in each case. If we assume that the drugs act on the nucleic acid of the virus, then we must assume that these low-molecular-weight substances are able to detect differences in the base sequence or the secondary structure of nucleic acids, since the fundamental chemical nature of the nucleic acids of both drug-resistant and drug-sensitive viruses is similar. But it is hard to envision in chemical terms how a molecule as small as guanidine (one of Tamm and Eggers's compounds) might recognize differences in nucleic acid base sequence. The development of drug-resistant mutants is also difficult to explain.

As is well known from enzyme chemistry, small molecules readily interact in particular ways with proteins, and it would be simple to visualize ways in which a drug could acquire its specific effects by interaction with a virus-specific protein. In our work, we have shown that streptomycin inhibits nucleic acid injection, and it might be postulated that one end of the antibiotic molecule combines with the nucleic acid, and the other end with a specific site on the protein coat, thus effectively sealing the nucleic acid within the head. Tamm and Eggers cited an alternative hypothesis in their system that suggested that guanidine might inhibit the formation of an active RNA polymerase through effects on a precursor protein.

The importance of these speculations for approaches to virus chemotherapy is that they may direct thinking along new lines. To date most antiviral chemotherapeutic work has concerned itself with the virus nucleic acid. Yet each virus is endowed with a protein or group of proteins, and it is easy to conceive of the existence of drugs which will interact specifically with these proteins. In this light, successful chemotherapy of many virus diseases seems a distinct possibility.

THOMAS D. BROCK
Department of Bacteriology, Indiana University, Bloomington

The recent demonstration by T. D. Brock and S. O. Wooley [*Science* **141**, 1065 (1963)] of specific inhibition of certain bacterial viruses by streptomycin has brought into focus in another system the question of binding of small-molecular virus inhibitors to nucleic acid or protein.

The primary sites of action of 2-(α-hydroxybenzyl)-benzimidazole (HBB) and guanidine, compounds which specifically inhibit the replication of picornaviruses, are not known. Last year, in discussing the probable mechanism of action of HBB, we proposed two alternative hypotheses, namely that this compound may combine with viral RNA or may inhibit directly a virus-specific RNA polymerase [I. Tamm and H. J. Eggers, *Cold Spring Harbor Symp. Quant. Biol.* **27**, 196 (1962); H. J. Eggers and I. Tamm, *Virology* **18**, 426 (1962)]. At about the same time, A. Lwoff proposed that both HBB and guanidine may combine with a hypothetical precursor of the virus-specific RNA polymerase [*Cold Spring Harbor Symp. Quant. Biol.* **27**, 159 (1962)]. To summarize our views again, we think that a virus-specific inhibitor of virus-controlled macromolecular synthesis may combine with viral nucleic acid itself, a virus-specific enzyme, or some other virus-specific component which plays an essential role in the process of virus reproduction [*Science* **142**, 24 (1963)]. Brock has expressed similar views. In his letter, however, he emphasizes the possibility of binding of inhibitors to virus-specific proteins, whereas in our recent review we emphasized the possibility of binding to virus nucleic acid. The experimental elucidation of the primary sites of action of HBB and guanidine should provide information of considerable interest.

IGOR TAMM
HANS J. EGGERS
The Rockefeller Institute, New York 21

Serendipity—the Last Word

Most of the letters from readers sparked by your editorial "Serendipity in research" [*Science* **140**, 1177 (14 June 1963)] center about S. Stewart West's letter [*ibid.* **141** (6 Sept. 1963)] rather than your editorial. H. J. Adler's letter, in the same issue as West's, is the only one that is addressed to and takes issue with your editorial. My compliments to Adler, who expressed the essence of serendipity as Walpole defined it.

I fear that your otherwise excellent editorial was based on the dictionary definition, which differs from Walpole's and therefore led you to some erroneous conclusions. The same error may be assigned to the late Walter B. Cannon, whose celebrated chapter and conclusions on serendipity contained in his autobiography, *The Way of an Investigator*, reflect this error. Therefore his adherence to Pasteur's postulate: "Chance favors the prepared mind." I have no quarrel with Pasteur or with you, but the postulate may be encompassed in serendipity or it may not.

Compare the definition you quoted —"a gift for finding valuable or agreeable things not sought"—with Walpole's "making discoveries, by accidents and sagacity, of things which they [the princes of Serendip] were not in quest of." In the same letter he amplified his meaning by referring to "*accidental sagacity*" (his underscoring). Walpole's definition applies equally to the trained scientist and to the uneducated oddball, provided each has that mysterious quality which Adler calls "a flash of insight." It is unfortunate that the pristine character of Walpole's definition has been lost. The word is now used to cover the sort of thing that you imply is covered by "a series of happy incidents."

West feels the need for an English translation from the German of *The Three Princes of Serendip*. He believes "that the literary background of science would benefit" by such a translation. Your correspondent Bard [*ibid.* **142**, 421 (8 Nov. 1963)] agrees. Another correspondent, Zeisberg (*ibid.*), advises that there is an English translation which was from a French translation from the Persian, and that the original was, he thinks, written sometime in the 1400's. Actually, the English translation (Chetwood) was from de Mailly's (Amsterdam, 1721). Walpole read the French translation as a child. The original from which de Mailly translated was not Persian, but Italian (*Peregrinaggio di tre giovani figliuoli del Re di Serendippo* (Venice, 1557).

As a matter of fact, there never has been a direct English translation of the Italian original. This points up the lack of information generally about Walpole's contribution of "serendipity," the identity of the original *Three Princes of Serendip*, its translations, and so on. To supply these data, my forthcoming book, *Serendipity and the Three Princes*, will be published next spring by the University of Oklahoma Press. The book will contain a free-flowing translation just completed by an Italian scholar.

The scientist in general, and the physician in particular, have been fascinated by the phenomenon of serendipity, as well they may be. However, it

would be an error to believe that serendipity, a precious gift, may be developed in the laboratories and in the libraries as a tool for research.

THEODORE G. REMER
230 North Michigan Avenue, Chicago 1, Illinois

To Remer, an attorney, goes the last word in these columns on this subject, at least for a while.—ED.

Basic Research on a Problem

Why does Norman Storer [*Science* **142**, 464 (25 Oct. 1963)] think that basic science is threatened by a "powerful imposter, 'basic research *on a problem*' "? (Italics are Storer's.) "Basic research on a problem" may be a contradiction in terms when applied to the physical sciences, where basic dimensions are well established, interactions among dimensions are minimal, and, therefore, completely adequate research designs can be prosecuted. In contrast, in many areas of the life sciences one must assume that there may be hundreds of variables which determine a particular phenomenon, and that many of these variables interact strongly with many others. In these areas, an ideal experiment would have to deal with a host of permutations of variables simultaneously. This being impossible, the researcher must select some rubric or organizing principle which will allow him to design a human-sized piece of research. A practical question often serves this purpose excellently.

Storer implies that a piece of basic research—and in the life sciences it must be done piecemeal—is more likely to involve breadth of variables or "heuristic cross fertilization" or "progress along all fronts" or "the interstitial areas of science" than is an attempt to answer a practical question. In most of the life sciences the reverse is true. In our clinic, a cardiologist, a neurologist, a biochemist, an ophthalmologist, and I (an experimental psychologist) are trying to find some immediately applicable answers to questions about the relations in both directions, between performance in certain very demanding occupations and cardiovascular diseases and defects. We have obtained help from a psychoanalyst, an audiologist, a biophysicist, and others. So far, our attempts have led us to dozens of areas, many not usually dealt with in our specialties: anthropology, biometrics, "competition" in its many forms, dietetics, ethnology, "fatigue" in its many definitions, genetics, hydraulics—the list is long and still growing. Our practical questions force us to go where the relevant variables lie. It is hard work, much harder than the cozy "basic" filigree-work that each of us might be doing in his own little corner. Aside from research results, each of us is getting the broad education in life science that could be offered by "pure" research environments, but seldom is.

It is wrong to think that applied science contributes less to basic science than vice versa. To take one example from experimental psychology—probably not the best one: In World War II, the British asked some of their applied psychologists to find out why sonar operators missed many physically detectable signals, and what could be done about it. The answers, in the form of some excellent experiments by Mackworth and others on "vigilance" in monotonous situations, not only provided powerful basic knowledge about the dynamics of consciousness but, more importantly, helped force experimental psychologists to face basic facts which had been evaded in the simple-minded stimulus-response and sensory psychologies then fashionable in many academies.

Scientific research is only good or bad, not basic or applied. Good science consists of original thinking about careful observations in interesting situations, and frequently a practical question is the stimulus for it. The false dichotomy of "basic" and "applied" too often reinforces a preciousness or snobbery in the graduate student that narrows his vision for years after leaving the academy. Some never recover.

WALTER SPIETH
Georgetown Clinical Research Institute, AM-130, Federal Aviation Agency, Washington 25, D.C.

Do Antimalarial Sprays Explain Declining Death Rates?

Your issue of 19 April [*Science* **140**, 281 (1963)] carried comments by D. S. Greenberg on the report of the Panel on Population Problems of the Committee on Science and Public Policy, "The Growth of World Population," published by the National Academy of Sciences (1963). The report is described as "brief, lucid, honest, and humane, and, on a subject that often elicits excess and astonishing logical gymnastics, it is informed, restrained and responsible. . . . it is not unlikely that the Academy report will exert considerable influence for a long time. . . ." Therefore it seems most unfortunate that the report should perpetuate a misleading description of the interrelation of economic and demographic transition in low-income countries, citing the demographic experience of Ceylon as example. Thus:

"The precipitous decline in the death rate that is occurring in the low-income countries of the world is a consequence of the development and application of low-cost public health techniques. . . .

"The use of residual insecticides to provide effective protection against malaria at a cost of no more than 25 cents per capita per annum is an outstanding example. Other innovations include antibiotics and chemotherapy, and low-cost ways of providing safe water supplies and adequate environmental sanitation in villages that in most other ways remain relatively untouched by modernization. The death rate in Ceylon was cut in half in less than a decade, and declines approaching this in rapidity are almost commonplace. . . .

"The result of a precipitous decline in mortality while the birth rate remains essentially unchanged is, of course, a very rapid acceleration in population growth, reaching rates of three to three and one-half percent."

Ceylon has been the classic example for those who would give modern medicine and public health undue credit for inducing a "population explosion." The postwar coincidence of a dramatic drop in the death rate and the introduction of insecticides has misled many. The decline in the death rate in Ceylon preceded the large-scale spraying of residual insecticides by at least 6 months. The postwar reduction in mortality was about the same in the malarious areas treated and the nonmalarious areas not treated with insecticides. There is no evidence that control of malaria was the sole or even the major factor inducing a "population explosion"; rather, malaria control has prevented the million of debilitating but usually nonfatal attacks of malaria that had been occurring annually. Thus malaria control had the paradoxical effect of reducing population pressure by removing an insurmountable obstacle to the development of the major part of the island, which had remained relatively sparsely populated. Actually, the sharp postwar decline in the death rate was a return