepted for publication in these the most prestigious journals in biomedical sciences. These journals, in particular, are in the hands of the scientific oligarchy. Why then has the oligarchy not done anything to stop the flood of papers dealing with trivial questions? Two answers are possible. Either, the oligarchy knows something that I don't know and the problem of tissue distribution *is* worthy of the 1000 publications. Or, the problem is trivial and the oligarchy has not realized it.

I do not want to be misunderstood: I realize that we all investigate certain trivial things because we believe that they may lead us to more important issues. This is a perfectly normal way of doing research. However, I think that 1000 failures should be more than enough to convince anyone that this particular path is not worth following.

There is also the question of economy. It is difficult to put a value on how much it has cost to produce one of the 1,000 papers but 10,000 dollars is probably a rather conservative estimate. For the 1,000 papers, this comes to about 10 million dollars. While one could argue that this money is still better spent than if it were used to build a bomber or a tank, it is also true that it could have been used to build a school, a hospital, or to support worthwhile research.

Studying tissue distribution of Mhc molecules is just one example of wasteful research. There are many others. Description of new Ir genes, antigens, and monoclonal antibodies; repeated demonstration of Mhc-restriction for this or that virus; description of a new suppressor system without any attempt to elucidate how it works or how it relates to systems already described; descriptions of factors, without any regard to the dozens of factors described before; description of the influence of this or that monoclonal antibody on this or that response; study of the effect of gamma interferon, cyclosporin, or interleukin on God knows what; and so on and so on.

Why is it that so much trivial research is

done today? My answer to this question is: Because the majority of immunologists are mediocre scientists, because the elite that rules contemporary immunology is mediocre, and because mediocre papers are favored by the editorial boards.

To have a paper accepted by a prestigious journal may seem like a lottery, but in fact it is a game with strict rules and little left to chance. I am not talking about the power play which is probably unavoidable in any system: If you are British, then of course you have a better chance of having your paper accepted by *Nature* than if you are, say, French. If you are a member of the East Coast power elite, and you are a member of the elite, and you are a member of the editorial board of the Journal of Experimental Medicine, then of course you have virtually unlimited access to its pages.

This is not what I mean. Rather, I am talking about a situation when you are located, say, in Kansas City, Canberra, or Tubingen and submit a manuscript to a prestigious journal:Then you have a chance only when you prepare the manuscript in a certain way.

First of all, the manuscript must not be a bad one. After all, the oligarchy is not unintelligent and they can tell a bad manuscript when they see one — except when it is their own. But the manuscript must not be a *very good* one either. It must not contain any radically new ideas, untested approaches, discoveries that open new vistas. It must conform to the usual standard, it must not tower above this standard. There is a long list of examples supporting this conclusion. The most outstanding of these is the paper by Hans Krebs describing the Krebs cycle, work later honored by a Nobel prize, but rejected by *Nature* where it was submitted originally.

It is not that the reviewers would not recognize the originality of the contribution. I repeat, they are not unintelligent and they realize that the paper contains something out of the ordinary. But is is precisely this "out of the ordinary" that disturbs them. They really do not know what to think of it and how to handle it. Under these circumstances, the safest thing for them to do is to turn down the manuscript.

The subject of the paper must be *fashionable*. A good topic for a paper these days is *gene conversion*. If you manage to produce meager data that can be interpreted as supporting gene conversion, you can put all modesty aside and aim for the most prestigious journal. Never mind that nobody knows what gene conversion is. Never mind that your data can be interpreted in a half-dozen other ways. Gene conversion is fashionable and that suffices for your manuscript to sail right through the reviewing system.

Also, you must use *sophisticated techniques*. T-cell clones, monoclonal antibodies, cell sorter, DNA sequencing — do wonders with reviewers. Again, never mind that you could have done the same work in a straightforward CML assay instead of T-cell clones; by a standard fluorescence test instead of the FACS; by serology instead of restriction enzyme mapping. The sophisticated techniques seem to add a dimension of credibility to your work, they decorate it — it is like decorating an old mare for a ride to a wedding party.

Finally, you must write your paper to conform with the established norm. Speculate as little as possible, and if you must speculate, do so along the well-established lines. Repeat the main points at least three or four times so that you drive them into the minds of the reviewers and the readers — should there be any. The *Abstract*, the final paragraph of the *Introduction*, the *Results*, and the opening paragraph of the *Discussion* are the places where the reviewer expects to find such repetitions. He feels cheated if you avoid some of this redundancy. A good thing is to give the reviewer an extra bonus by adding a summary at the end of the *Discussion*. The reviewer will appreciate your generosity and will take it into account when making recommendation on the manuscript.

Utmost care is required for putting your results into proper context. It is extremely important what and whom you cite. Here it is absolutely crucial that you stay in the mainstream of current thinking. Any deviation will be looked upon with suspicion, any negligence in acknowledging a popular idea

will be regarded as ignorance or, even worse, as conceit.

If you observe all these recommendations, you will be able to publish your manuscript in any journal you choose.

But all this is of course part of what is wrong with contemporary immunology. We have ended up with a system in which mediocrity begets mediocrity, in which mediocrity is strongly selected for and rewarded, and originality is selected against.

Now I come to the second manifestation of mediocrity in immunology, which is the *muddleness of the field.* You would probably agree with me that in many areas of immunology there is total chaos and that there are only very few questions that we can answer with certainty.

The situation reminds me of some institutions in modern Germany. There, each institution, be it a factory, a post office, or a research department, has a *Betriebsrat*, a sort of union representing the workers of that institution. At some institutions, however, the *Betriebsrat* has become so leftist that it opposes any decision of the leadership on principle, saying: You are the capitalists, we are the exploited workers, hence whatever you might want us to do must be incompatible with our interests, and therefore, we must be against it. In this way, the *Betriebsrat* has managed to incapacitate some of these institutions.

In immunology, I too, have the impression, that some workers oppose published observations and ideas on principle, or just for the heck of it. As soon as someone comes up with something positive, someone else comes up with an observation that completely negates the positive statement. I know of some immunologists who actually specialize on research negating the work of others. For years after a controversy has risen, there are then papers published, some supporting the original statement and others supporting the anti-statement. There are thus facts and antifacts, and the controversy lingers on and on, totally incapacitating certain areas of immunology. And the questions remain unanswered: Are T cells educated in the thymus? How do cells get into and out of the thymus? What actually happens in the thymus? Do T cells mature in the cortex or in the medulla? Is there a J molecule? What is the nature of nonresponsiveness? How do T cells interact with B cells? What is the nature of antigen presentation? Does a network of immune cells exist? What is the nature of tumor specific antigens? I could go on and on with the list; virtually anything you can think of in immunology is doubted by some immunologists.

Of course, controversies are a normal part of scientific process; they are part of the way knowledge increases in that they demonstrate incompleteness of the previously acquired knowledge. But what is happening in contemporary immunology is something else. Here it is not a question of replacing old views (paradigms) with new ones — it is a question of negating observations by counterobservations. Two opposing views can be reconciled, two opposing observations cannot; one of them must be wrong. By this reasoning there must be a lot of wrong observations in contemporary immunology!

How has this situation arisen?

There are several reasons why immunology is muddled and incapacitated. The first is that some of the questions we ask are *truly difficult to answer.* In immunology, we are working with the most complex thing on Earth — a mammal, and we study one of the most complex systems mammals possess. A system that is not localized to a region of the body but pervades the entire organism, a system in which variability is one of the defining features, in each experiment dealing with this system, we manage to control only *some* of the variables, we are never in control of all the variables, as an ideal experiment would require. It is therefore understandable that some of us get different results from others.

The second reason is related to the first: because of the system's complexity, *the techniques we use* are *extremely vulnerable* to errors in their execution and to errors in the interpretation of the results. Even when we simplify the system by doing as much as we can in tissue culture, we are still working with multitudes of unknowns. Anyone with experience in tissue culture work knows that there are periods when the cultures simply refuse to cooperate and that you may spend

many months trying to find out why. At the end, usually, the techniques begin to work again without your ever finding out why they did not work previously. The only advice the veterans of tissue-culture work can give you in such a situation is: When cultures stop growing — go on vacation! The chemists and the physicists sometimes scorn us: if you cannot standardize the conditions of the experiment to the degree that such things do not happen, you should not do the experiments in the first place. However, if biologists had followed this advice, there would not have been any biology. On the other hand, there is no doubt that our inability to control all the variables in our experiments contributes to the confusion so characteristic of contemporary immunology.

The third reason for the confusion is *cheating*. Much has been said about this topic recently and I shall, therefore, not deal with it in any depth, except to say that cheating does exist in contemporary immunology and it contributes to and *feeds* on chaos.

What do I mean by this last statement? In a controversy where facts and antifacts exist side by side, one side must be wrong and the other side right. But the cheater cannot lose, no matter which side he is on. If he is on the right side,nobody will question his results because, after all, he was right. If he happens to place his cards on the losing side, he again may escape detection because the explanation for his wrong results will be the same as that for all the others who were wrong, namely not that he cheated but that he designed, executed, or interpreted the experiments in a wrong way. Chaos thus provides a shelter for cheaters by making their discovery extremely difficult. And of course, as long as the cheater is not discovered, he contributes to the confusion by producing data that others must reckon on because they don't know that the data are worthless.

Recently, science has come under attack for harboring cheaters and not doing enough to discover them.

"Discover them!" — that is easier said than done. In fact, it is extremely difficult to catch a cheater in your own laboratory not to mention somebody else's laboratory. The only foolproof safeguard against cheating is that you yourself repeat and duplicate every experiment done in your laboratory. But this is impossible because first, you do not have the time, and second you have not mastered many of the sophisticated techniques to the degree that the originator of the experiment has. It takes many months to be really in control of some of these techniques, and this time, again, you do not have. To ask somebody else to duplicate the data of his colleague would be unfair for the obvious reason that everybody wants to do original work and not to serve as a verifier of somebody else's data. So when the journalists attack scientists for not being on the alert for cheaters, they do not know what they are talking about.

However, I believe that the main reason for the current confusion in immunology is the *low competence* of many immunologists. Again, I do not claim that there are many incompetent immunologists; but I do believe that there are many immunologists whose competence just does not measure up to the formidable problems they are studying.

There are two kinds of low competence, technical and intellectual. The technical low competence results in sloppy experimentation and overinterpretation of the data. As I mentioned earlier, the many immunological methods require considerable skill. Everybody can learn the techniques but to really master them requires a special talent. Not everybody who enters immunology has this talent and there is no selection procedure that screens candidates for it. As a result, many untalented researchers struggle with imperfect techniques to produce unreliable data. Often the data are cosmetically beautified when a manuscript is prepared for publication so that the reader does not have any way of knowing that they are not to be trusted. It is only when a researcher has been proven to be wrong on too many occasions that one begins to be suspicious of his papers.

The intellectual low competence manifests itself in the use of approaches that cannot answer the posed question. A good example is the use of radiation chimeras to study the effect of Mhc on the T cell repertoire. At first this approach looked promising and there was some justification in using it. However,

later it became clear that chimeras are, to a large degree, uncontrollable in terms of nongenetic variation. Yet, instead of searching for alternative ways of answering the question, some immunologists stubbornly stick to radiation chimeras, continue to produce contradictory data, and thus perpetuate the chaos surrounding the question whether the T cell repertoire is influenced by the thymus. In my opinion, this lack of sound judgment in choosing techniques appropriate to the problem under study is largely responsible for the long persistence of many of the current controversies.

Another sign of mediocrity in immunology is the *slow progress of this discipline.* An eminent immunologist has stated recently that "more progress has been made in immunology in the past 20 years than was made since this discipline was created by the original discovery of Pasteur." Perhaps this is true, although I am not so sure. But even if it is true, this does not mean that we are doing a good job. We must not forget that until 20 years ago, there was only a handful of immunologists, whereas now there is a whole army. Also, until 20 years ago, the support for immunology was very modest, whereas in the last 20 years it has been — all the recent cuts notwithstanding — extremely generous. If we take these two facts into account, there is not much to boast about. As I said earlier, most of the basic problems are not solved, and don't seem to be even near a solution. And some of the problems that we claim to have solved appear to be solved by acclamation rather than by decisive experiments. A glaring example of lack of progress is the question of T cell receptor. How much nonsense has been published about the T cell receptor in the last 10 or 20 years! Just recall the immunoglobulin-on-T-cells controversy of the 1970s! Or the more recent idiotype sharing between T and B cells! Yet the techniques with which the T cell receptor problem is now finally being solved have been available for some time, and the ideas, too. Why then have they not been used earlier?

I think the main reason is that we lack grandeur and courage — that we are mediocre. We prefer to study the tissue distribution of Mhc molecules because such a study will, for sure, produce results. And when we study the T cell receptor, we prefer to use familiar techniques and approaches that cannot solve the problem.

It has often been said that the reason why we prefer working on small but safe problems is the pressure of the grant system: we are afraid, so the argument goes, that if we do not publish anything in 2-3 years, we would lose our support. I think this is just an excuse. In many institutions in Europe, such pressure either does not exist or is minimal. Yet, I have not noticed that European immunologists go after more important problems than their American colleagues — if anything they may be doing just the opposite.

I think that the real reason for our failure to solve many of important problems is that we either do not realize that they are important or, if we do, we lack the greatness needed for solving them. We are mediocre.

How else can one explain that we continue describing one Ir gene system after another instead of taking one of them, exploring it in depth, and answering critical questions! Why have we not even seriously approached the problem of antigen processing at the molecular level; prethymic T cell differentiation; molecular mechanism of tolerance induction; site of tolerance induction; molecular mechanism of lymphocyte activation; mechanism of disease-HLA association; molecular mechanism of T cell suppression; etc. My answer is: Because we are used to thinking small.

Still another sign of mediocrity is *lack of critical exchange*, apparent at meetings and in our writings. When I attend a scientific conference, I often have the impression that I walk instead into a convention of traveling salesmen. Our conferences should be places where we exchange ideas and argue out differences. Instead, they have become vehicles for the advertisement and promotion of our own accomplishments. I don't remember ever being at a meeting at which there was ample time for discussion. Most meetings are just a series of presentations, with a few minutes for discussion after each talk and this discussion then centers on trivial questions mostly regarding details of the protocol. To be sure, scientists are ready to talk science at any place and

at any time — but talk their science. Such discussions always run the same course: You start on some topic, and your colleague soon interrupts you with: "Let me tell about some data we obtained..." or "We have found this or that..." It is difficult to argue with anyone about principles because he immediately bombards you with details of his data which he thinks you should know about. A discussion between two such partners is not a dialogue — it is a double dialogue, in which the partners hardly listen to what the other says. Not advancement of knowledge but promotion, selling, and advertising seem to be our main concern at meetings.

In our writings, it is the same. We usually pay only lip-service to other people's work — and only to those whom we do not care not to cite. Otherwise, we use the pages of the papers again for self-promotion. Our review articles are usually restatements of the findings we published in journals. A review article should be an opportunity to sit back, pause for a moment to see where we are and where we are going, to speculate, to put things together, to make a whole of the parts, to synthesize. But we rarely use the opportunity. It appears that we have largely lost the ability to speculate, to generalize, to see things in broader texts.

We have also lost the ability to criticize each other, to take a stand, side with someone and against somebody else. Criticism should be a normal part of science, for it is only through critical exchange that we can truly take advantage of the fact that science has become a collective endeavor. We should battle openly, argue things out, and try to find weaknesses in each other's data,theories, and arguments. But again, we rarely do any of these things. We do not criticize, at least not openly. And if somebody does dare to criticize us, we regard it as a personal attack and respond to it irrationally. And all this is a sign of insecurity and insecurity is a sign of smallness, of mediocrity.

Finally, I would like to mention one more sign of mediocrity and that is dominance of *fads and fashions* in contemporary immunology. As soon as something new and promising emerges from the chaos, many immunologists drop what they have been doing up until then and join the crowd gathering around this new topic. They join the bandwagon. There are great fashions, such as the Mhc has been for the last 10 years, and ephemeral fads, such as the alien specificities, syngeneic preference (hybrid resistance), gene conversion, dendritic cells, Langerhans cells, etc. Fads and fashions are a sign of mediocrity because they, too, reveal researcher's insecurity. A great scientist has his own program, goes his own way, makes a trail for others to follow. A mediocre scientist, on the other hand, tends to follow a beaten path. As the Chinese proverb says: "One dog barks at something and a hundred bark at the sound."

This concludes the "destructive" part of my talk. I can summarize it by saying that 50 or 100 years from now, when historians of science evaluate immunology of the 1970s and 1980s, they probably will conclude that those were the years of a mediocre government. Years of too many immunologists, spending too much money on too trivial projects.

The constructive part of my talk will be brief because it will be an excursion into science fiction, as most discussions of *What to do?* necessarily are, and somehow I have never acquired a taste for this kind of literature.

Indeed, what can we do? The first thing, of course, is to acknowledge that a problem exists. I don't expect that everybody will agree with everything I said today but if I have planted some seeds of disquietude in some of you, this would be more than I could have hoped to accomplish. A great majority of us is on a public payroll and we owe it to those whose money we are spending to evaluate from time to time how well we are doing our jobs. And I don't mean the kind of evaluation in which we count the number of HLA determinants we have identified or the number of genes we have sequenced, but an evaluation in which we ask *why* we have identified the determinants and why we have sequenced the genes. We should

talk about why we are doing what we are doing and whether, perhaps, we should not be doing something else. Even if I am wrong and things are not as black as I have painted them, we should constantly search our souls to make sure that we are doing all right — and I emphasize that I do not mean soul-searching about details but about general trends, about where we are going.

The question, of course, is whether in a state ruled by a mediocre government it is at all possible to acknowledge that things are not as they should be. I personally doubt this. In a hegemony of mediocrity there is bound to be a lot of back-patting and a tendency toward self-satisfaction. Actually, seen through the eyes of the governing body, we *are* doing a very good job, because we *are* producing a lot of mediocre research. Therefore, it may not be possible to escape the vicious circle from within the circle. Then what hope is there that the hegemony of mediocrity might some day be superseded by a hegemony of true greatness? I don't believe that this can be accomplished by a revolution in our midst: we are too old and too established to make revolutions. But there is a hope that some day some young scientists will see things with different eyes than we do and will also begin *doing* things differently than we have been doing them. And that they will grow up into a more intelligent elite than we have presently.

In the mean time, some changes in the quality of research may occur if the present trend in reducing research support continues. I know, it is extremely heretical to say this, but I really think that a reduction in support might at the end be beneficial to science. If nothing else, it will reduce the influx of people into, say, immunology, and this could only be good for this discipline. The reduction may also put some pressure on researchers to concentrate on important problems instead of trivial problems. However, the opposite may also happen — namely that the power of the mediocre elite will become even greater and the trend toward mediocrity even stronger.

All this does not sound too optimistic — but then, what is optimism? Voltaire wrote a whole novel on this theme and came to the conclusion that "Optimism is the stubborn belief that things are good when they are bad." By this definition, even I am an incurable optimist.

To summarize what I have said in this lecture. First, I believe that scientists are selected for one particular form of intelligence — mainly the ability to solve problems. Second, this ability is not enough to make a great scientist; it makes only a mediocre scientist. A great scientist must also possess the ability to seek and find important problems, an ability for which we are not selected and evaluated. Third, certain scientific disciplines, such as immunology, are ruled by an elite which is good at solving problems but mediocre at finding important problems. Fourth, as a consequence of the previous three points, a lot of mediocre research is done in contemporary immunology, and probably in some other sciences as well. Fifth, the signs of mediocrity are preoccupation with trivial problems, muddleness, slow progress, lack of critical exchange, and dominance of fashions. Sixth, as a first step in remedying the situation I have called for a debate on where we are, where we have come from, and where we are going. And I expressed the utopian hope that one day, one young generation will replace the hegemony of mediocrity by a hegemony of greatness.

Before closing, let me say this. You might be tempted to regard my criticism as an outrageous example of incredible arrogance.

Although you have every right to ask such a question, I would like to ask you to do something else, instead: To consider seriously whether there might be any truth in what I am saying, because if there is, then it is no longer important who is saying it.

I have no desire of becoming a prophet of a cause (particularly since I know that many prophets were stoned to death). On the other hand, since as long as I remember I have always had the urge to call out that the emperor had no clothes on when I saw emperors parading around naked.

To quote the French existentialist Albert Camus: "I think, therefore I am, said Descartes. I am, therefore, I am, wrote Augustine. I rebel, therefore we are."