

REPRINTS AND REFLECTIONS

Facts, opinions and affaires du coeur^{*†}

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Someone has suggested that any scientist should begin a scientific paper with the phrase: "Ladies and gentlemen, these are the opinions on which I base my facts . . ."

That scientists should have affairs of the heart with scientific theories marks them as being human, and to seek to defend one's lover against the attacks of others and to document her or his virtues is surely a worthy enterprise. This might be taken as implying that science is intuitive and irrational. In this paper, taking the epidemiology of coronary heart disease as my focus, I should like to present the case, made by some philosophers of science, that science does have a heavy dose of the intuitive and irrational and that these are fundamental to the way science proceeds. Even accepting this irrationality, however, there are rational methodological guidelines, which, if followed by epidemiologists, might improve the way epidemiologic research is conducted.

Why bother working epidemiologists with such philosophic speculations? My reasons are twofold. In the field of chronic disease epidemiology, as in many other branches of science, we seem to have considerable trouble choosing between and evaluating competing hypotheses, and we should be grateful for any methodological help the philosophers can give us. Secondly, I bring up this topic in a symposium on the history of epidemiology because I have been convinced by the argument that one cannot do philosophy of science without studying the actual history of science, and conversely.

To make the case, I should like to briefly consider the history of theories of causation of coronary heart disease. One can somewhat oversimplify the picture by saying that the majority of scientists working in the field of coronary heart disease have subscribed to one or other of two views – the lipid hypothesis or the thrombosis hypothesis. (See, for example, the brief review by Roberts¹.) The first group includes the vast numbers of scientists working on some aspect of diet, body lipids and coronary heart disease. In the second group, I have somewhat inaccurately lumped together a more diverse array of scientists

working on different etiologic factors in the disease, the common thread being that these factors are liable to affect coronary heart disease via the formation of thrombi, rather than via an effect on lipids.

These two views differ in whether they consider the primary event in the development of coronary atherosclerosis to be the accumulation of lipids in the arterial wall or whether they consider thrombosis to be the primary event in the development of the atherosclerotic plaque, and the accumulation of lipids to be only secondary. This is not merely an academic debate among pathologists, as it has profound importance for understanding the causes of coronary heart disease and has obvious implications for prevention. If the basic process were primarily a disorder of lipid metabolism due to faulty nutrition, this would suggest one approach to prevention. On the other hand, if the basic process were primarily an increased tendency to form arterial thrombi, this might suggest a different approach. It would therefore be of major importance if one had some way of sorting out the relative merits of these two basically opposed hypotheses.

I shall briefly sketch the history of these two views in an attempt to show that, although the two hypotheses are in direct opposition, evidence may be assembled to logically support either view. (In the historical sketches that follow, no attempt is made to present a comprehensive, documented history, but rather to present a few main points. Many documented histories of coronary heart disease are available elsewhere^{2–7}.) Controversy exists, in part, because epidemiologists do not follow consistent criteria in deciding to accept or reject a theory. My aim is not to choose between competing theories, but to use this historical example to examine what some philosophers have said about how scientific theories are accepted or rejected, and to ask what we, as epidemiologist, can learn from the suggestions of the philosophers.

The lipid hypothesis is based on a chain of evidence; pathological, animal-experimental, clinical, and epidemiologic. It begins with the observations of the 18th Century pathologists that patients with angina pectoris had lesions of the coronary arteries. These were best characterized by Virchow⁸ in the mid-19th Century who described the atherosclerotic lesion and its content of cholesterol and lipids. It was theorized that lipids from the circulating blood are imbibed into the intima of the coronary arteries.

* Presented at the Symposium on the History of Epidemiology at the Eighth Annual Meeting of the Society for Epidemiologic Research, Albany, NY, June, 1975.

† Facts, Opinions and Affaires du Coeur, *American Journal of Epidemiology*, 103: 519–526. Reprinted with permission.

The animal-experimental evidence came from the Russians at the beginning of this century. Ignatovski, Anitschkow and others fed milk, egg yolk and pure cholesterol to rabbits and produced the lesions of arteriosclerosis.⁹ Similar experiments with other animals have been successfully performed in the United States.¹⁰

The clinical evidence is based on the observations that patients with a myocardial infarction have a tendency to elevated blood lipids. In addition, it has been shown that under controlled conditions, the fat content of the diet may affect the level of serum cholesterol.

Epidemiologic studies have shown that, within population groups, there is a strong correlation between the level of serum cholesterol and subsequent incidence of coronary heart disease. Between countries, there is a correlation between the fraction of dietary calories provided by fat and frequency of coronary heart disease.¹¹

These epidemiologic studies have, of course, emphasized that other factors, in particular cigarette smoking and elevated blood pressure, are important in the disease.

This body of pathological, experimental, clinical and epidemiologic evidence appears so strong and compelling, one might wonder why it is still considered contentious by some.

In fact, it has been questioned at almost every level. The holders of the thrombosis view, Rokitsky¹², Duguid¹³ and others¹⁴ emphasize that mural thrombi are the primary initiating events in the formation of the atherosclerotic lesion and that the characteristic fatty deposits are only a secondary development. Pickering even quotes Virchow's later work as arguing against the lipid theory and in favour of the thrombosis theory.¹⁵ Morris's analysis of the pathology records of London Hospital over a 40-year period suggested that CHD mortality increased while the frequency and severity of the lipid containing lesion in the wall of the coronary arteries actually showed a decrease. He suggested that the luminal component of the disease, i.e., thrombi, determines the frequency of clinical coronary heart disease, not the frequency of the atheromatous plaque.^{16,17}

The thrombosis view can thus claim the advantage of parsimony. The one process, thrombosis, explains both the development of the mural plaque and the events that precipitate an acute occlusion, i.e., thrombosis could account for both the chronic and the acute disease. The lipid view cannot claim the same advantage.

Pickering¹⁵ also questions the relevance of the animal experiments to the lipid hypothesis because the doses of cholesterol fed to the animals are very large, and feeding cholesterol does not produce the thrombosis.

The epidemiologic evidence has been questioned because, although there is a strong indirect correlation

between average dietary fat for a population and average serum cholesterol and CHD rates for that population, there is no direct correlation, i.e., within a single free-living population group there has been a consistent failure to show a relationship between dietary fat for individuals and either serum cholesterol or CHD incidence.

It would thus appear that the epidemiologic evidence does not unequivocally support the lipid view. The original question posed in this paper was: are there simple epidemiologic criteria one can apply to help make a judgement of a hypothesized causal relationship? It would appear that there *are* criteria, but that these are not consistently applied. For example, the epidemiologic evidence supporting smoking (and elevated blood pressure) as risk factors for coronary heart disease is almost opposite to the evidence supporting the role of dietary fats. Within some population groups there is a strong direct correlation between an individual's smoking habits and his risk of coronary heart diseases; but, between countries, i.e., in indirect studies, there is very little correlation between the average smoking level for the population and that population's rate of CHD. The same is true for elevated blood pressure (see for example the summary of the Seven-Countries Study¹⁸). In contrast, as has been pointed out, the dietary fat-CHD correlation holds up in indirect studies between countries, but not at all within countries.

Of course, the conflicting observations sketched here with regard to the lipid hypothesis do not necessarily invalidate the theory; reasonable explanations can be created to account for these conflicts, especially multifactorial causation. The point I wish to make is that the thrombosis theory also has significant holes. In particular, the links between population characteristics and tendency to thrombosis are remarkably sketchy. Thus, here stand two completely opposed theories, one or other of which is subscribed to by medical scientists of the highest order. Each theory has its defects and each has its strong adherents. One might ask which one is the correct one? But that is not the question I want to ask here as I respect the judgment and follow the arguments of both the upholders and detractors of both theories. The question I wish to pose is a different one. Assuming that epidemiology is a fully-fledged science and that one has here an example from the history of a science, of the progress of a particular body of knowledge. Is it, then, possible to describe the way in which scientific hypotheses are accepted or rejected? In particular, are the philosopher's explanations of how science proceeds adequate to explain the failure of the scientific community to achieve consensus over which of these theories to accept or reject?

In wandering agog through the richness of the philosophy of science literature, I found as little consensus as in the sciences they attempt to describe. As a result of these tentative wanderings I shall report on

four different accounts of the scientific enterprise. The first two do not fit the history of heart disease any better than they fit the history of any other science, but the second two offer us important insights. (The accounts that follow have been directly influenced by the philosophic writings of Feyerabend^{19,20}, Popper^{21,22}, Lakatos^{23,24}, Hempel²⁵, and Medawar²⁶. If no specific reference is made in what follows, it is because the same point has been made by several of these authors.)

The first may be called the narrow inductive view. This view suggests that first all the relevant facts are gathered and from these facts a theory is derived, i.e., we pass from statements about particular facts to a general statement that comprehends these facts. This view of science has been soundly attacked since the 18th Century, and it clearly does not fit our heart disease example. Even applying Mill's canons of inductive logic, which are dear to the heart of epidemiologists, one cannot, starting with the facts, arrive at one single theory. A set of "facts" are currently available in coronary heart disease epidemiology, yet scientists who presumably subscribe to the same rules of logic have not reached a unanimous conclusion on the choice between the lipid theory and the thrombotic theory. Not only is it not possible to derive theories from facts, I suspect it is not even attempted. As far as I can discern, the lipid theory was in existence before most of the epidemiologic data were available. Dock⁴ suggests that Ignatovski performed his cholesterol feeding experiments in order to test out the lipid theory – or, if you will, the theory preceded the facts. I should add here that it is very difficult to find an accurate historical account of this point, for the history of science commonly gets reconstructed from an inductive viewpoint, i.e., it gets retold as if the theory were ineluctably derived from the facts, where the reverse may have been true.

It is thus fairly generally accepted that theories arise in the scientist's mind in mysterious and non-rational ways. You choose the facts that are relevant to the theory. We might say that the process of theory development is a psychological one, but the process of theory testing is a logical one.

This brings us to a second view of the philosophy of science. Karl Popper^{21,22} asserts that science proceeds by bold conjectures and refutations. He points out that theories may not be verified, they may only be falsified. Thus, to apply it to our heart disease example: If one theorized that *the* initiating event for a myocardial infarction was acute thrombosis of a major coronary artery, and if one were able to demonstrate this to be true in a select group of subjects, then this would not conclusively prove the hypothesis to be true. It could be reasonably argued that an acute thrombosis may cause a myocardial infarction in the people studied, but other individuals may suffer a myocardial infarction without a thrombosis. Thus, argues Popper, theories cannot be proved

by facts any more than by thumping the table. Rather, he argues that theories are put forward, conjectured, and then attempts made to falsify them by gathering the appropriate facts. One might measure the worth of a theory by its ability to withstand attempted falsifications. Theories are rejected by crucial experiments that show them to be false. This is an attractive view of science, but as Lakatos²³ has argued, it does not stand up to scrutiny. To take the lipid theory. The theory predicts that the risk of heart disease rises as the fat content of the diet rises. It might therefore be reasoned that a crucial experiment would be a direct study of the heart disease incidence of individuals consuming high fat diets compared to the CHD incidence of individuals consuming low fat diets. As was pointed out earlier, these data from prospective studies in the United States and the United Kingdom appear to directly refute the theory. Therefore, if Popper's account accurately described the progress of science, the lipid theory would have been discarded.

Of course, the theory has *not* been discarded. Instead, it has been argued, quite plausibly, that the failure to show the direct relationship between the diet of individuals and their heart disease risk has been owing to (a) the inaccuracy of dietary measurements for individuals and (b) the fact that all Americans or all Englishmen consume a diet that is high in fat and therefore a prospective study in the United States or the United Kingdom is not an adequate test of the theory. In fact, a moment's reflection will show that, with a little ingenuity, it is always possible to save a theory from refutation by erection of auxiliary hypotheses to explain away the anomalies. The Popperian response to this is to argue that such auxiliary hypotheses are acceptable if they are not ad hoc, i.e., if they flow naturally from the theory. But this does not really help very much in accounting for acceptance or rejection of theories. The lipid theory has comfortably survived a number of conflicting observations despite some apparently ad hoc maneuvers to account for these conflicts, the reason being, apparently, that the weight of evidence in favour of the lipid hypothesis is so great that no other explanation could easily account for the known facts about coronary heart disease occurrence.

Lakatos, in rejecting the Popperian view, puts forward a third view, from which we can learn much.^{23,24} He argues that a single theory is not judged on its merits alone, but rather a research program which develops and modifies a succession of theories is judged. As long as a research program is progressive, then the theories continue to be accepted, i.e., if a theory is found wanting in the face of new data, then the research program is progressive only if the explanation of the apparent conflicts predicts new empirical observations. Thus, for example, if a population eating a high fat diet is found to have a low heart disease risk, then the lipid theory could be

saved by postulating that it is not total dietary fat that is important but saturated fats and the explanation for this low observed CHD is therefore that the fat was unsaturated. This is progressive if it leads to new predictions, e.g., that feeding individuals a diet high in saturated fat would raise the serum cholesterol level, whereas an unsaturated fat diet would not. On the other hand, arguing that individual variability is too great might be non-progressive or degenerative if it did not lead to new predictions, but merely saved the old theory.

The Lakatos argument is important because it provides guidelines for scientists to follow in choosing between competing research programs. To choose a degenerating research program is irrational unless one works to make it progressive, i.e., to develop the theory such that new empirically testable predictions can be made. I shall return to this point again. It would appear, however, that the criterion of progressive versus degenerative has not been applied in recent years in our heart disease example. The lipid hypothesis has been saved by some auxiliary hypotheses which by and large have not led to new empirical observations. Although perhaps it could be argued, in a sense, that the attempt to modify CHD risk by modifying diets is a progressive prediction. Similarly, the thrombosis hypothesis has not been specified in such a way that it can account for the epidemiologic variations in CHD occurrence, and thus it, too, cannot be considered progressive. Lakatos' account thus might leave us wondering why a majority of scientists in this field continue to work within these theoretical approaches.

Thomas Kuhn²⁷ offers such an explanation. Loosely paraphrased Kuhn's argument states that, in general, scientists work within paradigms; the word paradigm encompassing theory, methods and world view. (It has been pointed out, that Kuhn uses the term "paradigm" in a variety of different senses²⁸.) The reason that general theories (or paradigms) persist is that they are not seriously put to the test. Kuhn posits the existence of revolutionary science and normal science. During periods of revolutionary science, whole paradigms are called into question, and the result is that subsequently scientists work in new traditions. Famous examples are the Copernican revolution and the change from a Newtonian view of the universe to an Einsteinian view. In biology, we might cite the germ theory of disease.

However, Kuhn asserts that what scientists do most of the time is normal science, i.e., the general paradigm or theoretical framework is accepted and not questioned and scientists spend their time filling in the little pieces and, in Kuhn's terms, solving puzzles. This surely is what most of us in epidemiology do, most of the time. The long-term prospective study is of incomparable importance in epidemiology, but it is the example, par excellence, of normal science. Thus, to return to our two schools of thought of the etiology

of CHD. Workers in both traditions spend their time trying to explain conflicting findings in terms of the accepted theories. Why does one country have a higher CHD rate than another? It can, of course, all be explained in terms of the standard risk factors and we spend our time puzzling over the complexities of the interrelationships, without ever questioning the theory.

Kuhn asserts that all theories have anomalies or observations that conflict with them. The paradigm collapses and revolutionary science occurs only when the anomalies become so numerous and so great that the paradigm can no longer support a puzzle-solving tradition. However, Kuhn is not critical of normal science and does not consider it a lower cultural form. He says that it is only by committed scientists taking a stand and tenaciously defending a theory against all opposition that we discover how well it performs and its limits, and thereby increase our knowledge and understanding.

It would thus appear that Kuhn's normal and revolutionary science that he used to describe the physical sciences give a reasonable description of the way heart disease epidemiology has proceeded. It seems that scientists make a decision, ill-understood, to accept a certain paradigm or theory (in our case the lipid view or the thrombosis view), and work within that framework. Hence, the theories will persist as long as scientists are prepared to work within the framework without questioning it. While this may be an accurate description of the way science is, if we accept this as a complete picture of the way science ought to be, the choice between competing theories becomes a propaganda campaign. Each side campaigning for its own beliefs.

To return to Lakatos, however, I think he makes an important methodological suggestion that would reintroduce rationality to the scientific debate. Lakatos takes his criterion of progressiveness of scientific research programs from a study of the great scientists, Copernicus, Newton, Einstein. Their methods are set up as models for other scientists to follow. His implication would be that if we wish to defend our pet theories à la Kuhn, then the best way to do so would be to make them progressive. If a research program is found to be degenerative, then it is acceptable for workers in that "paradigm" to attempt to save it by making it progressive. Otherwise, it should be discarded in favour of a more progressive program. Lakatos stresses that any theory can be twisted to account for old data. The real test of progressiveness is if it predicts new data.

To apply this to our heart disease example: if our current theories cannot do what is asked of them then they should be drastically modified or discarded. For example, the concept of a multifactorial causation has saved many a good epidemiologic theory from destruction, but unless the multifactorial theory of heart disease epidemiology can *predict* whether or

not a particular population group will have a high CHD rate, then it cannot be considered progressive. What may be called for is a new paradigm or new research program. Such a program might, as others have argued, concentrate on individual susceptibility to illness in general rather than on exposure to specific heart disease producing agents. Alternatively, other new programs might be suggested. This new research program would then have to make predictions and be evaluated by the same criteria of progressiveness or degeneration.

To return to the opening phrase: "These are the opinions on which I base my facts ..." I have argued that, as with other sciences, epidemiology does not proceed by simple induction, deriving theories from facts. Rather, as described by Kuhn, scientists choose paradigms or research programs in which to work and then attempt to defend their positions. This may reflect the current situation, but from Lakatos, the suggestion has been gleaned that all need not be reduced to a survival of the loudest. His proposal of the criterion of progressiveness of research programs may allow our opinionated scientist to conclude by saying ... "it is reasonable for me to hold my opinion for my theory has successfully predicted the following new facts."

I would suggest that the injection into epidemiology of some set of methodological criteria such as Lakatos' would do much to help us out of our present dilemmas.

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