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Pointers

The Centenary of Mendel's Discovery

This week we celebrate the centenary of one of the greatest contributions to the science of life. No other single contribution can be compared to it. Gregor Johann Mendel was the son of poor peasants, taught schoolchildren though without any teacher's diploma, studied at the University in Vienna but failed his examinations, became a priest who found it difficult to preach in the Czech language, and was so respected and loved by his fellow monks that they elected him Abbot of the Monastery of Brünn, now Brno. Modesty, honesty, and great loyalty were among the characteristics which attracted those who knew him and sent him into headlong opposition against the tax-gatherers, the kind of opposition which more worldly prelates learnt to avoid. To commemorate the centenary of Mendel's discovery we publish in the middle pages long extracts of Mendel's original paper with reproductions of the first text page in facsimile and of his manuscript. On page 333 we publish an invited contribution on the man and his work by Professor Arnold Sorsby, Editor of the *Journal of Medical Genetics* published by the British Medical Association.

It has been well put by C. D. Darlington[1]: "Before the year 1900, we may say, almost all that we believed of the principles of heredity that was not in Lucretius was wrong." Yet in 1865 Mendel had published an account of scientific experiments that were flawless in design and perfect in execution. It was, however, in the interpretation of his results that his full genius emerged. He produced a theoretical model which predicted with complete accuracy the nature, the properties, and the behaviour which the physical hereditary mechanism, then totally unknown, must possess. As, step by step, understanding has grown, his model has been completely vindicated, and the wealth of further developments have appeared as natural extensions of one of the most inspired conceptions in the history of science.

A great part of Mendel's achievement must be attributed to the fact that he was a more than competent mathematician. He saw things in symbolic and mathematical form—in some ways perhaps being not unlike his great contemporary, Boole. This caused great difficulty to the biologists not only of his own day but to their successors for many a long year. The mixing of mathematics and biology aroused feelings of positive revulsion, as Karl Pearson was to find to his cost thirty years later.

There was a deeper reason why the significance of Mendel's work could not be grasped. As has so often happened in science, he was ahead of his time. His were observations whose significance could not be appreciated in the light of the knowledge existing at the time. There are many analogies. The rules for the transmission of haemophilia were established with complete correctness in 1820. But this made no

contribution to the study of heredity in general. It remained a sterile piece of empirical knowledge until the nature of sex-linked inheritance was elucidated in 1908. It was the greatness of Mendel, and the reason why we honour him to-day, that on the basis of his observations he formulated a theory of hereditary transmission which time has proved to be completely right. His paper was of course freely available in many leading libraries, but it was not until 1900 that a rather small company of biologists were ready to see that here was a key to their problems.

Geneticists of the early school of 1900 onwards had to face bitter opposition. The main line of attack was not to deny the reality of Mendel's observations but to refuse to accept their generality, and, far less, their universality. Naturally, and as we well understand to-day, those inherited characters which clearly demonstrate simple Mendelian ratios tend to be rare abnormalities or somewhat trivial characteristics. The major differences of evolutionary and biological importance are usually complicated in their inheritance as well as being subject to environmental influences. As Morgan and Bateson, for example, contended, their opponents wanted an analysis of what for the time being was unanalysable. The conventional biologists complained that the geneticists were concerning themselves solely with trivialities.

It would be easy to select many instances of frontal or oblique attacks on Mendelism, but one entertaining example which may not be familiar to many English readers was delivered by E. Rabaud[2] to L'Institut Français d'Anthropologie. His title was "Le Mendelisme chez l'Homme." Rabaud gave a clear enough account of Mendelian principles, but he could not conceal his scorn in the phrases he chose (here translated): "What meaning, what value could we really attach to formulas which miss the essence of a phenomenon?" he exclaims. And again: "Why then should we in the face of the facts try to apply a formula which leaks at all its seams? A whole edifice has been erected on a few superficial facts: the edifice collapses." Rabaud proposed a theory of physico-chemical constitution, and goes on to say: "For him [the biologist] such a language has flexibility and general application; it is less hypothetical than the language of Mendel, for, while physico-chemical constitution is a fact, determinants are a conception of the mind. To the biologist, the physico-chemical language is a sure guide, capable of leading him in all possible directions. At the present time, it is free of formulas and does not permit the drawing up of any 'law.' Therein lies its strength."

The Pearson school, however, went further and sought to attack the basic correctness of Mendel's observations. In careful and painstaking work of abysmal sterility Pearson's followers showed that if numbers were large enough there were significant departures from the 3 : 1 ratio. The reasons, primarily differential viability, are obvious enough now, and really should have been obvious then. Up to the time of his death in 1936, Pearson refused to accept Mendelism in any shape or form, and Mendelian terms were outlawed from the publications he edited. The importance of this is that undoubtedly many hostile biologists were glad to have the backing of so justifiably eminent a statistician for the view that Mendelian principles were mathematically unsound.

[1] Darlington, C. D., *The Facts of Life*, 1953. London.
[2] Rabaud, E., *Anthropologie*, 1912, **23**, 169.
[3] Fisher, R. A., *Trans. roy. Soc. Edinb.*, 1918, **52**, 399.
[4] Baur, E., in Baur, E., Fischer, E., and Lenz, F., *Human Heredity*, 1931. London.
[5] Iltis, H., *Life of Mendel*, 1932. London.

The Pearson school had produced a wealth of fine biometrical data, and in 1918 there appeared a paper of classical importance by R. A. Fisher. He showed that so far from the observations on continuously distributed metrical characters being inconsistent with Mendelian theory they could not be rationally explained in any other way. It is said that when Fisher submitted this paper to the Royal Society the Society, wishing to be fair, submitted it to the leaders of both schools. They proved to be in agreement for perhaps the only time in their lives: both recommended rejection. The paper was subsequently published in the *Transactions of the Royal Society of Edinburgh*.[3] From this time on all was set for a full synthesis, but the old doubts lingered for many years. Thus E. Baur,[4] writing as late as 1931, could say that much inheritance was non-Mendelian and that this applied especially to human racial crosses.

In recent times the progress of genetics has been smooth and continuous. The framework so ably established by Mendel has proved completely sound, and developments in biochemical genetics, in the idea of one gene controlling the development of one enzyme, in theories on the mode of action of genes, in the elucidation provided by the genetics of bacteria and viruses, and in the inspired work of the molecular biologists—all have made the study of genetics central in biology. In these developments medicine has both profited and contributed.

Professor Sorsby's paper provides a valuable conspectus of Mendel and Mendelism. He has perhaps not brought out the essential modesty of the man, or his generosity. Mendel was unfortunate in some ways. His experiments with *Hieracium* (hawkweeds) were a disappointment. He had been lucky in choosing the edible pea, and this luck might not have been repeated. And he was in no better a position than his contemporaries to unravel the complexities that soon faced the early geneticist; the necessary basis of knowledge did not exist. So he remains famous for a single dazzling contribution, whose lustre can never be dimmed.

Measuring Sputum

The amount of sputum coughed up in the first hour of the morning has been used in epidemiological studies of chronic bronchitis to establish the diagnosis and give some idea of the severity of the disease.[1] In the *B.M.J.* of 30 January Dr. T. Ashcroft (page 288) and Dr. C. M. Fletcher and his colleagues (page 291) reported their investigations into the relation between the amount coughed up in the first hour and that produced in 24 hours, and the day-to-day variation. In addition, with the object of reducing the chance of error, Dr. Ashcroft has compared the first half hour's production with that of the first hour and he has investigated the daily pattern of sputum production.

Ashcroft's investigations were carried out with the co-operation of forty-eight male patients recovering from chronic bronchitis but free from obvious infection; only two were coughing up less than 10 ml. in 24 hours. Drs. D. L. Miller, C. M. Tinker, and C. M. Fletcher studied sputum collected from 243 subjects in all—people selected as early or pre-clinical cases. Most of them produced less than 10 ml. a day. Both studies showed a large day-to-day variation in the 24-hour volume and in the percentage of it produced in the first