The Case of the Floppy-Eared Rabbits: An Instance of Serendipity Gained and Serendipity Lost
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THE CASE OF THE FLOPPY-EARED RABBITS: AN INSTANCE OF SERENDIPITY GAINED AND SERENDIPITY LOST

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ABSTRACT

Two distinguished medical scientists independently observed the same phenomenon in the course of their research: reversible collapse of rabbits' ears after injection of the enzyme papain. One went on to make a discovery based on this serendipitous or chance occurrence; the other did not. Intensive tandem interviews were conducted with each of these scientists in order to discover similarities and differences in their experiences with the floppy-eared rabbits. These interview materials are analyzed for the light they shed on the process of scientific discovery in general and on the serendipity pattern in particular.

As with so many other basic social processes, the actual process of scientific research and discovery is not well understood.[1] There has been little systematic observation of the research and discovery process as it actually occurs, and even less controlled research. Moreover, the form in which discoveries are reported by scientists to their colleagues in professional journals tends to conceal important aspects of this process. Because of certain norms that are strongly institutionalized in their professional community, scientists are expected to focus their reports on the logical structure of the methods used and the ideas discovered in research in relation to the established conceptual framework of the relevant scientific specialty. The primary function of such reports is conceived to be that of indicating how the new observations and ideas being advanced may require a change—by further generalization or systematization—in the conceptual structure of a given scientific field. All else that has occurred in the actual research process is considered "incidental." Thus scientists are praised for presenting their research in a way that is elegantly bare of anything that does not serve this primary function and are deterred from reporting "irrelevant" social and psychological aspects of the research process, however interesting these matters may be in other contexts. As a result of such norms and practices, the reporting of scientific research may be characterized by what has been called "retrospective falsification." By selecting only those components of the actual research process that serve their primary purpose, scientific papers leave out a great deal, of course, as many scientists have indicated in their memoirs and in their informal talks with one another. Selection, then, unwittingly distorts and, in that special sense, falsifies what has happened in research as it actually goes on in the laboratory and its environs.

Public reports to the community of scientists thus have their own function. Their dysfunctionality for the sociology of scientific discovery, which is concerned with not one but all the components of the research process as a social process, is of no immediate concern to the practicing research scientist. And yet what is lost in "retrospective falsification" may be of no small importance to him, if only indirectly. For it is not unlikely that here, as everywhere else in the world of nature, knowledge is power, in this case power to increase the fruitfulness of scientific research by enlarging our systematic knowledge of it. The sociology of scientific discovery would seem to be an especially desirable area for further theoretical and empirical development.

One component of the actual process of scientific discovery that is left out or concealed in research reports following the practice of "retrospective falsification" is the element of unforeseen development, of happy or lucky chance, of what Robert K.

[1] For an account of what is known see Bernard Barber, *Science and the Social Order* (Glencoe, Ill.: Free Press, 1952), chap. ix, "The Social Process of Invention and Discovery," pp. 191–206.

Merton has called "the serendipity pattern."[2] By its very nature, scientific research is a voyage into the unknown by routes that are in some measure unpredictable and unplannable. Chance or luck is therefore as inevitable in scientific research as are logic and what Pasteur called "the prepared mind." Yet little is known systematically about this inevitable serendipity component.

For this reason it seemed to us desirable to take the opportunity recently provided by the reporting of an instance of *serendipity gained* by Dr. Lewis Thomas, now profesor and chairman of the Department of Medicine in the College of Medicine of New York University and formerly professor and chairman of the Department of Pathology.[3] Then, shortly after hearing about Dr. Thomas' discovery, we learned from medical research and teaching colleagues of an instance of *serendipity lost* on the very same kind of chance occurrence: unexpected floppiness in rabbits' ears after they had been injected intravenously with the proteolytic enzyme papain. This instance of serendipity lost had occurred in the course of research by Dr. Aaron Kellner, associate professor in the Department of Pathology of Cornell University Medical College and director of its central laboratories. This opportunity for *comparative* study seemed even more promising for our further understanding of the serendipity pattern. Here were two comparable medical scientists, we reasoned, both carrying out investigations in the field of experimental pathology, affiliated with distinguished medical schools, and of approximately the same level of demonstrated research ability (so far as it was in our layman's capacity to judge). In the course of their research both men had had occasion to inject rabbits intravenously with papain, and both had observed the phenomenon of ear collapse following the injection.

In spite of these similarities in their professional backgrounds and although they had both accidentally encountered the same phenomenon, one of these scientists had gone on to make a discovery based on this chance occurrence, whereas the other had not. It seemed to us that a detailed comparison of Dr. Thomas' and Dr. Kellner's experiences with the floppy-eared rabbits offered a quasi-experimental opportunity to identify some of the factors that contribute to a positive experience with serendipity in research and some of the factors conducive to a negative experience with it.

We asked for and were generously granted intensive interviews with Dr. Thomas and Dr. Kellner.[4] Each reported to us that they had experienced both "positive serendipity" and "negative serendipity" in their research. That is, each had made a number of serendipitous discoveries based on chance occurrences in their planned experiments, and on other occasions each had missed the significance of like occurrences that other researchers had later transformed into discoveries. Apparently, both positive and negative serendipity are common experiences for scientific researchers. Indeed, we shall see that one of the chief reasons why Dr. Kellner experienced serendipity lost with respect to the discovery that Dr. Thomas made was that he was experiencing serendipity gained

[2] For discussions of serendipity see Walter B. Cannon, *The Way of an Investigator* (New York: W. W. Norton & Co., 1945), chap. vi, "Gains from Serendipity," pp. 68–78; and Robert K. Merton, *Social Theory and Social Structure* (rev. ed.; Glencoe, Ill.: Free Press, 1957), pp. 103–8. Our colleagues, Robert K. Merton and Elinor G. Barber, are now engaged in an investigation and clarification of the variety of meanings of "chance" that are lumped under the notion of serendipity by different users of that term.

[3] Lewis Thomas, "Reversible Collapse of Rabbit Ears after Intravenous Papain, and Prevention of Recovery by Cortisone," *Journal of Experimental Medicine,* CIV (1956), 245–52. This case first came to our attention through a report in the *New York Times.* The pictures printed in Dr. Thomas' original article and in the *Times* will indicate why we have called this "the case of the floppy-eared rabbits."

[4] These interviews lasted about two hours each. They are another instance of the "tandem interviewing" described by Harry V. Kincaid and Margaret Bright, "Interviewing the Business Elite," *American Journal of Sociology,* LXIII (1957), 304–11.

with respect to some other aspects of the very same experimental situation. Conversely, Dr. Thomas had reached a stalemate on some of his other research, and this gave him added incentive to pursue intensively the phenomenon of ear collapse. Partly as a consequence of these experiences, in what were similar experimental situations, the two researchers each saw something and missed something else.

On the basis of our focused interviews with these two scientists, we can describe some of the recurring elements in their experiences with serendipity.[5] We think that these patterns may also be relevant to instances of serendipity experienced by other investigators.

SERENDIPITY GAINED

Dr. Thomas.—Observing the established norms for reporting scientific research, in his article in the *Journal of Experimental Medicine,* Dr. Thomas did not mention his experience with serendipity. In the manner typical of such reports he began his article with the statement, "For reasons not relevant to the present discussion rabbits were injected intravenously with a solution of crude papain." (By contrast, though not called by this term, serendipity was featured in the accounts of this research that appeared in the *New York Times* and the *New York Herald Tribune.* "An accidental sidelight of one research project had the startling effect of wilting the ears of the rabbit," said the *Times* article. "This bizarre phenomenon, accidentally discovered . . ." was the way the *Herald Tribune* described the same phenomenon. The prominence accorded the "accidental" nature of the discovery in the press is related to the fact that these articles were written by journalists for a lay audience. The kind of interest in scientific research that is characteristic of science reporters and the audience for whom they write and their conceptions of the form in which information about research ought to be communicated differ from those of professional scientists).[6]

Although Dr. Thomas did not mention serendipity in his article for the *Journal of Experimental Medicine,* in his interview he reported both his general acquaintance with the serendipity pattern ("Serendipity is a familiar term. . . . I first heard about it in Dr. Cannon's class . . .") and his awareness of the chance occurrence of floppy-eared rabbits in his own research. Dr. Thomas first noticed the reversible collapse of rabbit ears after intravenous papain about seven years ago, when he was working on the effects of proteolytic enzymes as a class:

> I was trying to explore the notion that the cardiac and blood vessel lesions in certain hypersensitivity states may be due to release of proteolytic enzymes. It's an attractive idea on which there's little evidence. And it's been picked up at some time or another by almost everyone working on hypersensitivity. For this investigation I used trypsin, because it was the most available enzyme around the laboratory, and I got nothing. We also happened to have papain; I don't know where it had come from; but because it was there, I tried it. I also tried a third enzyme, ficin. It comes from figs, and it's commonly used. It has catholic tastes and so it's quite useful in the laboratory. So I had these three enzymes. The other two didn't produce lesions. Nor did papain. But what the papain did was always produce these bizarre cosmetic changes. . . . It was one of the most uniform reactions I'd ever seen in biology. It always happened. And it looked as if something important must have happened to cause this reaction.

[5] In this paper we shall concentrate on the instances of serendipity gained by Dr. Thomas and lost by Dr. Kellner and give somewhat less attention to elements of negative serendipity in Dr. Thomas' experiments and elements of positive serendipity in those of Dr. Kellner.

[6] Further discussion of this point lies beyond the scope of this paper. But in a society like ours, in which science has become "front-page news," some of the characteristics and special problems of science reporting merit serious study. A recently published work on this topic that has come to our attention is entitled *When Doctors Meet Reporters* (New York: New York University Press, 1957). This is a discussion by science writers and physicians of the controversy between the press and the medical profession, compiled from the record of a series of conferences sponsored by the Josiah Macy, Jr., Foundation.

Some of the elements of serendipitous discovery are clearly illustrated in this account by Dr. Thomas. The scientific researcher, while in pursuit of some other specific goals, accidentally ("we also happened to have papain . . .") produces an unusual, recurrent, and sometimes striking ("bizarre") effect. Only the element of creative imagination, which is necessary to complete an instance of serendipity by supplying an explanation of the unusual effect, is not yet present. Indeed, the explanation was to elude Dr. Thomas, as it eluded Dr. Kellner, and probably others as well, for several years. This was not for lack of trying by Dr. Thomas. He immediately did seek an explanation:

> I chased it like crazy. But I didn't do the right thing. . . . I did the expected things. I had sections cut, and I had them stained by all the techniques available at the time. And I studied what I believed to be the constituents of a rabbit's ear. I looked at all the sections, but I couldn't see anything the matter. The connective tissue was intact. There was no change in the amount of elastic tissue. There was no inflammation, no tissue damage. I expected to find a great deal, because I thought we had destroyed something.

Dr. Thomas also studied the cartilage of the rabbit's ear, and judged it to be "normal" (". . . The cells were healthy-looking and there were nice nuclei. I decided there was no damage to the cartilage. And that was that . . ."). However, he admitted that at the time his consideration of the cartilage was routine and relatively casual, because he did not seriously entertain the idea that the phenomenon of ear collapse might be associated with changes in this tissue:

> I hadn't thought of cartilage. You're not likely to, because it's not considered interesting. . . . I know my own idea has always been that cartilage is a quiet, inactive tissue.

Dr. Thomas' preconceptions about the methods appropriate for studying the ear-collapsing effect of papain, his expectation that it would probably be associated with damage in the connective or elastic tissues, and the conviction he shared with colleagues that cartilage is "inert and relatively uninteresting"—these guided his initial inquiries into this phenomenon. But the same preconceptions, expectations, and convictions also blinded him to the physical and chemical changes in the ear cartilage matrix which, a number of years later, were to seem "obvious" to him as the alterations underlying the collapsing ears. Here again, another general aspect of the research process comes into the clear. Because the methods and assumptions on which a systematic investigation is built selectively focus the researcher's attention, to a certain extent they sometimes constrict his imagination and bias his observations.

Although he was "very chagrined" about his failure, Dr. Thomas finally had to turn away from his floppy-eared rabbits because he was "terribly busy working on another problem at the time," with which he was "making progress." Also, Dr. Thomas reported, "I had already used all the rabbits I could afford. So I was able to persuade myself to abandon this other research." The gratifications of research success elsewhere and the lack of adequate resources to continue with his rabbit experiments combined to make Dr. Thomas accept failure, at least temporarily. As is usually the case in the reporting of scientific research, these experiments and their negative outcome were not written up for professional journals. (There is too much failure of this sort in research to permit of its publication, except occasionally, even though it might be instructive for some other scientists in carrying out their research. Since there is no way of determining what might be instructive failures and since space in professional journals is at a premium, generally only accounts of successful experiments are submitted to such journals and published by them.)

Despite his decision to turn his attention to other, more productive research, Dr. Thomas did not completely forget the floppy-eared rabbits. His interest was kept alive by a number of things. As he explained,

the collapse of the rabbit ears and their subsequent reversal "was one of the most uniform reactions I'd ever seen in biology." The "unfailing regularity" with which it occurred is not often observed in scientific research. Thus the apparent invariance of this phenomenon never ceased to intrigue Dr. Thomas, who continued to feel that an important and powerful biological happening might be responsible. The effect of papain on rabbit ears had two additional qualities that helped to sustain Dr. Thomas' interest in it. The spectacle of rabbits with "ears collapsed limply at either side of the head, rather like the ears of spaniels,"[7] was both dramatic and entertaining.

In the intervening years Dr. Thomas described this phenomenon to a number of colleagues in pathology, biochemistry, and clinical investigation, who were equally intrigued and of the opinion that a significant amount of demonstrable tissue damage must be associated with such a striking and uniform reaction. Dr. Thomas also reported that twice he "put the experiment on" for some of his more skeptical colleagues. ("They didn't believe me when I told them what happened. They didn't really believe that you can get that much change and not a trace of anything having happened when you look in the microscope.") As so often happens in science, an unsolved puzzle was kept in mind for eventual solution through informal exchanges between scientists, rather than through the formal medium of published communications.

A few years ago Dr. Thomas once again accidentally came upon the floppy-eared rabbits in the course of another investigation:

> I was looking for a way . . . to reduce the level of fibrinogen in the blood of rabbits. I had been studying a form of fibrinoid which occurs inside blood vessels in the generalized Schwartzman reaction and which seems to be derived from fibrinogen. My working hypothesis was that if I depleted the fibrinogen and, as a result, fibrinoid did not occur, this would help. It had been reported that if you inject proteolytic enzyme, this will deplete fibrinogen. So I tried to inhibit the Schwartzman reaction by injecting papain intravenously into the rabbits. It didn't work with respect to fibrinogen. . . . But the same damned thing happened again to the rabbits' ears!

This time, however, Dr. Thomas was to solve the puzzle of the collapsed rabbit ears and realize a complete instance of serendipitous discovery. He describes what subsequently happened:

> I was teaching second-year medical students in pathology. We have these small seminars with them: two-hour sessions in the morning, twice a week, with six to eight students. These are seminars devoted to experimental pathology and the theoretical aspects of the mechanism of disease. The students have a chance to see what we, the faculty, are up to in the laboratory. I happened to have a session with the students at the same time that this thing with the rabbits' ears happened again. I thought it would be an entertaining thing to show them . . . a spectacular thing. The students were very interested in it. I explained to them that we couldn't really explain what the hell was going on here. I did this experiment on purpose for them, to see what they would think. . . . Besides which, I was in irons on my other experiments. There was not much doing on those. I was not being brilliant on these other problems. . . . Well, this time I did what I didn't do before. I simultaneously cut sections of the ears of rabbits after I'd given them papain *and* sections of normal ears. This is the part of the story I'm most ashamed of. It still makes me writhe to think of it. There was no damage to the tissue in the sense of a lesion. But what had taken place was a quantitative change in the matrix of the cartilage. The only way you could make sense of this change was simultaneously to compare sections taken from the ears of rabbits which had been injected with papain with comparable sections from the ears of rabbits of the same age and size which had not received papain. . . . Before this I had always been so struck by the enormity of the change that when I didn't see something obvious, I concluded there was nothing. . . . Also, I didn't have a lot of rabbits to work with before.

Judging from Dr. Thomas' account, it appears that a number of factors contributed

[7] Thomas, *op. cit.*, p. 245.

to his reported experimental success. First, his teaching duties played a creative role in this regard. They impelled him to run the experiment with papain again and kept his attention focused on its implications for basic science rather than on its potentialities for practical application. Dr. Thomas said that he used the experiment to "convey to students what experimental pathology is like." Second, because he had reached an impasse in some of his other research, Dr. Thomas had more time and further inclination to study the ear-collapsing effect of papain than he had had a few years earlier, when the progress he was making on other research helped to "persuade" him to "abandon" the problem of the floppy-eared rabbits. Third, Dr. Thomas had more laboratory resources at his command than previously, notably a larger supply of rabbits. (In this regard it is interesting to note that, according to Dr. Thomas' article in the *Journal of Experimental Medicine,* 250 rabbits, all told, were used in the experiments reported.) Finally, the fact that he now had more laboratory animals with which to work and that he wanted to present the phenomenon of reversible ear collapse to students in a way that would make it an effective teaching exercise led Dr. Thomas to modify his method for examining rabbit tissues. In his earlier experiments, Dr. Thomas had compared histological sections made of the ears of rabbits who had received an injection of papain with his own mental image of normal rabbit-ear tissue. This time, however, he actually made sections from the ear tissue of rabbits which did *not* receive papain, as well as from those which did, and simultaneously examined the two. As he reported, this comparison enabled him to see for the first time that "drastic" quantitative changes had occurred in the cartilaginous tissue obtained from the ears of the rabbits injected with papain. In the words of the *Journal* article,

> The ear cartilage showed loss of a major portion of the intercellular matrix, and complete absence of basophilia from the small amount of remaining matrix. The cartilage cells appeared somewhat larger, and rounder than normal, and lay in close contact with each other. . . . (The contrast between the normal ear cartilage and tissue obtained 4 hours after injection is illustrated in Figs. 3*A* and 3*B* of this article.)

Immediately thereafter, Dr. Thomas and his associates found that these changes occur not only in ear cartilage but in all other cartilaginous tissues as well.

How significant or useful Dr. Thomas' serendipitous discovery will be cannot yet be specified. The serendipity pattern characterizes small discoveries as well as great. Dr. Thomas and his associates are currently investigating some of the questions raised by the phenomenon of papain-collapsed ears and the alterations in cartilage now known to underlie it. In addition, Dr. Thomas reported that some of his "biochemist and clinical friends" have become interested enough in certain of his findings to "go to work with papain, too." Two of the major problems under study in Dr. Thomas' laboratory are biochemical: the one concerning the nature of the change in cartilage; the other, the nature of the factor in papain that causes collapse of rabbits' ears and lysis of cartilage matrix in all tissues. Attempts are also being made to identify the antibody that causes rabbits to become immune to the factor responsible for ear collapse after two weeks of injection. The way in which cortisone prolongs the reaction to papain and the possible effect that papain may have on the joints as well as the cartilage are also being considered. Though at the time he was interviewed Dr. Thomas could not predict whether his findings (to date) would prove "important" or not, there was some evidence to suggest that certain basic discoveries about the constituents and properties of cartilaginous tissue might be forthcoming and that the experiments thus far conducted might have "practical usefulness" for studies of the postulated role of cortisone in the metabolism of sulfated mucopolysaccharides and of the relationship between cartilage and the electrolyte imbalance associated with congestive heart failure.

In the research on reversible ear collapse that Dr. Thomas has conducted since his initial serendipitous discovery, the planned and the unplanned, the foreseen and the accidental, the logical and the lucky have continued to interact. For example, Dr. Thomas' discovery that cortisone prevents or greatly delays the "return of papain-collapsed ears to their normal shape and rigidity" came about as a result of a carefully planned experiment that he undertook to test the effect of cortisone on the reaction to papain. On the other hand, his discovery that "repeated injections of papain, over a period of two or three weeks, brings about immunity to the phenomenon of ear collapse" was an unanticipated consequence of the fact that he used the same rabbit to demonstrate the floppy ears to several different groups of medical students:

> I was so completely sold on the uniformity of this thing that I used the same rabbit [for each seminar]. . . . The third time it didn't work. I was appalled by it. The students were there, and the rabbit's ears were still in place. . . . At first I thought that perhaps the technician had given him the wrong stuff. But then when I checked on that and gave the same stuff to the other rabbits and it *did* work I realized that the rabbit had become immune. This is a potentially hot finding. . . .

SERENDIPITY LOST

Dr. Kellner.—In our interview with Dr. Thomas we told him that we had heard about another medical scientist who had noticed the reversible collapse of rabbits' ears when he had injected them intravenously with papain. Dr. Thomas was not at all surprised. "That must be Kellner," he said. "He must have seen it. He was doomed to see it." Dr. Thomas was acquainted with the reports that Dr. Kellner and his associates had published on "Selective Necrosis of Cardiac and Skeletal Muscle Induced Experimentally by Means of Proteolytic Enzyme Solutions Given Intravenously" and on "Blood Coagulation Defect Induced in Rabbits by Papain Solutions Injected Intravenously."[8] He took it for granted that, in the course of these reported experiments which had entailed papain solution given intravenously to rabbits, a competent scientist like Dr. Kellner had also seen the resulting collapse of rabbits' ears, with its "unfailing regularity" and its "flamboyant" character. And, indeed, our interview with Dr. Kellner revealed that he had observed the floppiness, apparently at about the same time as Dr. Thomas:

> We called them the floppy-eared rabbits. . . . Five or six years ago we published our first article on the work we were doing with papain; that was in 1951 and our definitive article was published in 1954. . . . We gave papain to the animals and we had done it thirty or forty times before we noticed these changes in the rabbits' ears.

Thus Dr. Kellner's observation of what he and his colleagues dubbed "the floppy-eared rabbits" represents, when taken together with Dr. Thomas' experience, an instance of independent multiple observation, which often occurs in science and frequently leads to independent multiple invention and discovery.

Once he had noticed the phenomenon of ear collapse, Dr. Kellner did what Dr. Thomas and any research scientist would have done in the presence of such an unexpected and striking regularity: he looked for an answer to the puzzle it represented. "I was a little curious about it at the time, and followed it up to the extent of making sections of the rabbits' ears." However, for one of those trivial reasons that sometimes affect the course of research—the obviously amusing quality of floppiness in rabbits' ears—Dr. Kellner did not take the phenomenon as seriously as he took other aspects

[8] See, Aaron Kellner and Theodore Robertson, "Selective Necrosis of Cardiac and Skeletal Muscle Induced Experimentally by Means of Proteolytic Enzyme Solutions Given Intravenously," *Journal of Experimental Medicine,* XCIX (1954), 387–404; and Aaron Kellner, Theodore Robertson, and Howard O. Mott, "Blood Coagulation Defect Induced in Rabbits by Papain Solutions Injected Intravenously," abstract in *Federation Proceedings,* Vol. X (1951), No. 1.

of the experimental situation involving the injection of papain.

In effect, Dr. Kellner and his associates closed out their interest in the phenomenon of the reversible collapse of rabbits' ears following intravenous injection of papain by using it as an assay test for the potency and amount of papain to be injected. "Every laboratory technician we've had since 1951," he told us in the interview, "has known about these floppy ears because we've used them to assay papain, to tell us if it's potent and how potent." If the injected rabbit died from the dose of papain he received, the researchers knew that the papain injection was too potent; if there was no change in the rabbit's ears, the papain was not potent enough, but "if the rabbit lived and his ears drooped, it was just right." Although "we knew all about it, and used it that way . . . as a rule of thumb," Dr. Kellner commented, "I didn't write it up." Nor did he ever have "any intention of publishing it as a method of assaying papain." He knew that an applied technological discovery of this sort would not be suitable for publication in the basic science–oriented professional journals to which he and his colleagues submit reports of experimental work.

However, two factors apparently were much more important in leading Dr. Kellner away from investigating this phenomenon. First, like Dr. Thomas, Dr. Kellner thought of cartilage as relatively inert tissue. Second, because of his pre-established special research interests, Dr. Kellner's attention was predominantly trained on muscle tissue:

> Since I was primarily interested in research questions having to do with the muscles of the heart, I was thinking in terms of muscle. That blinded me, so that changes in the cartilage didn't occur to me as a possibility. I was looking for muscles in the sections, and I never dreamed it was cartilage.

Like Dr. Thomas at the beginning of his research and like all scientists at some stages in their research, Dr. Kellner was "misled" by his preconceptions.

However, as we already know, in keeping with his special research interests, Dr. Kellner noticed and intensively followed up two other serendipitous results that occur when papain is injected intravenously into rabbits: focal necrosis of cardiac and skeletal muscle and a blood coagulation defect, which in certain respects resembles that of hemophilia.[9]

It was the selective necrosis of cardiac and skeletal muscle that Dr. Kellner studied with the greatest degree of seriousness and interest. Dr. Kellner told us that he is "particularly interested in cardio-vascular disease," and so the lesions in the myocardium was the chance observation that he particularly "chose to follow . . . the one closest to me." Not only did Dr. Kellner himself have a special interest in the necrosis of cardiac muscle, but also his "laboratory and the people associated with me," he said, provided "the physical and intellectual tools to cope with this phenomenon." Dr. Kellner and his colleagues also did a certain amount of "work tracking down the cause of the blood coagulation defect"; but, because this line of inquiry "led [them] far afield" from investigative work in which they were especially interested and competent, they eventually "let that go" as they had let go the phenomenon of floppiness in rabbits' ears. Dr. Kellner indicated in his interview that the potential usefulness of his work with the selective necrosis of cardiac and skeletal muscle cannot yet be precisely ascertained. However, in his article in the *Journal of Experimental Medicine* he suggested that this serendipitous finding "has interesting implications for the pathogenesis of the morphological changes in rheumatic fever, periarteritis nodosa, and other hypersensitivity states."

Thus Dr. Kellner did not have the ex-

[9] See Kellner and Robertson, *op. cit.*, and Kellner, Robertson, and Mott, *op. cit.*

perience of serendipity gained with respect to the significance of floppiness in rabbits' ears after intravenous injection of papain for a variety of reasons, some trivial apparently, others important. The most important reasons, it seems, were his research preconceptions and the occurrence of other serendipitous phenomena in the same experimental situation.

In summary, although the ultimate outcome of their respective laboratory encounters with floppiness in rabbits' ears was quite different, there are some interesting similarities between the serendipity-gained experience of Dr. Thomas and the serendipity-lost experience of Dr. Kellner. Initially, the attention of both men was caught by the striking uniformity with which the collapse of rabbit ears occurred after intravenous papain and by the "bizarre," entertaining qualities of this cosmetic effect. In their subsequent investigations of this phenomenon, both were to some extent misled by certain of their interests and preconceptions. Lack of progress in accounting for ear collapse, combined with success in other research in which they were engaged at the time, eventually led both Dr. Thomas and Dr. Kellner to discontinue their work with the floppy-eared rabbits.

However, there were also some significant differences in the two experiences. Dr. Thomas seems to have been more impressed with the regularity of this particular phenomenon than Dr. Kellner and somewhat less amused by it. Unlike Dr. Kellner, Dr. Thomas never lost interest in the floppy-eared rabbits. When he came upon this reaction again at a time when he was "blocked" on other research, he began actively to reconsider the problem of what might have caused it. Eventual success was more likely to result from this continuing concern on Dr. Thomas' part. And Dr. Kellner, of course, was drawn off in other research directions by seeing other serendipitous phenomena in the same situation and by his success in following up those other leads.

These differences between Dr. Thomas and Dr. Kellner seem to account at least in part for the serendipity-gained outcome of the case of the floppy-eared rabbits for the one, and the serendipity-lost outcome for the other.

Experiences with both serendipity gained and serendipity lost are probably frequent occurrences for many scientific researchers. For, as Dr. Kellner pointed out in our interview with him, scientific investigations often entail "doing something that no one has done before, [so] you don't always know how to do it or exactly what to do":

> Should you boil or freeze, filter or centrifuge? These are the kinds of crossroads you come to all the time. . . . It's always possible to do four, five, or six things, and you have to choose between them. . . . How do you decide?

In this comparative study of one instance of serendipity gained and serendipity lost, we have tried to make inferences about some of the factors that led one investigator down the path to a successful and potentially important discovery and another to follow a somewhat different, though eventually perhaps a no less fruitful, trail of research. A large enough series of such case studies could suggest how often and in what ways these factors (and others that might prove relevant) influence the paths that open up to investigators in the course of their research, the choices they make between them, and the experimental findings that result from such choices. Case studies of this kind might also contribute a good deal to the detailed, systematic study of "the ways in which scientists actually . . . think, feel and act," which Robert K. Merton says could perhaps teach us more "in a comparatively few years, about the psychology and sociology of science than in all the years that have gone before."[10]

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[10] See his Foreword to *Science and the Social Order* by Bernard Barber, p. xxii.