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Nobel Prize in Medicines 1960

Sir Frank Macfarlane Burnet

Peter Brian Medawar

The Nobel Prize in Physiology or Medicine 1960 was awarded jointly to Sir Frank Macfarlane Burnet and Peter Brian Medawar "for discovery of acquired immunological tolerance"

A person's individuality finds many different expressions. In daily life we rely upon such vague means of recognition as facial features, general build, manner of being, moving, and speaking. All these characteristics can be recorded by our sense organs and can be classified and distinguished in more or less conscious perception processes but they could hardly be analysed by physical or chemical methods or expressed in a formula.

There exist, however, individual characteristics which can be registered in a more objective fashion. Fingerprints might be mentioned as one wellknown example. The fine ridges of the skin of the finger tips form a pattern of unlimited variability and therefore apt to serve as an unfailing identification mark.

Similarly, the surface of each separate body cell represents a chemical pattern. In this pattern several distinct motives repeat themselves; some are typical of the species or genus, others of the organ to which the cell belongs; finally, some are characteristic of the

individual. The differences between individual patterns are too subtle to be detectable by chemical means but they are promptly recognized by those elements of the organism which serve the function to neutralize invading foreign substances.

As a consequence, attempts at grafting of tissue will lead to different results depending upon the origin of the tissue. Moving of tissue from one site of the body to another in the same person does not meet with any fundamental difficulties; if only the operation is technically correct, the tissue will heal into its new surroundings. Likewise, tissues or organs can be exchanged between genetically identical individuals, such as identical twins or animals of the same, through systematical inbreeding purebred line. In other situations the result will be less good. At first, perhaps, success appears to have been achieved; healing proceeds as usual and the tissue may start functioning normally. After about two weeks, however, a reaction evolves around the graft which is demarcated and soon degenerates and is rejected. If the experiment is repeated with tissue from the same donor, the recipient will prove to have been sensitized to tissue from that particular donor; the reaction now develops within a few days.

Grafting of normal tissue was systematically studied by Medawar who was able to show among other things that the graft reaction is an immunity phenomenon of the same nature as the tuberculin reaction and that the cellular immunological pattern is an expression of the individual genetic constitution.

The observations on graft reactions served as a basis on which Burnet in 1949 attempted to build a general theory on the nature of immunity. Previously the interest had been mainly directed toward those immune substances which appear in the blood, their chemical nature and modes of production. To Burnet, viewing immunity from the widest possible angle, this was only a small part of a larger problem.

All higher beings fight a running battle against the myriads of micro-organisms that make up our immediate surroundings. The capacity of developing immunity is one of the most important means of defence, of decisive importance for the survival of the individual and the species. It is imperative that the tissues, responsible for the protective reactions, be

able immediately to identify a substance as foreign and therefore presumably harmful. It is equally important, however, that they do not react against the body's own substance. In such cases when this type of abnormal reactions occur, the consequences are fatal. In other words, there must exist a mechanism enabling the organism to distinguish between «self» and foreign substance. To Burnet this emerged as the central problem in the field of immunology.

As already mentioned the individual immunological pattern is genetically determined and is fully developed already in the earliest developmental stages. The capacity to produce immunity, on the other hand, develops relatively late; it is completely lacking in the fetus and full immunological maturity is only reached weeks or months after birth. On this basis Burnet concluded that the capacity of recognizing self substance cannot be an inherited property but is gradually acquired in the course of fetal life. During the constant contact with self substance the developing immunity-producing tissue supposedly learns to recognize and to «remember» its pattern. If this assumption is correct, a foreign pattern should also impress itself upon the immunological memory, on the condition that it be introduced in the fetus at the right time. Burnet predicted the possibility of experimental preparation of an individual so as to make him later accept a certain foreign substance as self.

It was not Burnet himself but instead Medawar and his co-workers who first were able to present experimental evidence to prove the validity of this prediction. Grafting experiments in twin calves supported the theory and indicated that the graft reaction might provide a specially suited test system. Direct experiments were therefore performed in mice, of which a great number of genetically homogeneous, inbred lines are available. Foreign tissue was inoculated into mouse embryos in the womb. The young were later delivered at right term and developed normally. After their immunological maturation grafts were performed. The mice then accepted not only self but also foreign tissue of the same immunological pattern as that introduced during fetal life. Against other foreign

tissues they reacted as vigorously as nontreated animals. They had thus acquired a specific «immunological tolerance».

This observation has now been amply confirmed and expanded in various directions. Experimentally produced tolerance has developed into a biological research tool of great usefulness. Application in practical medicine is still in its very early stages. Naturally it has been close at hand to attempt to apply the laboratory experience gained in the field of surgery, where the problem of substitution of defective or damaged, vitally important organs not infrequently presents itself. Theoretically, the problem is solved; in practice great technical difficulties must first be overcome. The first successful operations of this kind were recently reported, however, and there are thus reasons to await the future development with confidence.

So far, however, the principal importance of the discovery has been in the field of research. It has been said that it has opened a new chapter in the history of experimental biology. In a decisive way it has made a direct study of immunologically active tissue feasible, which in turn has created conditions for a further penetration of the problem of the nature of immunity and of such disturbances of immunization processes as might result in serious disease.

However, immunology is not the only field in which Burnet's and Medawar's work has left its imprints. They have also provided tumour research and genetics with invaluable tools by which new important discoveries were made possible. Sir Macfarlane Burnet. Doctor Peter Brian Medawar. Immunity is our perhaps most important defense against a hostile surrounding world. By penetrating analysis of existing data and brilliant deduction, and by painstaking experimental research you have unveiled a fundamental law governing the development and maintenance of this vital mechanism. On behalf of the Caroline Institute, I extend to you our warm congratulations, and ask you to receive the Nobel Prize for Physiology or Medicine from the hands of His Majesty the King.

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http://www.nobelprize.org/nobel_prizes/medicine/laureates/1960/press.html