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William Bateson, human genetics and medicine

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Abstract The importance of human genetics in the work of William Bateson (1861–1926) and in his promotion of Mendelism in the decade following the 1900 rediscovery of Mendel's work is described. Bateson had close contacts with clinicians interested in inherited disorders, notably Archibald Garrod, to whom he suggested the recessive inheritance of alkaptonuria, and the ophthalmologist Edward Nettleship, and he lectured extensively to medical groups. Bateson's views on human inheritance were far sighted and cautious. Not only should he be regarded as one of the founders of human genetics, but human genetics itself should be seen as a key element of the foundations of mendelian inheritance, not simply a later development from knowledge gained by study of other species.

Introduction

In the year 1900, the forgotten work of Gregor Mendel was rediscovered almost simultaneously by three workers, Hugo De Vries, Carl Correns and Eric von Tschermak, and modern genetics can be considered to have been born. The man who did most, however, to promote and establish Mendelism as the foundation for heredity was not one of these three discoverers but William Bateson, trained as a zoologist and at this time working at Cambridge, who immediately recognised the importance of Mendel's work and set himself the task of furthering it both by his own experimental studies and by his lectures. Bateson soon became the focal point for experimental research in genetics (a term which he

himself introduced) and is rightly recognised today as the principal founder of Mendelism.

Bateson was not medically qualified and his experimental subjects ranged widely across animal and plant species. In his later career he became director of the John Innes Horticultural Institution, Britain's principal plant breeding centre. As a result, he is now largely identified with the early development of plant and animal genetics and his contributions to human genetics are less widely recognised. This paper aims to correct this perception and to show that Bateson was not only intensely interested and involved in human genetics and inherited disorders, but that this field provided vital evidence for the validity and importance of Mendelism generally which was independent of that obtained from other species. Bateson's work makes it quite clear that human genetics played a central role in the development of thought and knowledge about genetics from the very beginning and was not just a late-comer to the subject.

In this process Bateson's role was particularly important as an interface between basic biologists working on inheritance in experimental animal and plant species and those numerous clinicians interested, but rarely expert, in documenting the wealth of data on inherited disorders already available by the beginning of the twentieth century. Without this interface role, it is unlikely that human genetics would have developed so rapidly, particularly given the virtual absence of meaningful human cytogenetic data for another 50 years. Nor would soundly based observations on human genetic disorders, independent of eugenic prejudices, have reached the point of giving secure foundations for the later development of medical genetics in the decades after World War II.

William Bateson's life

We are fortunate that Bateson's life, correspondence and experimental records are all well preserved and archived, principally at the John Innes Centre, Norwich, UK,

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including a large series of photographs, three of which are reproduced in Fig. 1. A detailed biography of Bateson (Harvey 2000) has also been written by the former archivist at the John Innes Centre, which is available for consultation there and it is planned to publish a shortened version of this. Bateson's widow Beatrice also wrote a memoir shortly after his death, combined with a selection of his addresses (Bateson B. 1928). Other biographical articles are by Bateson's colleague (Punnett 1950) and, more recently, by a distant relative, himself a distinguished scientist (Bateson P. 2002). The present short outline has relied on these sources.

William Bateson was born on 8 August 1861 in Cambridge, England, where his father was Master of St. John's College. After undergraduate years at Cambridge University, he made summer visits in 1883 and 1884 to America to work under William Brooks at the Chesapeake Bay Marine Biological station, part of Johns Hopkins University, on the primitive chordate *Balanoglossus*, following this by further major field expeditions to Russian Central Asia and Egypt.



Fig. 1 William Bateson, **a** as a young man, **b** in later life, **c** Bateson working in the grounds of the John Innes Horticultural Institute, Merton. (Courtesy of the John Innes Archive)

From 1889, he began a 6-year-study on the mechanisms of variation, both structural and developmental, as a research student in Cambridge, which established his views on the importance of discontinuous variation and led to his 1894 book, 'Materials for the Study of Variation (Bateson 1894). In 1896, he married and his wife Beatrice became a key worker in his plant and animal breeding and later his biographer (their marriage had for some years before been strongly opposed by her father).

An increasing focus on mechanisms of heredity and on experimental breeding, meant that on receiving a letter from Hugo de Vries on 8 May 1900, containing a copy of Mendel's paper, he immediately recognised its fundamental importance. The famous story that he opened the letter on the train between Cambridge and London to give a lecture on heredity to the Royal Horticultural Society, and changed the lecture en route to announce Mendel's work, is only documented in Beatrice Bateson's biography and is open to question (Olby 1987). However, there is no doubt that he at once became Mendel's most effective protagonist, demonstrating the general validity and importance of mendelian inheritance in his lectures, books (Mendel's principles of Heredity; Bateson 1902, 1909) and also in his experimental work. His visit to America in 1902 reinforced this position, despite acrimonious debates in Britain with the 'biometric' school of workers, notably Weldon and Pearson (Cock 1973). It was in 1905, exactly a century ago, that he coined the word 'genetics' for the study of heredity when writing (unsuccessfully) to urge the university to establish a Chair in the field.

'If the Quick Fund were used for the foundation of a Professorship relating to Heredity and Variation, the best title would, I think, be 'The Quick Professorship of the Study of Heredity'. No simple word in common use quite gives this meaning. Such a word is badly wanted, and if it were desirable to coin one, 'Genetics' might do.' (Letter dated 18 April 1905, in John Innes Archive.)

Despite Bateson's efforts, and the eventual award of a Chair at Cambridge (in Biology not in Genetics) it proved impossible to obtain major university or government support for his breeding programmes, while in America these had moved rapidly ahead, leaving Bateson to see his own work and ideas overtaken. When the privately funded John Innes Horticultural Institution was established at Merton, near London in 1909, Bateson moved from Cambridge to become its first director, leaving his colleague Reginald Punnett to become the first Professor of Genetics in Cambridge. In his new post Bateson was now able to place plant breeding in Britain on firm genetic foundations, but his more theoretical work was hampered by a persistent reluctance to accept chromosomes as the physical basis for heredity. The *Drosophila* work of Morgan and his colleagues in America, by contrast, was able to advance rapidly by

combining chromosome research with fundamental genetics.

Nevertheless, the John Innes Institution became the international focus for plant breeders across Europe and Bateson had a profound influence on the next generation of workers who established their own centres in different countries, as outlined later. Bateson died on 8 February 1926, aged 64, while still in post as director, being succeeded initially by Daniel Hall and then by Cyril Darlington (Harman 2004), already at the John Innes with Bateson, who would be a key figure in the field of cytogenetics which Bateson had for so long underestimated.

Bateson, Garrod and 'Inborn errors of metabolism'

Archibald Garrod (Fig. 2) now rightly regarded as the father of biochemical genetics and whose key concept of inborn errors of metabolism was brought together as the series of Croonian Lectures to the Royal College of Physicians of London (Garrod 1909), published his first paper on alkaptonuria in 'Lancet' in 1901, mentioning that the parents in three of the four families containing 11 affected individuals, while themselves healthy, were first cousins (Garrod 1901).

In January 1902, Bateson began to correspond with Garrod, whose family material on alkaptonuria had grown considerably with data on 32 families worldwide. Garrod's interest in and appreciation of Bateson's ideas can be seen in his reply (Fig.3), while Bateson was able to cite Garrod's work as a footnote in the report by himself and Elizabeth Saunders to the Evolution Committee of the Royal Society, pointing out the high frequency of consanguinity and the lack of transmission to offspring as evidence for human mendelian recessive inheritance.



Fig. 2 Archibald Garrod (1858–1936). From Garrod's *Inborn Errors of Metabolism*, ed H. Harris 1963. (Courtesy Oxford University Press)

One feature of Bateson's Neurological Society address that seems strikingly modern today is how both his text and illustrations move effortlessly between different species to illustrate particular points. It is striking to see on a single plate (Fig. 4) an X-ray of a human hand (brachydactyly), a series of sheep (to show hornlessness) and a plant (Primula). Admittedly, these probably were not shown together on a single slide, but the concept of 'model organisms', now part of everyday thought and experimental practice in human genetics, was clearly part of Bateson's thinking also. What the neurologists thought of being required to switch from one species to another in this way is not known; there is no printed record of discussion following the lecture.

Bateson's evidence for human Mendelian disorders came from a range of specialties, notably from eye and skin diseases, whose readily observed phenotypes and frequent occurrence in large kindreds made them especially suitable. By the time that the second edition of his book 'Principles of Mendelian Inheritance' was published in 1909 (Bateson 1909), he was able to cite a wide range of disorders (Table 1) that he considered to follow Mendelian inheritance. Much of the material is likely to have come from a 'debate' on heredity and disease, held at the Royal Society of Medicine, London, the previous year and subsequently published (Church et al. 1909).

Bateson's most important clinical collaboration was undoubtedly with the London based ophthalmologist

Fig. 4 Plate from Bateson's address (1906) to the Neurological Society of London, showing his use of evidence from different species applied to human genetics



A



B



C



D

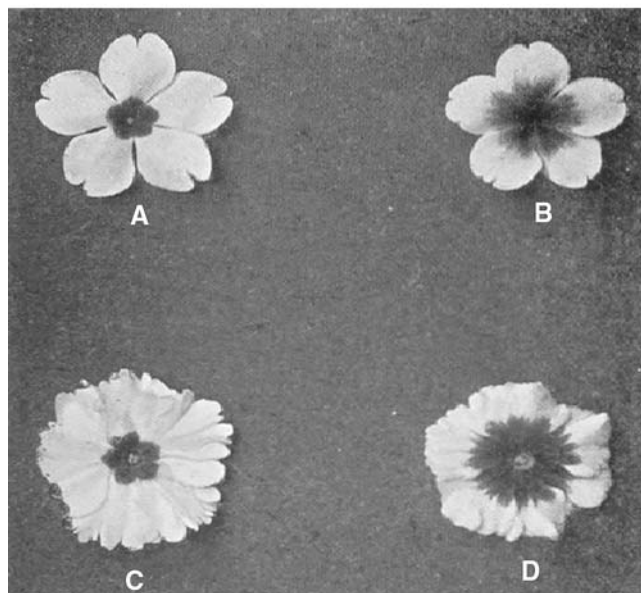


Table 1 Human inherited disorders considered by Bateson to follow Mendelian inheritance

Based on 'Mendel's Principles of Heredity', (2nd edition, 1909), chapter 12, 'Evidence as to Mendelian Inheritance in Man'.8 (modern disease names in square brackets). *Dominant*

Skin disorders	Epidermolysis bullosa	
	Multiple telangiectasis [hereditary haemorrhagic telangiectasis]	
	Monilethrix	
	Porokeratosis	
	Tylosis [hyperkeratosis palmaris plantaris]	
	Xanthoma	
	Eye disorders	Coloboma/irideraemia [aniridia]
		Congenital cataract
		Ectopia lentis
	Other	Stationary night blindness (one large kindred only)
Brachydactyly		
<i>Recessive</i>	Split hand/ectrodactyly	
	Huntington's chorea	
<i>'Sex-limited'</i>	Albinism	
	Alkaptonuria	
	Colour blindness	
	Haemophilia	
	Pseudohypertrophic [Duchenne] muscular dystrophy	
	Stationary night-blindness (most families)	

Edward Nettleship, with whom he corresponded regularly and frequently over a 10-year-period from 1904 until Nettleship's death in 1913. The letters from Nettleship to Bateson are preserved in the Bateson archive at the John Innes Centre and the series shows a warm and lively exchange of ideas, not limited to eye disorders.

Rushton, in a valuable review (Rushton 2000) has pointed out how Nettleship was able to act as a link not only with Bateson but with Karl Pearson, retaining the respect of both despite the conflict between 'Mendelian' and 'biometric' viewpoints. Nettleship repeatedly stressed his ignorance of heredity, but in fact asked questions which showed his insight and which not only stimulated Bateson's work but helped him to avoid serious error on occasion, notably in relation to colour-blindness, discussed below.

Bateson's notes during this period, also preserved in the archive at the John Innes Centre, show that his thoughts were ranging over a wide range of human disorders, including Huntington's disease and sickle cell anaemia, though the information on many was too inconclusive to include as examples of mendelian inheritance in either his book or his lectures.

Bateson's approach to human genetics

It has already been noted that Bateson's links with Garrod had a two way value, providing important explanations for Garrod's findings of consanguinity and

absence of transmission from parent to offspring, while giving Bateson a clear example of mendelism in action. The same is true for Bateson's wider observations on human inherited disorders and on human genetics in general.

Bateson was notably cautious in drawing mendelian conclusions from human data, especially in relation to normal inherited characteristics, such as eye, hair and skin colour, all of which were seized on by other workers to give over-simplified or erroneous conclusions. Thus for hair and eye colour:

'With respect to hair-colour in our own population nothing can yet be said with much confidence. The segregation of red hair from black hair may be seen in many families and this red is presumably a recessive, but to work out the interrelations of hair-colours in general would be a very difficult undertaking. Just as in the case of eye-colours, so here, the attempt to force the various colours into a continuous colour-scale and to classify the material by reference to that scale is useless; for though probably intermediates could be found existing in such gradations as to

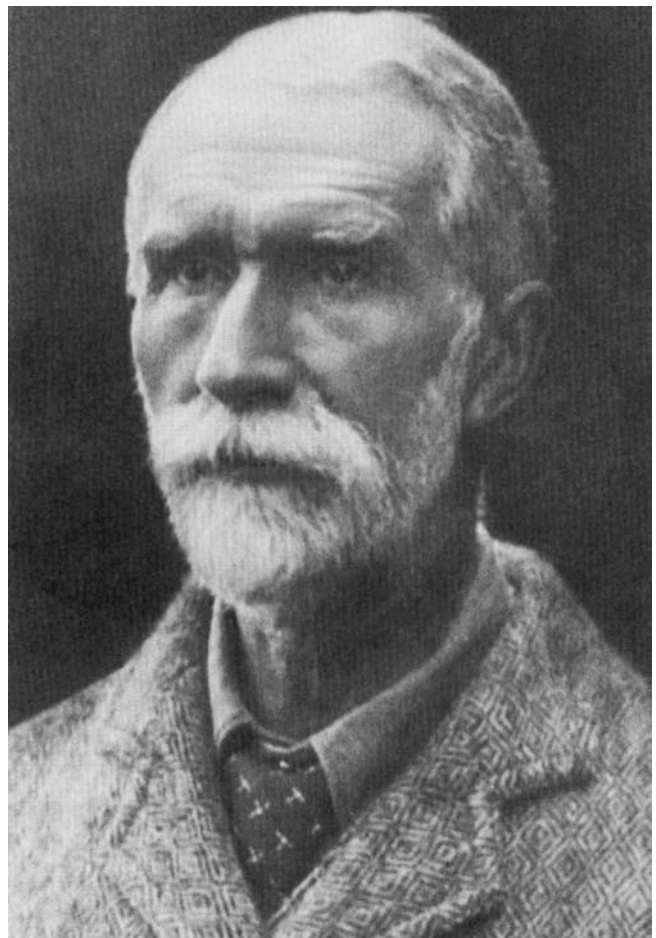


Fig. 5 Edward Nettleship, (1845–1913). Ophthalmologist and collaborator of Bateson. (From Beighton P and Beighton G (1997). *The Person behind the Syndrome*. Springer. Reproduced by courtesy of the authors)

bridge the gaps between the more distinct types, there cannot be the least doubt that so soon as a strict method of analysis is instituted the various intermediates will be shown to be caused by the interactions of a limited number of definite factors. In the analysis of such phenomena research must proceed by the detection of the pairs of factors, beginning with the more obvious, and when their behaviour and powers are thoroughly understood, a search for the remainder may be attempted.'

While for skin colour:

'With regard to skin-colour the general trend of evidence is in favour of the conclusion that if definite determining factors are responsible for the colour seen, the number of such factors or of their subtraction-stages must be considerable.'

It can be seen that while Bateson is here rejecting the 'biometric' approach of totally continuous distributions, he is equally cautioning against trying to fit complex phenotypes into a simple mendelian framework. Importantly, he clearly recognises that a relatively small number of specific inherited factors can produce what appears to be a smoothly continuous distribution of phenotype. This is the essential point, taken forward later by Fisher, which resolved the largely unnecessary conflict between 'Biometricians' and 'Mendelians', and which has given the foundations for the later (and continuing) analysis of complex phenotypes involving most common disorders.

Bateson's foresight (and concern) that these complexities might be ignored is well seen in the conclusion of his address to the Neurologists:

'In conclusion, I should warn you that the detection of these systems of heredity is, except in a few cases, not a simple matter, even when experimental breeding is applied.... We cannot suppose that the complexities there encountered can be absent in man (Bateson 1906).'

Bateson provided a series of simple and practical points to be followed by clinicians keen to document inherited disorders. They are remarkably similar to those to be found in modern introductory texts on medical genetics (and are often still ignored a century later!). They include:

1. Collecting information on normal family members in as much detail as on those affected.
2. Documenting sex, age, and age at onset of the disorder.
3. Tabulating data on each family separately.
4. If families have to be added together, it must be certain that they are in reality similar.
5. Accurate diagnosis is essential.
6. Consanguinity to be noted as present or absent.

Bateson was not himself medically trained, and made no attempt to collect or analyse large-scale family

material, apart from the early data on alkaptonuria. Ironically this approach was taken up by Francis Galton and Karl Pearson, opponents of Mendelism and of Bateson himself, and later resulted in the remarkable work, 'The Treasury of Human Inheritance', whose first part appeared in 1909 (Pearson 1909; Harper 2005). The abundant published and unpublished pedigrees collected and recorded in successive sections of this monumental work, provided more evidence for human mendelian inheritance that Bateson could ever have done himself, especially for rare disorders. Indeed, the Treasury can be regarded as a worthy forerunner of later and more systematic catalogues such as McKusick's 'Mendelian Inheritance in Man (McKusick 1966).'

Bateson's ideas on human mendelian disorders

It can be seen from Table 1 that within a few years of Mendel's work being rediscovered, well before the end of the first decade of the 20th century, all three fundamental patterns of mendelian inheritance had been recognised in human diseases, though there were limitations. Bateson brought this material together in a specific chapter of the second (1909) edition of his 'Principles of Mendelian Inheritance', essentially a completely different book to the original (1902) edition (Bateson 1902).

Autosomal dominant inheritance was the easiest inheritance pattern to be recognised, starting with the report of Farabee in 1905 on brachydactyly (Farabee 1905), cited in detail by Bateson, but followed by a series of other disorders. Indeed much material had already been published and simply needed interpreting in a Mendelian framework. It is perhaps fortunate that a number of those dominantly inherited conditions were reported as single very large pedigrees, such as that of Farabee and also the huge family with stationary night-blindness given as a folding pedigree in Bateson's 1909 book (where he specifically notes that most other families follow a different 'sex-limited' pattern). This avoided problems due to heterogeneity, though transmission by occasional unaffected members (probably due to incomplete study as well as to lack of penetrance) proved puzzling in some instances.

Regarding autosomal recessive disorders, apart from alkaptonuria and other 'inborn errors of metabolism' discussed at the beginning of this paper, Bateson was unable to add significantly to what Garrod had already established, except to note that an increased consanguinity rate would be an indicator of this form of inheritance. He noted the possibility that some families with retinitis pigmentosa might be recessively inherited on account of this, but in general the small size of most kindreds with recessive disorders made it difficult to establish a clear inheritance pattern outside specific and thorough studies, such as those of Garrod. As was stated earlier, it is surprising that autosomal recessive inheri-

tance was recognised at all at this early point, and it would probably have had to wait for a decade or more had it not been for the fortunate conjunction of Bateson and Garrod.

Turning to what we now recognise as X-linked disorders, we find that Bateson, like all workers at that time, was uncertain and at times confused. For this to become clear required not just the concept of genes as definite particles, but the involvement of chromosomes differing by sex, something only fully established by Wilson (1911), though much debated over the preceding decade.

A range of human genetic disorders had already been recognised as following 'sex-limited inheritance', the term generally used at this time and not distinguishing true X-linkage from autosomal inheritance with secondary modification by sex. Haemophilia, colour blindness and pseudohypertrophic (Duchenne) muscular dystrophy had all long been known to be largely confined to males but transmitted through healthy females, but Bateson regarded them (at least before 1910) as atypical examples of dominant inheritance, possibly dominant in males, recessive in females.

Interestingly, the closest he came to the true situation was because of an error on colour-blindness in his 1909 work detected by the ophthalmologist Nettleship with whom he was in frequent correspondence, as already discussed, and to whom he must have shown the proof of the manuscript. Bateson had suggested that half the sons of colour-blind males were themselves affected, but included an erratum note, dated April 1909, which states that Nettleship had documented all sons of colour-blind men (23 of 23) to be normal and for the only previous reports to be where there was a maternal family history of colour-blindness also. He then raises the important possibility that

'It will be evident that the question of a sexual dimorphism among spermatozoa is thus prominently raised'.

As well as making it clear for both clinicians and biologists generally that the different forms of mendelian inheritance were responsible for many genetic disorders, Bateson made an important contribution to thought on how genes acted in producing disease. Again the starting point was Garrod's far sighted concept that inborn errors of metabolism resulted from absence of a necessary enzyme. Bateson broadened this to suggest that absence of a factor would prove to be a feature of recessive disorders generally, while dominantly inherited conditions were the result of something 'added'.

'If, for example, a disease descends through the affected persons, as a dominant, we may feel every confidence that the condition is caused by the operation of a factor, or element, added to the usual ingredients of the body'.

Of course, the underlying pathogenesis of dominant conditions is now recognised as being much more com-

plex and variable than this, but if 'altered' is used instead of 'added', Bateson is not far from the truth for many situations, while even his original concept of 'added' has proved correct for some dominant mutations, notably those tri-nucleotide repeat disorders where a 'toxic' mechanism is involved at either the protein (e.g. expanded polyglutamine sequence in Huntington's disease (Harper and Perutz 2001) or RNA (e.g. expanded CUG repeat in myotonic dystrophy (Mankodi et al. 2000) levels.

Bateson, Punnett and the Hardy-Weinberg formula

While not particularly related to human genetics, this expression of the stable way in which genes are related to genotypes in a population is an integral part of human genetics, as are the factors which result in departure from it. It was also a question raised as to why a human dominantly inherited disorder should not eventually increase in relation to its normal counterpart, that made Bateson and his colleague Reginald Punnett (Fig. 6) take the problem to their colleague George Hardy, Professor of Mathematics at Cambridge.

Punnett's description of the event (Punnett 1950) gives a further interesting view on how informal social networks influenced the development of scientific ideas.



Fig. 6 Reginald Punnett, Bateson's closest colleague at Cambridge, later appointed to the first Professorship of genetics in the university. (Courtesy of the Master and Fellows of Gonville and Caius College, Cambridge, and Professor Anthony Edwards)

'On my return to Cambridge I at once sought out GH Hardy with whom I was very friendly. For we had acted as the joint secretaries to the committee for the retention of Greek in the Previous Examination and we used to play cricket together. Knowing that Hardy had not the slightest interest in genetics I put my problem to him as a mathematical one.. He replied that it was quite simple and soon handed me the now well known formula $pr = q^2$ (Punnett 1950)

The somewhat disdainful attitude of mathematician towards the (implied) inferior species of biologist is made clear also in the beginning of Hardy's short report (Hardy 1908) (appearing in Science as he felt that to publish such trivia in a British journal might damage his reputation!)

'To the Editor of Science: I am reluctant to intrude in a discussion concerning matters of which I have no expert knowledge, and I should have expected the very simple point which I wish to make to have been familiar to biologists. However, some remarks of Mr Udney Yule, to which Mr C Punnett has called my attention, suggest that it may still be worth making.

In the *Proceedings of the Royal Society of Medicine* (vol I, p 165) Mr Yule is reported to have suggested, as a criticism of the Mendelian position, that if brachydactyly is dominant 'in the course of time one would expect, in the absence of counteracting factors, to get three brachydactylous persons to one normal.'

It is not difficult to prove, however, that such an expectation would be quite groundless.'

It should not be forgotten that Weinberg in Germany, both a geneticist and a physician, reached and

published the same conclusions simultaneously (Weinberg 1908).

Bateson and the Genetical Society

One of Bateson's most important and enduring achievements was to found the Genetical Society, whose preliminary meeting on 25 June 1919 inaugurated one of the first societies in the world specifically devoted to genetics (Jinks 1969). All the records of the society since its inception are archived, alongside Bateson's own records, at the John Innes Centre (now in Norwich, UK), including the original minute book (Harper 2004), from which Fig. 7 shows the initial members, a number of whom had interests in human inheritance.

This brought together and consolidated the previously scattered workers in the field of heredity and gave them a forum for scientific discussion that rapidly achieved world-wide influence.

Bateson's wider links

Bateson's early travels in America, Russia and elsewhere provided a wide range of important links that bore fruit after the Mendelian discovery and made him the acknowledged leader of the new Mendelism world-wide. Although his contacts with medical workers were primarily British, the new field of genetics had not yet differentiated to form specific human genetics, so he became the focus for those interested in human heredity, despite or possibly because of, his reluctance to be associated with the eugenics movement founded by Galton and his followers.

Fig. 7 Inauguration of the Genetical Society. Minutes of the initial meeting to form the Society. (From the original minute book, courtesy of the Genetical Society and the John Innes Centre Archive).

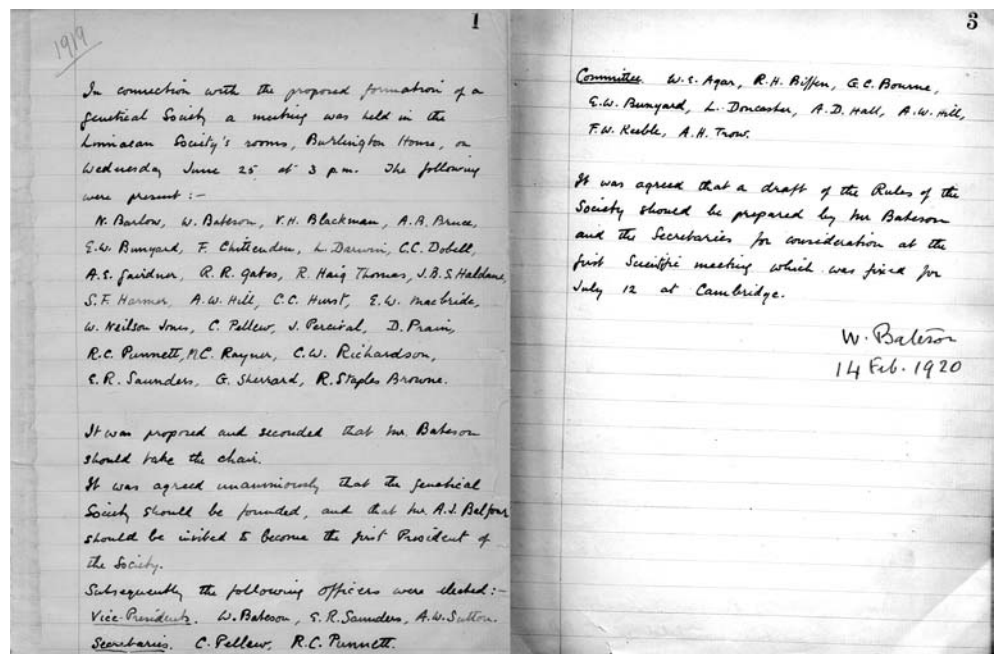


Fig. 8 Bateson with Nikolai Vavilov (1887–1943). (Courtesy of the John Innes Archive).



Bateson's move to the John Innes Horticultural Institution naturally enhanced the links with other workers in plant breeding world-wide, but again the work of these people ranged far beyond the plant field and in many cases had major influences (not all beneficial) on ideas of human genetics across Europe. Notable links were with Denmark (Johannsen), Norway and Sweden (Nilsson-Ehle), France (Cuénot), Baur (Germany) and, perhaps most important of all, Vavilov in Russia (Fig. 8).

Vavilov was a visiting worker at the John Innes Institution in 1913–1914, narrowly escaping with his life when his return ship was hit by a mine in 1914, with the loss of all his records. Despite this, Vavilov returned to Russia to found and develop genetics and plant breeding to an outstanding level; Bateson visited his centre in the new Soviet Union in 1925 and had visible evidence of what could be achieved with the extensive funding and central direction that he himself was never able to obtain to an adequate extent.

Vavilov provides an excellent example of the importance of the 'second generation' geneticists who were able to build on the foundations of Bateson's work and apply them to fields he never could (or in the case of cytogenetics was unwilling to) achieve. In addition this second generation was able to adopt fruitful aspects from different sources (and discard others), so that Vavilov could incorporate the *Drosophila* work of Morgan and Muller alongside the plant breeding studies of Bateson. Vavilov's broad interests and influence had major effects on Russian human genetics leading to the establishment under Solomon Levit of the world's first and largest Institute for Medical Genetics. Alas, both for Russia and the world, the entire structure of Russian Genetics was before long to be destroyed, with the Medical Genetics Institute closed and Levit shot in 1937, Vavilov him-

self imprisoned and dying in a concentration camp in 1943, while after the war genetics was systematically eliminated by Stalin, through the activities of Lysenko, for more than a generation (Medvedev 1969; Soyfer 1994).

Closer to home, Bateson's work at the John Innes Institution was developed by Cyril Darlington, who, as mentioned earlier, had started his career as Bateson's student and who later became the Institution's third director (Harman 2004). Perhaps Bateson would have taken comfort, after neglecting chromosomes for so long, in seeing his Institute become, under Darlington, the world's leading centre for plant cytogenetics.

Conclusion

Human inheritance, especially inherited disorders, formed a central part of the initial evidence for mendelism and was extensively used by Bateson in furthering the recognition and wider acceptance of mendelian principles. Bateson interacted widely and productively with clinicians and may be truly said to have laid the foundations for human genetics. Rather than being a later addition based on the experimental genetics of other species, human genetics has been a key part of genetics since the rediscovery of Mendel's work in 1900.

Acknowledgements I should like to express my thanks to the staff of the library and archive of the John Innes Centre, Colney, Norwich, UK, especially to Kenneth Dick, librarian, for help in consulting, copying and scanning documents and for allowing their reproduction. I am also grateful to Mrs Rosemary Harvey, former Archivist of the John Innes Centre, for allowing access to her biography of Bateson prior to its formal publication and for much valuable advice. Both she and Dr Alan Rushton, New Jersey, provided helpful comments on this paper, though I myself remain responsible for any errors or misinterpretations.

References

- Harvey R (2000). William Bateson and the emergence of genetics. Norwich, The John Innes Centre
- Bateson B (1928) William Bateson, FRS., naturalist. His essays and addresses, together with a short account of his life. Cambridge University Press, Cambridge
- Punnett RC (1926) William Bateson. *Edinb Rev Crit J* 244:71–86
- Bateson P (2002) William Bateson: a biologist ahead of his time. *J Genet* 81(2):49–58
- Bateson W (1894) Materials for the study of variation. Cambridge, Cambridge University Press
- Olby R (1987) William Bateson's introduction of mendelism to England: a reassessment. *Br J Hist Sci* 20(67):399–420
- Bateson W (1902) Mendel's principles of heredity: a defence. Cambridge University Press, Cambridge (Facsimile edition published 1996 by Genetics Heritage Press)
- Bateson W, (1909). Mendel's Principles of Heredity. Cambridge University Press, Cambridge (Facsimile edition published 1990 by Classics of Medicine Library)
- Cock W (1973) William Bateson, mendelism and biometry. *J Hist Biol* 6:1–36
- Harman SO (2004) The man who invented the chromosome: a life of Cyril Darlington. Harvard University Press, London
- Garrod AE (1909) Inborn errors of metabolism. Henry Frowde, Hodder and Staughton, London. (Reissued as Harris H (ed) (1963). Garrod's Inborn Errors of Metabolism. Oxford, Oxford University Press)
- Garrod AE (1901) About alkaptonuria. *Lancet* 2:1484–1486
- Bateson W, Saunders ER (1902) Experimental studies in the physiology of heredity. *Rep Evol Comm Royal Soc Lond* 1:133–134
- Garrod AE (1902) The incidence of alkaptonuria: a study in chemical individuality. *Lancet* 2:1616–1630
- Bateson W (1906) An address on mendelian heredity and its application to man. *Brain* 29:157–179
- Church WS, Gowers W, Lashman A., Bashford EP (eds) (1909) Influence of heredity on disease. Longmans, London
- Rushton AR (2000) Nettleship, Pearson and Bateson: the biometric-mendelian debate in a medical context. *J Hist Med Allied Sci* 55(2):134–57
- Pearson KE (1909) The Treasury of Human Inheritance, parts 1 and 2. London, Dulau
- Harper PS (2005) Julia Bell and the Treasury of Human Inheritance. *Hum Genet* (in press)
- McKusick VA (1966) Mendelian Inheritance in Man (1st edn). Johns Hopkins University Press,
- Farabee WC (1905) Inheritance of digital malformation in man. *Pap Peabody Mus Am Archeol Ethnol* 3:69–77
- Wilson EB (1911) The sex chromosomes. *Mikrosk Anat Entwicklunsmech* 77:249–271
- Harper PS, Perutz M (2001) (eds) Glutamine repeats and neurodegenerative diseases: molecular aspects. Oxford University Press, Oxford
- Mankodi A, Logigian E, Callaghan L et al. (2000) Myotonic dystrophy in transgenic mice expressing an expanded CUG repeat. *Science* 289(5485):1769–73
- Punnett RC (1950) Early days of genetics. *Heredity* 4:1–10
- Hardy GH (1908) Mendelian proportions in a mixed population. *Science* 28:49–50
- Weinberg W (1908) Über den Nachweis der Vererbung beim Menschen. *Jahreshefte des Vereins für Vaterländische Naturkunde in Württemberg*, Stuttgart 64:368–382
- Jinks J (1969) Fifty years of genetics. In: Proceedings of a symposium held at the 160th meeting of the Genetical Society on the 50th anniversary of its foundation. Oliver and Boyd, Edinburgh
- Harper PS (2004) The Genetical Society, William Bateson and human genetics. *Genet Soc News*
- Medvedev Z (1969) The rise and fall of TD Lysenko. New York, Columbia University Press
- Soyfer V (1994) Lysenko and the tragedy of Soviet Science. Rutgers University Press, New Brunswick
- Cock AG (1983) William Bateson's rejection and eventual acceptance of the chromosome theory. *Ann Sci* 40:19–59
- Harvey RD (1985) The William Bateson letters at the John Innes Institute. *Mendel Newslett* 25:1–11