THE CENTENARY OF THE RE-DISCOVERY OF MENDELIAN GENETICS

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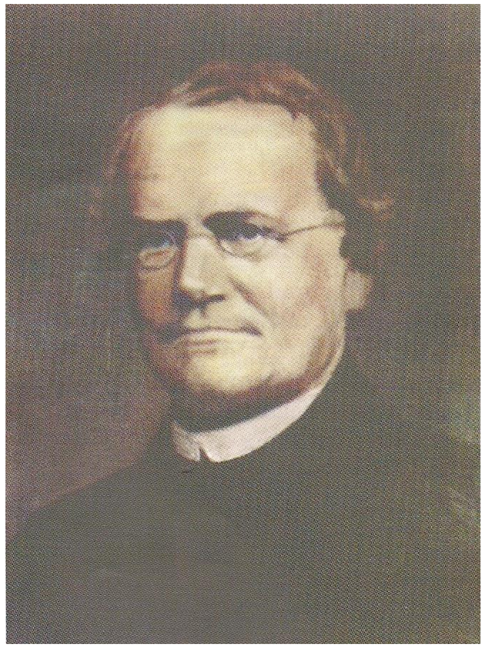

Gregor Johann Mendel

As a Society the BBTS rightly celebrates this year the centenary of Landsteiner's original announcement concerning the existence of blood groups (see Newsletter No. 55, and apologies for the faulty translation - on which no-one has yet commented).

1900 was also the year in which Mendel's laws were re-discovered. Gregor Mendel (b. 1822) was a monk in the Augustinian Abbey at Brünn (now Brno, Czech Republic). The Abbott supported his interest in horticulture by arranging the construction of a glasshouse. In 1865, Mendel announced - to his somewhat bemused fellow small-town scientists - the results of seven years hard work crossing, back-crossing and double-crossing generations of peas. This had involved over 300,000 plants. As a result he introduced the words and concepts of Dominance and Recessiveness. In his enthusiasm he allowed the welter of numbers to bury his interpretations which undoubtedly had the touch of genius; although the simple 3:1 ratio of dominant-to recessive characters inherited in the second hybrid generation was apparent, Mendel could not make his audience appreciate its significance.

Mendel published his findings in German and sent copies to several leading scientists in Europe and America, including Charles Darwin (whose copy was found, unopened, on his death in 1882). The only person of note to respond was Carl Nägeli with whom Mendel entered some correspondence. As a result he was persuaded to work on the less suitable flower "Hieracium" (hawkweed, a kind of multi-headed dandelion). This failed to produce convincing results and the correspondence petered out in 1873. By this time Mendel had become Abbott himself and was taken up with administration; he died in 1884.

Although the simultaneous re-discovery of Mendel's work in 1900 by three 'independent' workers seems remarkable, the story is more complicated. The reports were by the Dutchman Hugo de Vries (in French in March, and in German in April); the German Carl Correns (April, with a postscript on the 16th May); and the Austrian Erich von Tschermak (June). All three were botanists and thought that they were making original discoveries. The Cambridge-based naturalist William Bateson (1861 - 1926) was hot on their heels having been made aware of Mendel by de Vries, possibly during a meeting of the Royal Horticultural Society in London on 11th July 1899. Indeed, the next day another botanist referred to Mendel specifically. De Vries had been working on plant hybridisation throughout the 1890s. He received a copy of Mendel's text, probably some time in 1898 or 1899, before writing his 1900 papers entitled "Concerning the Law of Segregation of Hybrids" which described inherited characters in 11 species of plant. Although he used the terms 'Dominant' and 'Recessive' he did not mention Mendel in the French version of the report, although a brief mention was inserted into the German version. On the other hand, Correns gave clear precedence to Mendel, as shown by his title ("G Mendel's Law Concerning the Behaviour of Progeny of Varietal Hybrids"). He published this after receiving a courtesy copy of de Vries' paper, the rapidity of his response indicating that he was already aware of Mendel's work (Nägeli happened to be his wife's father). Like Mendel he was working with peas - and, like de Vries, with maize. Correns saw De Vries' action as pre-empting his own work and, by implication, that of Mendel himself; but his insight into Mendel's contribution was probably better. R.M. Henig, (see list for further reading) indicates that the normally calm Correns was so upset by de Vries' paper (de Vries had pipped him to the post previously on another matter) that he felt urged to 'correct' de Vries' interpretation of Mendel. In a postscript Correns had written *"1 must emphasise that in many pairs of characters there is no dominant member; and that Mendel's law of segregation cannot be applied universally".* Although this appears to be a caveat to Mendel's discovery, it was made to rebuke de Vries for claiming that in all pairs of differentiating characters one must always be dominant, and to vindicate Mendel's work for those characters which *did* show clear dominant/recessive patterns of inheritance.

Tshermak - the most junior of the three - had also worked with peas and ends his paper by writing *"the simultaneous discovery of Mendel by Correns, de Vries and myself, appears to me especially gratifying. Even in the second year of experimentation, I too still believed that I had found something new".* He later became a Nazi sympathiser and eugenicist. When, in 1910 and largely through Bateson's enthusiasm, the City authorities of Brünn erected a statue in honour of Mendel, de Vries refused to come, Correns' presence was rather grudging, but Tshermak was enthusiastic.

Throughout the last third of the 19th century many people had been working on the mathematics of inheritance. In Britain, the main protagonist was Francis Galton (a cousin of Charles Darwin) who - like Mendel - was born in 1822, but survived to 1911. Galton passed his concepts to Karl Pearson (1857 - 1936) - the first holder of the Chair of Genetics founded through Galton's will at the University of London. Pearson was a major pioneer in the statistical analysis of biological and medical sciences. His students included W.S. Gosset ("Student") and R.A. Fisher (1890 - 1962). Pearson's mathematical style had appealed to W.F.R. Weldon (1860 - 1906), Professor of Zoology at University College London from 1891, and of Comparative Anatomy at Oxford in 1899. Weldon and Bateson had been good friends while students at Cambridge but became estranged after Weldon took up the Galton-Pearson view of biology. Weldon admitted his need to improve his understanding of statistical methods, whereas Bateson had made something of a virtue of his own mathematical limitations (although in 1899 he had urged a statistical analysis of data on inheritance). Weldon's attitude was particularly appreciated by Pearson when Mendel's work was re-discovered.

Following de Vries' lead, Bateson took to Mendel's laws immediately; but Pearson and Weldon, and probably Galton, at first frankly did not believe them. This is not surprising given that much of their work had applied to animals, and often to humankind, where it was more difficult to spot clear cut dominant / recessive patterns, particularly in illnesses. This was at a time when even conditions such as tuberculosis were thought to have a profound inherited element. Pearson's reaction to the difficulties in getting the biological community to accept his approach was to found - with Weldon's help - the Journal 'Biometrika' in 1901, which has always featured complicated mathematical analytical concepts, but caused the biologists to refer to them rather disparagingly as 'biometricians' (to rhyme with 'technicians'?). Interestingly, back in the 1870's Galton had experimented, in a somewhat "dilettante" fashion, on sweet peas. From this study he introduced the term *"reversion"* to describe the findings when offspring of plants with extreme characteristics reverted towards a more average ancestral type. A few years later he replaced this with *"regression"* and began to apply it statistically, in which sense it is still used. In spite of his typically Victorian obsession with numbers, Galton failed to spot the diminishing simple proportions of the 'non-reversant' peas among succeeding generations of hybrids. Had he done so, he might have realised that they signified something special.

In 1902, Archibald Garrod reported on alkaptonuria, a harmless human condition in which - through an inherited block in the metabolism of tyrosine - an accumulation of homogentisic acid is passed into the urine. This darkens upon oxidation in air, so that any stained clothing becomes embarrassingly noticeable. He noted that people with this rare condition were commonly children of first-cousin marriages, which Bateson explained in Mendelian terms. Garrod published these descriptions, along with albinism (which Pearson had told him was also increased among children of cousin marriages), creatinuria and pentosuria, as *"Inborn Errors of Metabolism".* The Mendelian nature of ABO blood group inheritance was first hinted at in 1909 by Reuben Ottenburg and confirmed in 1911 by Von Dungern and Hirszfeld (see Newsletter No.48 - *"It All Happened Around 1911* ").

The controversy between Bateson and the Galton / Pearson school was not resolved in their lifetimes. Before 1900 Bateson had disagreed with Weldon by advocating a 'discontinuous' process of evolution; in other words a species could proceed for generations in an apparently stable state, then suddenly change. This concept was not far from that of mutation, and Bateson quickly adapted it to the Mendelian approach. Bateson and Pearson certainly respected each other, paying tribute to each others' integrity, but were deeply divided and vigorously defended their own viewpoints. It was a classic encounter between analytically inclined minds at home with numbers, and minds more inclined to descriptive observations. As Pearson's son wrote, the two schools were not actually incompatible; indeed Weldon, who understood the biologists' ways of thinking, tried to mediate between the two schools - as, somewhat later, did Fisher. However, even at Weldon's death in 1906 Bateson - after much heart searching - felt he could not send a note of condolence to his widow.

Mendel's discoveries, and the re-discoveries, represent major advances in the understanding of biological inheritance. Within ten years T.H. Morgan (from whom the unit of genetic distance, the 'centimorgan' is derived) had begun his work on the fruit fly *Drosophila,* and by 1915 had published a remarkable genetic map showing the loci of several genes on each of *Drosophila's* four chromosomes. Before his death Bateson came to agree with Morgan about the 'string' theory of gene disposition along the chromosomes, in spite of initial reluctance (which - according to Henig - might have been coloured by Bateson's prejudice against Americans). From this time the era of modern genetics really began.

Further reading

Gregor Mendel - A Monk and Two Peas, Robin Marantz Henig, Weidenfeld and Nicolson, London, 2000.

Translations into English of Mendel's correspondence with Nägeli, and the original publications of de Vries (in French) and of Correns and Tschermak (in German) were issued in Volume No 35 of the journal *Genetics* in September 1950.

Bateson W, 1900. *Problems of Heredity as a Subject for Horticultural Investigation.* Journ. Roy. Hort. Soc. Vol 25, read to the RHS on 8th May 1900 and reprinted in *'William Bateson,* FRS; *Naturalist'* by B Bateson, Cambridge University Press 1928. This gives an excellent summary of Mendel's original work as seen in 1900, but Henig indicates that the written version contains material additional to the delivered speech - as indicated by contemporary press accounts of the meeting.

Morgan TH, Sturtevant AR, Muller HJ, Bridges EB, 1915, *'Mechanism of Mendelian Hereditary'.* Constable & Company Ltd, London.

Garrod AE 1902. *'The incidence of alkaptonuria: a study in chemical individuality'.* Lancet ii 1616. 1909 *'Inborn errors of metabolism'* (the Croonian Lectures, June 1908) Oxford Medical Publications.

DW Forrest *"Francis Galton: the life and work of a Victorian genius"* (Elek Books Ltd, 1974).

ES Pearson. *'Karl Pearson. An appreciation of some aspects of his life and work';* Cambridge University Press 1938.

It may be of interest to note that, among other contributions, 'Student' analysed the variations in analysis, or errors of observation, of red cell counts in haemocytometers. In 1918, R.A. Fisher tried to reconcile the population-orientated Galtonian concepts of genetics with the individual Mendelian concepts, and in the 1930s was also an early exponent of the randomised clinical (and experimental) trial. In the 1940s he helped Rob Race to elucidate the nature of the inheritance of the 'Rhesus blood factors'. Galton founded the ill-fated 'Eugenics' movement, with its advocacy of the duty of the intelligent to have lots of children (although he was childless); Fisher, and several more recent academics, continued to advocate this 'duty'. The Eugenics movement got perverted into ideas of Anglo-Saxon, and then German, racial superiority, although Pearson's views of innate British superiority were severely knocked by the ineptness of the British conduct of the Boer War.