Middle Articles

As part of the programme of the XIXth General Assembly of the World Medical Association, held recently in B.M.A. House, a session was devoted to a conference of medical editors. We print below in full the opening contribution by Lord Brain.

Structure of the Scientific Paper

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I have been asked to comment on a provocative B.B.C. address by Sir Peter Medawar (1964) entitled, "Is the Scientific Paper a Fraud?" Medawar explains that he means by this that "the scientific paper may be a fraud because it misrepresents the processes of thought that accompanied or gave rise to the work that is described in the paper." Consider, he says, the traditional form of a scientific paper, upon which, incidentally, editors themselves often insist. "First, there is the section called the 'Introduction,' in which you merely describe the general field in which your scientific talents are going to be exercised, followed by a section called 'Previous Work' in which you concede, more or less graciously, that others have dimly groped towards the fundamental truths that you are now about to expound. Then a section on 'Methods'—that is O.K. Then comes a section called 'Results.' The section called 'Results' consists of a stream of factual information in which it is considered extremely bad form to discuss the significance of the results you are getting . . . . You reserve all appraisal of this scientific evidence until the 'Discussion' section, and in the 'Discussion' you adopt the ludicrous pretence of asking yourself if the information you have collected actually means anything; of asking yourself if any general truths are going to emerge from the contemplation of all the evidence you have brandished in the section you have called 'Results.'"

Medawar goes on to maintain that "the conception underlying this style of scientific writing is that scientific discovery is an inductive process . . . . It starts with simple observation—simple, unbiased, unprejudiced, naive, or innocent observation—and out of this sensory evidence, embodied in the form of simple propositions or declarations of facts, generalizations will grow up and take shape, almost as if some process of crystallization or condensation were taking place. Out of a disorderly array of facts, an orderly theory, an orderly general statement, will somehow emerge." On the contrary, he says, naive observation is a mere philosophic fiction, and it is logically impossible to arrive with certainty at any generalizations containing more information than the sum of the particular statements upon which that generalization was founded. In fact, he maintains that all scientific work of an experimental or exploratory character starts with a hypothesis which arises by guesswork or by inspiration. The scientific work consists in putting the hypothesis to the test, "a strictly logical and rigorous process, based upon deductive arguments."

Scientific Criteria

Medawar (1965) returns to this general topic in an article in *Encounter*. A good deal of what he says in that is not relevant to our present purpose, but one passage is. He is discussing "the criteria used by scientists when judging their colleagues' discoveries and the interpretations put upon them. Foremost is their *explanatory value*—their generality, span of relevance, or rank in the grand hierarchy of explanations. A second is their clarifying power, the degree to which they resolve what has hitherto been perplexing; a third, the feat of originality involved in the research, the surprisingness of the solution to which it led, and so on."

In both of these papers Medawar is directing attention to a process of scientific discovery which, he suggests, is misrepresented by the form of the communication in which it is expressed. I agree with much of what he says. Many scientific discoveries are not based upon inductive reasoning: the hypothesis comes first, even though the scientist himself may hardly be conscious of this. Even so, it does not seem to me to follow that the structure of the scientific paper, the object of which is to communicate something to the reader, should necessarily correspond to the logical process by which the discovery was made. But medicine may be exceptional among the biological sciences Medawar was discussing in that there is often another very important factor in discovery, which he does not mention, but which is related in a complex way both to his hypothetico-deductive system and to the structure of the scientific paper. I propose to call this the serendipity principle—serendipity, you will remember, being "the faculty of making happy and unexpected discoveries by accident." Philosophical discussions are apt to be arid, so I will illustrate my point by some concrete instances.

Medical Discoveries

Consider Fleming's discovery of penicillin. Here is how he describes his famous observation: "What was very surprising was that the staphylococcal colonies in the neighbourhood of the mould, which had been well developed, were observed now to be showing signs of dissolution. This was an extraordinary and unexpected appearance and seemed to demand investigation" (Fleming, 1946). Here is the serendipity principle at its best. Then the hypothetico-deductive principle begins to operate. It is assumed that there is some substance in the mould which inhibits the growth of the bacteria, and an attempt is made to concentrate it. This broke down. Fleming says, "I had failed to advance further for the want of adequate help, Raistrick and his colleagues had lacked bacteriological co-operation, so the problem of the effective concentration remained unsolved." As we know, seven years later Florey and Chain solved it, having been led through their study of lysozyme to tackle the question of antibiotics generally. They proved the truth of Fleming's hypothesis, and their achievement surely substantiates another of Medawar's points—that there is no inherent difference between pure and applied science.

Now let us trace the development of knowledge which began with the problem of the treatment of pernicious anaemia. If you read Minot and Murphy's (1926) original paper you will find that, although it offends against Medawar's canon, it traces very precisely the course of reasoning by which they arrived at their conclusion. It is true that this is a hypothetico-deductive process, but it depends upon past observations made by others, and the historical account which the authors give therefore corresponds to the logical development of their own thought. They begin with the ancient observation that patients suffering from pernicious anaemia are the better for a nutritious diet. They quote Whipple as having suggested that the anaemia might be due either to a scarcity of material from which the stroma of the red cells is formed or to a disease of the stroma-forming cells of a bone-marrow. (Bone-marrow had in fact been given to patients with pernicious anaemia.) Minot and Murphy therefore thought that "perhaps liver and other foods rich in complete proteins may enhance the formation of red blood cells in this disease, especially by supplying materials to build their stroma." They also thought that fats had a bad effect on anaemia, so the diet should be low in fats.

These and similar observations, they say, "led us to investigate the value of a diet with abundance of food rich in complete protein and iron, particularly liver, and relatively low in fat, as a means of treatment for pernicious anaemia." Thus, though they were right in regarding pernicious anaemia as a nutritional disorder—this was a fortunate inspiration—the rest of their reasoning was faulty, and it was through a happy chance, but for the wrong reasons, that they gave large amounts of liver among other things to their patients. This discovery, then, owed much more to the serendipity than to the hypothetico-deductive principle. But then the hypothetico-deductive method gets into its stride. Castle and his collaborators, starting from the gastric achylia, separated the intrinsic and extrinsic factors, and the biochemist had only to persevere to isolate cyanocobalamin, vitamin B_{12}, from the effective liver extract. So the hierarchy of explanations builds up, and now pernicious anaemia is entering the wider synthesis of auto-immune disease.

Rarity-priority Principle

There is a third principle which enters into the construction of medical scientific papers and which to some extent overlaps the serendipity principles. I shall call it the rarity-priority principle. The author's motive is primarily to describe something rare; the wish to be the first to describe it is an independent variable. (Incidentally he very rarely is.) The history of Wilson's disease is an outstanding example.

Kinnier Wilson (1912) drew attention to "progressive lenticular degeneration: a familial nervous disease associated with cirrhosis of the liver" in 1912. He began quite frankly with the rarity-priority principle. "The object of this paper is to give a full description of a rare nervous disease, of which, as far as I am aware, no instance has been recorded during the last 20 years—a disease to which, for reasons which will hereinafter become evident, the name of 'progressive lenticular degeneration' may be conveniently applied." He devotes two pages to a brief clinical and pathological description, and then refers to the six previously published cases, before describing in great detail the clinical and pathological features of his own six new cases, and going on to consider the pathogenesis and the physiological basis of the symptoms.

Wilson could only speculate as to its cause, and his speculations were wide of the mark. The very next year Rumpel (1913) noted an increase of copper in the liver in a case of this disease, and this observation was confirmed, both for the liver and the brain, several times in the next 30 years, but it was not until 1948 that Cumings (1948) suggested hypothetico-deductively that Wilson's disease might be "an inborn error of mineral metabolism."

Further Research into Subacute Cerebellar Degeneration

Finally, let me quote some work in progress in which I am myself interested. Brouwer (1919), on the rarity-priority principle, reported a case of subacute cerebellar degeneration which occurred in a patient who also had a neoplasm. Several more examples of this association were reported later because subacute cerebellar degeneration is a rare condition, but the neoplasm was mentioned only incidentally as the cause of death, until Brouwer and Biemond (1938) first suggested that the association was significant. Brain, Daniel, and Greenfield (1951) reported four such cases, in three of which there was carcinoma. We discussed the meaning of the association and mentioned other reported cases of neuropathy occurring in patients with carcinoma. A paper in the current issue of *Brain* (Brain and Wilkinson, 1965) quotes 20 cases of subacute cerebellar degeneration associated with a neoplasm from the literature and adds 19 new ones. It is now clear that this disorder is only part of a broad spectrum of neuropathies associated with neoplasms, and nearly half a century after Brouwer's first observation we have reached a high level of the hierarchy of explanation but not yet the top, for we do not know the link between the carcinoma and changes in the nervous system. Here, then, as in the history of Wilson's disease, the rarity-priority principle led to the reporting of facts, but their significance was missed for a generation.

We reach this perhaps rather obvious conclusion. Neither hypotheses nor facts can do without the other. The hypothesis, the primary importance of which Medawar stresses, can spring only from the apprehension of some facts; and the rarity-priority facts, as we have seen, lead nowhere if the hypothetico-deductive principle does not come to grips with them. The outstanding need for clear thinking on this point is evident in the study of the effects of new drugs. It is certainly important to report all unexpected happenings to patients on new drugs, but equally important to realize that assessing their significance is a hypothetico-deductive process of much greater complexity than is realized by some agitators of the correspondence columns of medical journals.

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After Lord Brain had read his paper Sir Austin Bradford Hill spoke on the same theme. Further contributions were then made on (i) "The Medical Newspaper," by Dr. W. A. R. THOMSON, *Editor-in-Chief of "Medical News" and Editor of the "Practitioner," and by* Dr. MARTIN WARE, *Editor-designate, "British Medical Journal"; and on (ii) "A Journal and its Readers,"* Dr. JOSEPH GARLAND, *Editor, "New England Journal of Medicine," and* Dr. IAN DOUGLAS-WILSON, *Editor of the "Lancet." At the end of the meeting the panel of speakers answered questions from the audience.*