NATIONAL ACADEMY OF SCIENCES

WILLIAM ERNEST CASTLE

1867—1962

A Biographical Memoir by
L. C. DUNN

W. E. Castle

WILLIAM ERNEST CASTLE

October 25, 1867–June 3, 1962

BY L. C. DUNN

THE LIFE OF William Ernest Castle was so intimately connected with the development of the science of genetics in the United States that an account of his scientific career is also a story of the early years of genetics in this country. His scientific lifetime included the period from the rediscovery of Mendel's laws in 1900 until 1961 when his last paper on inheritance of coat color in horses was published. For all these years he devoted himself exclusively to this field—as an exponent and pioneer of the methods and views introduced by Mendel, as a research worker who with his students established the field of mammalian genetics, and as one of the first university teachers of genetics whose students became university teachers and themselves begat other generations of Castle's intellectual descendants. In all of this he spoke in direct and simple terms to a wide audience, attracted to the new science by its potential usefulness in agriculture, in medical and social problems, and especially in the interpretation of the mechanism of evolution. In fact, before the introduction of the term "genetics" by William Bateson in 1906, Castle referred to the

A chronology of Castle's life is appended to this memoir together with a bibliography of his writings. References to the latter will be by ordinal number of publication.

field he had entered just before 1900 as "experimental evolution." The birthplace of this kind of study was the Harvard Zoological Laboratory, where from 1891 to 1899 Charles B. Davenport was instructor in zoology and Castle was first a student and later (1897) also instructor. It was Davenport, later (1904-1934) Director of the Station for Experimental Evolution at Cold Spring Harbor, New York, who helped to form Castle's first interests in heredity and variation.

What happened at Harvard happened also at other laboratories in Europe and the United States in the period just following 1900. Young biologists took fire from the spark set off by the rediscovery of Mendel's principles. In the United States, the generation born in the 1860s and 1870s to which Castle belonged was most strongly affected, and contributed the first generation of leaders of the new science: T. H. Morgan (1866), C. B. Davenport (1866), W. E. Castle (1867), H. S. Jennings (1868), B. M. Davis (1871), R. A. Emerson (1873), G. H. Shull (1874), E. M. East (1879). The members of this group had another distinction—they received their advanced training and doctoral degrees in the United States, although, in general, the previous generation had been trained in Europe. They were zoologists and botanists of the classical schools until in the first decade of this century they diverted to genetics. All of these except Davenport had long careers as university teachers and trained many students in genetics, thus creating within the first twenty years of this century a very active and productive school of genetics in the United States.

Castle was the first of this group to devote himself exclusively to genetics—and had the longest active career. His ancestry and the course of his early life rendered him well fitted to be a pioneer in the development of American genetics.

W. E. Castle was born October 25, 1867, on his father's farm near Alexandria, Ohio. His father, William Augustus Castle, was born in 1824 in Granville, Ohio, as the third son of Augustus Castle (known as Deacon Augustus) who had been born in Underhill, Vermont. Augustus Castle was said to have served for four days in the War of 1812 and later to have migrated to Ohio. William Augustus, son of Augustus, attended for a short time Granville College, a Baptist school which in 1831 became Denison University; but being unable to afford further schooling he withdrew and thereafter educated himself. He became a school teacher in Johnstown, Ohio (near Granville), and there married one of his pupils, Sarah Fassett, daughter of Dr. Harry Fassett, who had himself migrated (on horseback, it was said) from northern Vermont to Ohio. The newly married pair then went to break prairie soil near Galesburg, Illinois, but William Augustus had an attack of typhoid fever and they soon returned to farm near Granville, Ohio. There the six children of William Augustus and Sarah Fassett Castle were born: Clarence Fassett, Albert, Edward, William Ernest, Mary, and Walter. Two of W. E. Castle's brothers also followed academic careers: Clarence taught classics at the University of Chicago and Edward at Teachers College, Columbia University. Of the six siblings, only William Ernest and Walter left descendants. William Ernest's two surviving sons both became professors (William Bosworth Castle, Professor of Medicine; Edward Sears Castle, Professor of Biology) in Harvard University; while Walter's oldest son, William Augustus Castle, became Professor of Zoology at Mary Washington College, Fredericksburg, Virginia.

Deacon Augustus Castle, grandfather of William Ernest, had besides his son William Augustus two other sons and three daughters. The eldest son, Orlando, graduated from Granville College and became Professor of Belles Lettres at a college at Upper Alton, Missouri. The other son, Judson, set out upon the Oregon Trail but died of cholera at Council Bluffs; one daughter succeeded in reaching Oregon, while the other two married and left descendants in Ohio and Indiana.

Another branch of the same Vermont Castle family furnished some of the early American settlers in Hawaii.

William E. Castle was thus derived both biologically and culturally from early British emigrants who with their descendants settled first New England, then the Middle West and the Far West—chiefly as farmers but with interests in education and culture which difficult conditions emphasized rather than discouraged.

Castle's interest in natural science was first expressed when as a farm boy he collected wild flowers and learned to graft trees and to identify and prepare the bones of animals which had died in fields and woods.

Denison University in Granville, Ohio, from which W. E. Castle graduated in 1889, was one of many sectarian colleges (Baptist in this case) established throughout the Middle West almost as soon as the emigrants from the East had broken the soil. It was here that Castle became interested in biology. He attributed the decisive influence in this direction to Clarence J. Herrick, who taught geology, zoology, and botany. It was from Herrick that he learned about organic evolution and the work of Darwin, which was taught in spite of strong theological opposition.

The chief emphasis in the college was on the classics and ancient languages, and upon graduation Castle went to teach Latin in another Baptist college in Ottawa, Kansas, called Ottawa University. It is not surprising, however, that he took with him Gray's manual and an interest in flowering plants that led him to spend his afternoons collecting and identifying plants from the prairie flora, which was new to him. This led to the publication of his first scientific paper (1), a list of several hundred flowering plants collected in the neighborhood of Ottawa.

Confirmed in his interest in botany, Castle, after three years of teaching Latin, aspired to learn more about plants and planned to study at Harvard University. Here a college friend, H. L. Jones, also inspired by Herrick, had preceded him. With scholarship aid, Castle entered the senior class of Harvard College in 1892 and in 1893 took a second A.B. degree (with honors). In that year he had taken all except the beginning courses in zoology and botany; finding the zoological work more interesting, and having made an excellent scholastic record, he applied for and obtained an appointment as laboratory assistant in zoology, under C. B. Davenport. This enabled him to take an A.M. degree in 1894 and a Ph.D. degree (under E. L. Mark) in 1895. Upon completing his doctoral requirements he was appointed instructor in zoology at the University of Wisconsin, where he spent one year. In the summer of 1896 he married Clara Sears Bosworth, whom he had met while teaching at Ottawa. That happy marriage, to which three children were born, was terminated by Mrs. Castle's death in 1940.

In September 1896 he became instructor in zoology at Knox College and served until in 1897 he was called back to Harvard, where, as instructor, and professor, he remained until his retirement in 1936. He was then appointed Research Associate in Mammalian Genetics at the University of California in Berkeley, where he was provided with facilities for continuing his research, which he pursued actively until his death, after a brief illness, on June 3, 1962.

SCIENTIFIC CONTRIBUTIONS

Castle's first extensive scientific publication was his doctoral dissertation, submitted in 1895 and published (4) in January 1896. Under the direction of Professor E. L. Mark, director of the Zoological Laboratory at Harvard, he had undertaken to work out the embryological development of an ascidian—

Ciona intestinalis—in an effort to elucidate certain disputed questions concerning the mode of origin of the primary germ layers of the tunicates. Castle did this in a very thorough manner which led him to take issue with the then prevailing views concerning the origin of the mesoderm and the ancestry of the chordates, both questions of intense interest to zoologists. But before coming to these larger questions, he began his paper with his most important observation—the discovery of self-sterility. He proved that in Ciona, an hermaphrodite ascidian, self-fertilization is prevented not, as had been supposed, by ripening of eggs and sperm at different times but by a different means which Castle revealed for the first time in an animal. This was that, in general, sperm and eggs produced by the same individual are unable to unite in fertilization. The failure of sperm, in Ciona, to penetrate eggs of the same individual was comparable, in Castle's view, to the self-sterility (later called incompatibility) which had been found in certain flowering plants. He speculated that the block to self-fertilization was probably chemical in nature.

This observation, confirmed by later investigators, revealed problems concerning the nature of the fertilization process which still occupy the attention of biologists. It is an interesting fact that T. H. Morgan spent many years studying the self-sterility phenomena which Castle had discovered, chiefly the years following his work with Drosophila, an animal which Castle had also introduced into experimental zoology.

This early paper of Castle's also gives indication of the direction of his future interest. During the course of publication of Castle's paper, Boveri had named and defined the "centrosome," that is, the "attraction sphere" introduced into the egg by the sperm. Castle commented that this organ "is not a bearer of heredity since in fertilization it may be derived from the sexual product of one parent only."

Castle's other publications of 1900 and before dealt with developmental problems in invertebrates, such as the origins of the metameric pattern in leeches. Then there occurred a sudden break. No publications of his are listed for 1901 or 1902 but in January 1903 he published a paper on Mendel's laws of heredity. After that all of his biological publications for the next fifty-eight years dealt with genetics and its relation to evolution and animal breeding. The change in his research interests and materials which occurred in 1901 seems to have been complete and never to have reversed itself. The cause of the change was clear: he had recognized the significance of Mendel's principles.

His mind had been prepared, as we learn from his writings, by Darwin, Weismann, de Vries, and Bateson. In a letter to me (October 21, 1959) he wrote speaking of the period just before 1900: "The rediscovery of Mendel's work threw a flood of light on the situation, the full significance of which was first realized by Bateson. Here was where genetics began."

It is uncertain just how Castle first learned of Mendel's work, but there was ample opportunity, for in addition to the papers of de Vries, Correns, and Tschermak published in 1900, there appeared in 1901 in the *Biological Bulletin* a paper by C. B. Davenport on "Mendel's Law of Dichotomy in Hybrids." Bateson's reports to the Evolution Committee of the Royal Society began to appear in 1902. Castle said later that it was from the first of these reports (Bateson and Saunders 1902) that he got the idea that the difference between males and females in higher animals was a Mendelian one (32, p. 395). He had already (before 1900) begun to study the role of heredity in determining the sex ratio in mice and guinea pigs by testing experimentally the effects of selection upon it. Although the results of this work were not published, and were presumably indecisive, he did publish several papers on genetic interpretations of sex heredity (7, 14, 32). While these had the merit of showing that the sex difference could be treated as Mendelian, he had been anticipated in this by Correns and Strasburger and (as appeared later) by Mendel in his correspondence with Nägeli.

Castle's own experimental work did not contribute to the clarification of sex determination although his theoretical discussions focused attention on the essential questions involved. The chief importance of this early work for Castle's future research was that it turned his attention to small mammals and to the wealth of discontinuous variations in external characters which they showed. Beginning in 1901, therefore, his interest clearly came to center on the Mendelian analysis of coat colors and similar traits in rats, guinea pigs, rabbits, and mice and in the application of results of this analysis to questions of general importance for theories of evolution. In this he had the long-continued support of the Carnegie Institution of Washington, from which he received research grants from 1904 until 1943. He was Research Associate of the Station for Experimental Evolution (1904-1905) and thereafter of the Carnegie Institution, retaining this appointment until 1943, seven years after his retirement from Harvard.

He stated the problems toward which his work for the period 1900-1910 was directed as follows (228, p. 67):

"1. First came the problem, how extensive is the applicability of Mendel's law? Does it apply to all discontinuous variations? Does it apply to cases of intermediate or blending inheritance?

"2. The assumed purity of the gametes produced by a hybrid after the association of contrasted characters in the same zygote for many cell generations. Is it true?

"3. The assumption that a character segregating as a unit in hybridization cannot be modified by selection however long and persistently continued. Is it true?

"4. The conclusion of Weismann that germ cells and body cells are distinct, germ cells alone being the vehicle of heredity, and consequently that acquired characters are not inherited. Is it true?"

These were the questions of the hour and Castle was not alone in attacking them. Bateson and Punnett, Darbishire, Doncaster and Hurst in England, and Cuénot in France set out upon the same course but none exceeded Castle in the vigor and pertinacity with which he pursued these questions. His analysis of the independence of several Mendelian factors in guinea pigs, some of which interacted to produce a variety of coat colors, provided textbook illustrations of Mendelian heredity which remain useful today. The general applicability of Mendel's principles became apparent as such work proceeded, but concerning blending or intermediate inheritance the questions remained obscure and Castle's position vacillated between the possibility that permanent blends might occur between contrasted characters (as in ear length or weight in rabbits), which would constitute a negation of Mendel's first principle, and the acceptance of the multiple factor hypothesis to which he was later driven by results of his own work.

Concerning the second question, it is interesting to find that Castle, who was so often to play the role of defender and introducer of Mendelism, remained skeptical about some of its primary assumptions. On page 619 of his first paper on the heredity of albinism (11), he says: "It is not necessary to suppose, as Mendel did, that the segregated elements of a composite character pass invariably into different gametes." This doubt about "the purity of the gametes," a cornerstone of Mendel's principles, remained with Castle until 1919 when he finally convinced himself, after arduous experiments, that genes were not altered by selection nor subjected to conversion in hybrids.

One of his elegant and convincing experiments was directed to the fourth question. He and his volunteer associate, the surgeon John C. Phillips, transplanted the ovaries from an immature black guinea pig to an albino female whose own ovaries had been completely removed. This albino foster mother was then mated to an albino male and in three successive litters bore only black offspring. The heredity of the offspring was determined by the germ cells uninfluenced by the body in which they resided. This decisive demonstration had a great influence at a time when there were still widespread doubts about the inheritance of acquired characters and the influence of the soma on germ cells.

Also in this decade came other evidence that Castle was a true pioneer in genetics. In 1901 he found a useful experimental animal in *Drosophila ampelophila*—the vinegar or pomace fly. The reproductive behavior and general biology of this insect were worked out by Castle with the help of four students and in February 1906 the first paper on breeding experiments with Drosophila was published (18). This was an account of the effect on fertility of brother-sister inbreeding carried on for sixty generations, of the inheritance of low and high productiveness, and of the effects of crossing different inbred lines. Inbreeding in Drosophila, contrary to expectations based on experiments with other animals and plants, did not reduce vigor or productivity and crosses between some inbred lines gave unmistakable evidence of heterosis. The experimental results were reported but no general interpretation such as emerged later (e.g., East and Jones 1919) was given, and although often cited, the experiments of Castle and his students did not figure prominently in the genetical theories of inbreeding. The paper's most important effect may have been the introduction of Drosophila as the genetical animal par excellence, an eminence which it attained after Morgan's discovery of the first mutant in 1909.

The question which dominated Castle's scientific life for fifteen of his most productive years was, as he put it in 1951, "whether Mendelian characters are, as generally assumed, incapable of modification by selection, whether or not attended by outcrossing. My own early observations indicated that they were modifiable, and to this view I stubbornly adhered, like Morgan in his early opposition to Mendelism, until the contrary view was established by a crucial experiment" (228). The question, in fact, came to be whether a gene could be modified by selection—and the fact that the question could take two forms reveals a lack of clarity, in the first years of Mendelian study, concerning the concepts of characters and of genes. For Castle in 1904 "unit-character" or "unit-factor" meant what after 1909 "gene" came to mean, but the earlier terms permitted, as Mendel's "differentiating character" had permitted, a looser or vaguer distinction between the phenotypic effect and the transmitted element, the gene. At any rate Castle with a succession of collaborators, chiefly J. C. Phillips, proved that a black-and-white spotting pattern, called "hooded," known to segregate as a "unit-character" in rats, could be modified by selection in both directions toward more black and toward more white and that crossing with wild rats increased the amount of white in the hooded pattern of the spotted animals extracted from the cross. This happened to a conspicuous extent when the line selected toward more white was outcrossed, but there was a slight effect of this kind when the dark-selected line was used. This seemed to contradict the dogma of "purity of the gametes," so an extensive study involving some 50,000 rats was carried out between 1907 and

1919. This showed that the character was modifiable, but the crucial test (suggested by Castle's student Sewall Wright) showed that the modifications were due to genes separable in crosses from the hooded gene, which had not itself been changed. The results were shown to be due to the operation of multiple modifying factors and Castle was thus led, by his own experiment, to accept an interpretation of apparently blending or intermediate inheritance which he had long resisted, and to renounce the views on selection and the variability of the gene which he had defended so vigorously for nearly twenty years. Characteristically he made the correction in a seminar attended by his students and colleagues, some of whom had previously voiced their disagreement with his earlier interpretation. He introduced his remarks by saying that when he had told his wife that morning that he was to "correct" his long held views about selection, she had commented that he had spent a good deal of time recently in unsaying what he had said in previous years. "I agree," said Castle, "and consider that it represents progress."

In his published "correction" (101) he went the whole way and withdrew all claim for alteration in a gene except by its mutation to a different allelic state. In discussing genetic variability as largely due to multiple genes he took occasion to comment also on the lack of human control over the production of such variability. It forms an interesting contrast to the views later expressed by the Lysenko faction in the USSR to read Castle's view expressed in 1919. "We certainly at present have to follow nature's lead rather than to lead nature, as regards the course of evolutionary change."

Orthodoxy or easy agreement with generally held notions seemed not to be a normal position for Castle. He was a hard man to convince, and this led him into some serious controversies. In 1919 he attacked the very citadel of the chromosome theory of heredity as it had been erected by the Drosophila geneticists led by Morgan. Castle attempted to show (95, 96) that the Drosophila linkage data did not fit the single linear order of genes assumed by Sturtevant and Morgan. The controversy raged in the pages of the *Proceedings* of this Academy and at one meeting of the Academy Castle appeared with a three-dimensional model, in wire, which he believed more adequately fitted the breeding data. Sturtevant, Bridges, and Morgan replied that Castle had failed to understand the key to the linear arrangement theory, namely double crossing-over, and that in reaching his nonlinear model he had combined Drosophila data derived from different and not always comparable breeding experiments. H. H. Plough and later (1920) Alexander Weinstein of the Morgan group entered the controversy with new experimental data compatible with the linear but not with the nonlinear interpretation.

Castle's failure to understand (or to accept) some of the subsidiary hypotheses of the chromosome theory caused the Drosophila workers a lot of trouble, but it also caused them to re-examine their own evidence, in which some minor errors were found, to carry out additional experiments, and to scrutinize their assumptions more rigorously. The linear arrangement hypothesis survived all this and was strengthened by the controversy. If Castle went down to defeat he earned at least the gratitude of many students who had at first encounter failed to appreciate the subsidiary hypotheses such as interference required by the linear theory. Rereading these old battles after a lapse of forty years, we are reminded that the mechanism underlying recombination of linked genes has still not been elucidated. There were significant clues revealed in the replies of Morgan and his colleagues to Castle, such as the sensitiveness of crossing over to age, other genes, temperature, and other ambient conditions, but these have not yet yielded a general theory. Perhaps it is time for another "doubting Castle" to arise.

Castle subsequently devoted many years to the study of linked genes in mammals, of which he and Wright (81) described the first case in 1915. The construction of the linkage maps of the rat, the mouse, and the rabbit began in his laboratory and after his retirement his special interest was to localize the new mutations in the rat as they were discovered in his and other laboratories.

Castle's forte was to reduce scientific problems to simple terms capable of being tested by experiments. He was, as he himself said, better at carrying out rigorous testing of hypotheses than at inventing new ones. The first adequate proof of the existence of a lethal gene in animals was given in a paper by Castle and C. C. Little in 1910 (40). Cuénot had pointed out in 1905 that the yellow mice bred by him and others all proved to be heterozygous for a gene which distinguished yellow from non-yellow fur color; and that the litters produced by matings of yellow by yellow were smaller on the average than those of matings of yellow by non-yellow. Cuénot had supposed this to be due to repulsion, in fertilization, between sperm and eggs bearing the yellow allele. But Castle and Little's experimental data were better than Cuénot's and permitted them to discriminate decisively between the above hypothesis and another, first employed by Erwin Baur (1907) to explain a similar case found in the breeding of snapdragons. That was the assumption that the missing homozygous embryos were formed but always died, which was the first statement of the hypothesis of lethal factors. Castle was thus not the first to discover the anomalous facts nor the first to propose the essential element of the interpretation, but with his student Little he provided the proof.

The idea that genes could, by mutation, assume more than two alternative states (multiple allelism) had a somewhat similar history. Castle observed this relationship early in his studies of rabbit coat color and in 1909 (35) showed that the color factor in Himalayan albino rabbits (white with black "points") was not the same as in either fully-colored (C) or the usual albino varieties (*c*) but a new state which he referred to as C^1 since offspring of crosses between Himalayans and albinos did not show reversion to full color. His concept of 1909 was similar to the one which emerged much later: "The various independent factors may have a basis no more complicated than that of so many atoms attached to a complex molecular structure. Factors are components merely of complex molecular bodies" (35, p. 68). He was obviously thinking of the kinds of alterations which would occur in a gene to change its allelic state, but he did not generalize nor develop from that beginning the theory of multiple allelism with its important connotations concerning structure and function in the hereditary unit. That remained for others. G. H. Shull gave a more thorough discussion of this in 1911, assuming three forms of a sex gene, acting as multiple alleles, in *Lychnis Dioica* and concluding that such changes were incompatible with the hypothesis of Bateson that the recessive allele was merely the absence of something present in the dominant. Sturtevant (1913) gave the first clear analysis and generalization of multiple allelism, insisting on the importance of the theoretical distinction between allelism and complete linkage which had eluded Castle. But he and most subsequent workers with this problem and the writers of textbooks all used Castle's evidence from the Himalayan rabbit, which became, because of its clarity, the classical case.

Castle's research after about 1920 was dominated by two main interests—analysis of the inheritance of size in mammals and the construction of genetical maps of the chromosomes of the rat and the domestic rabbit through the study of linked genes. The questions about the inheritance of quantitatively varying characters such as size had arisen out of the doubts that Castle had entertained, almost from the beginning of his work in genetics, about the application of a Mendelian explanation to blending or intermediate inheritance. His first work with rabbits (body size, ear length) confirmed his doubts. But later intensive studies together with P. W. Gregory, using the methods of both genetics and embryology (148, 149, 156, 157, 158, 162, 174, 180), traced differences in size between different races of rabbits to differences in the rates of early development of the fertilized eggs, and these were clearly determined by genes in the chromosomes of both egg and sperm. Size differences among certain races of the house mouse were shown to be influenced by genes which had previously been identified by their effects on coat color and similar "qualitative" traits (160, 184, 187, 192, 202, 205). Some of these were found also to influence differentially the growth of special parts such as tail or cranium. Although questions as to whether the effect was exerted by the gene which had been recognized by its effect on color or by other genes closely linked to it were never satisfactorily resolved, these experiments disposed finally, in Castle's mind, of blending inheritance as a non-Mendelian category.

The breeding tests for linked genes, first in the rabbit and later concentrated on the rat, were of a more routine character but formed the basis for the chromosome maps of both species.

It was perhaps as a relief from the arduous breeding experiments which the above-mentioned studies required that he turned to the study of inheritance of coat colors in horses. This could be done by examination of pedigrees and stud books and became the most satisfying work, both as research and as hobby, of the last fifteen years of his life. He was especially interested in the beautiful Palomino breed, and together with W. R. Singleton presented in 1961 an outline of the inheritance and interaction of genes concerned with this and other horse colors and patterns. This was his last published paper and brought to full circle his interest in color inheritance in mammals which he had begun to analyze sixty years before.

CASTLE AS TEACHER

Castle began his teaching career in 1893 as assistant in zoology at Harvard College under Charles B. Davenport and continued as instructor for one year each at the University of Wisconsin (1895) and Knox College (1896) before returning to Harvard as instructor in 1897. There he began with an introductory course in invertebrate zoology which he taught for twenty years. In 1900 he began to offer a course devoted to new developments in evolution that quickly became what must have been one of the first university courses dealing primarily with genetics. His interests had already turned in this direction before Mendel's work came to his attention in 1901. His prompt recognition of the fundamental nature of this discovery determined his future course as scientist and as teacher, and he was eager to share his interest both with college classes and with a wider audience. The introductory paragraph of a paper (8, 8a) which he prepared in 1902 reads as follows:

MENDEL'S LAW OF HEREDITY[1]

"What will doubtless rank as one of the great discoveries in biology, and in the study of heredity perhaps the greatest, was made by Gregor Mendel, an Austrian monk, in the garden of his cloister, some forty years ago. The discovery was announced in the proceedings of a fairly well-known scientific society, but

[1] This paper was originally published in January, 1903 (ref. 8).

seems to have attracted little attention and to have been soon forgotten. The Darwinian theory then occupied the center of the scientific stage and Mendel's brilliant discovery was all but unnoticed for a third of a century. Meanwhile the discussion aroused by Weismann's germ-plasm theory, in particular the idea of the non-inheritance of acquired characters, had put the scientific public into a more receptive frame of mind. Mendel's law was rediscovered independently by three different botanists engaged in the study of plant-hybrids—de Vries, Correns and Tschermak—in the year 1900. It remained, however, for a zoologist, Bateson, two years later, to point out the full importance and the wide applicability of the law. Since then the Mendelian discoveries have attracted the attention of biologists generally. Accordingly a brief statement of their underlying principles may not be without interest to others also."

Castle recognized one of the important consequences of the new view of heredity in the following words: "Acceptance of Mendel's principles of heredity as correct must lead one to regard discontinuous (or sport) variation as of the highest importance in bringing about polymorphism of species and ultimately the formation of new species." The motive force for Castle's interest, as for the work of many of his contemporaries, was clearly this new opportunity to elucidate the mechanism of evolution, and it was appropriate that a course of instruction in evolution should evolve into one in genetics. In 1910 he began to share this course with his newly appointed colleague in plant genetics, E. M. East. Beginning in 1915-1916, both graduate and undergraduate courses in genetics were offered, again with Castle and East alternating as instructors.

Castle was an orderly and thorough lecturer, usually speaking from a prepared text. His textbook *Genetics and Eugenics* (1916) reproduced these lectures in clear and simple language. Evolution was the main theme of both lectures and book. A sentence in the introduction to the textbook gives Castle's general orientation: "From the philosophical standpoint genetics is only a subdivision of evolution." This view was widely shared by the founders of the field who came to it under the influence of Darwin, Weissman, and de Vries. As Bateson had said (1908): "The facts of heredity and variation are the materials out of which all theories of evolution are constructed."

Castle thus shared the general views of his English contemporary William Bateson (born 1861) and came to occupy in the United States a role similar to that of Bateson in Great Britain. In his *Mendel's Principles of Heredity, a Defence* (1902) Bateson had begun by saying: "In the study of evolution, progress had well-nigh stopped." Then had come the rediscovery of Mendel, and Bateson described his relation to it as follows: "In many well-regulated occupations there are persons known as 'knockers up' whose thankless task it is to rouse others from their slumber and tell them work time is come round again. This part I am venturing to play this morning and if I have knocked a trifle loud, it is because there was need."

Castle was a quieter but equally persistent advocate of what he (and Bateson) referred to as Mendelism; and the rapid spread of interest in the new views of heredity and variation in the United States among biologists, students, plant and animal breeders, and the public owed much to Castle's writings and lecturing in the period 1903-1912.

His primary influence as a teacher was on graduate students and his work in this direction began to bear fruit when facilities and freedom for research with advanced students were provided. This came about with the establishment of the Bussey Institution for Applied Biology in 1908. The Bussey had been an undergraduate school of husbandry and gardening from 1871 until in 1908 it became the newly established graduate school of biology, with William Morton Wheeler, the entomologist, as dean. The main building of grey stone had been built some forty years before in the midst of the fields adjacent to the Arnold Arboretum in that part of Jamaica Plain known as Forest Hills, some ten miles distant from Cambridge. There were in addition greenhouses, barns and outhouses, and a frame dwelling used by the graduate students as a dormitory.

Castle moved his rabbits into the basement of the main building, his rats into the large west room on the first floor, and his guinea pigs into an out building known as the pigeon house. Soon a mouse-room was established in what had been a greenhouse attached to the front of the main building. Here Castle for the first time had the space and freedom to develop an extensive program in mammalian genetics. He was fortunate in having the help of a foreman who acted also as janitor—Mr. Patch—a former Maine farmer who tilled the fields, grew food for the animals, and invented devices for feeding, watering, and keeping the animals securely in their cages. Here he received as fellow-workers the first of the graduate students who took their degrees under his direction.

Soon Castle was joined at the Bussey by East, and together, between 1909 and 1936, when the Bussey closed its doors, they prepared forty doctoral candidates. The list of these follows.

Mammalian Genetics

J. A. Detlefsen	W. H. Gates
E. C. MacDowell	L. H. Snyder
C. C. Little	C. E. Keeler
Sewall Wright	G. W. Hervey
L. C. Dunn	Gregory Pincus
W. L. Wachter	P. W. Gregory
Tage Ellinger	E. A. Livesay
H. W. Feldman	R. C. Robb

Paul B. Sawin	F. H. Clark
N. F. Waters	S. C. Reed

Plant Genetics

R. A. Emerson	R. A. Brink
O. E. White	H. C. McPhee
O. F. Burger	P. C. Mangelsdorf
J. B. Park	W. S. Hsu
G. F. Freeman	A. J. Mangelsdorf
D. F. Jones	W. R. Singleton
E. F. Gaines	S. H. Yarnell
H. K. Hayes	F. A. McCray
Edgar Anderson	H. H. Smith
Karl Sax	E. R. Sears

There was also a succession of visiting investigators from the United States and other countries. Nearly all of these continued in research and teaching in genetics in universities, agricultural colleges, and experiment stations. Castle and East and the Bussey thus exercised an important formative influence on American genetics and, through the foreign guest investigators, on other countries as well.

There were several features of this development which were traceable to the character and behavior of the two leaders. Both were strong and positive personalities and in temperament and general views they were destined to be often in disagreement. When this happened it was not concealed from students, who were not expected to conform to the views of their particular sponsor. East's door was open to Castle's students and vice versa. No sharp distinctions between botanical and zoological materials or methods were made; genetics was one sharply defined set of problems which could be stated in more or less abstract terms. Nor was any distinction between "pure" and "applied" genetics ever broached. Castle and East were both interested in evolution, in animal and plant breeding, in agriculture, and in human social problems, and each was actively engaged in experimental analysis of problems which they conceived as of basic and general biological significance. The result was that the restricting influence of specialization, which might have been expected to accompany the rise of a new field that had to push its way into an established discipline such as zoology or botany, was largely avoided.

Castle and East and other members of the small staff of the Bussey probably preferred the freedom and simplicity of the Bussey to the more academic atmosphere of the university departments in Cambridge where they went to lecture during term time. But the rich odors of an old building which housed hundreds or thousands of rats and mice and rabbits and guinea pigs, and the spaciousness (and often the low temperature) of its high-ceilinged rooms failed in the end to compensate for its physical separation from the main center of the University. The completion of the new Biological Laboratories in Cambridge marked the end of the Bussey and in 1936 its work was transferred to Cambridge. Castle's retirement was timed to coincide with that move. He wrote to me on February 20, 1936: "I have just been advised, this last week, that the Bussey will be closed up July 1st and so my experimental work must come to an abrupt termination. I am trying to salvage some of the uncompleted projects." He then described tentative plans for three graduate students who could not finish their work under him. "I don't know what I shall do. Men of my race are long lived and die hard. I shall retire on pension in September. Of course we knew this was coming, in fact was overdue, but I kept right on with the experiments as if I had all the time there is for them, and I am glad that I did, for we got quite a number of problems cleared up.—

"I am grateful for the long continued opportunities which I have enjoyed for scientific research, which is indeed a privileged status. Now I shall take a vacation and look around for something worth doing while I continue so damned healthy and so am unable to die, as I should."

Several of his former students were apparently more disturbed than he was by the absence of provision for mammalian genetics in the new laboratories in Cambridge; but when he heard of our inquiries as to facilities with which he might continue his experimental work, he gently chided us with failure to learn at least one lesson from him. This, as he expressed it at a luncheon given for him in June 1936 on the occasion of his retirement, was that the progress of science was often impeded by old men with stereotyped ideas who get in the way of young men with fresh ideas.

Castle's influence as a teacher derived in large degree from the human qualities which guided his scientific life. His enthusiasm was quiet and firm and controlled but never concealed. It extended to all parts of the work of an animal breeding laboratory and students came to enjoy even the menial parts of the work (in which they participated on equal footing with the professor and the laborers) as much as he did. Sometimes it seemed a bit grim, as when I reported to him that the chief infestation site of a parasite which had brought breeding in the rat colony almost to a standstill was under the scales of the tail. "In that case," he said, "we shall have to remove the tails"; and we stood at two chopping blocks with butcher knives and amputated the tails of several hundred rats, discussing at the same time the construction of the linkage maps to which end the rats were being bred.

His courtesy and patience never seemed to fail. This lent a certain formality to his manner. All persons in the laboratory were addressed and referred to as Mr. or Mrs. or Miss. This was quite in keeping with the starched wing collar which usually appeared above his long brown laboratory coat. The essential kindliness of his nature was not worn externally, but students and associates knew they could count on it. Simplicity and directness characterized his manner as they did his approach to scientific problems. He had a natural aversion to complicated experiments and I believe regarded abstractions with suspicion. This led him to make mistakes when dealing with problems requiring mathematical or statistical methods—but once discovered the mistake was always acknowledged. Except in his lectures he did not give the impression of being a conscious teacher. Rather he behaved with students as a fellow-investigator; and the memory of him which his former students probably treasure most is that of being treated, even as beginners, as responsible persons and as intellectual equals.

CASTLE'S ATTITUDES ON SOCIAL APPLICATIONS OF GENETICS

Castle's influence on his contemporaries was exerted in another way which now calls for recognition. This was his steady maintenance of an attitude of critical, scientific objectivity toward such questions as eugenics, race-crossing, and the other social applications of genetics at a time when other voices tended to become strident and extreme positions were often expressed by his fellow scientists. His textbook of 1916 was called *Genetics and Eugenics* and in all four of its editions (the last in 1930) there was a statement of the then meager facts of human heredity and a discussion of eugenics. Beginning in 1915, five additional publications of his dealt with such questions. The first of these (82), a review of H. H. Goddard's book of 1914, *Feeble-mindedness: Its Causes and Consequences,* set the atmosphere for the others. He compared the attitudes of the English and American schools as represented by the Eugenics Laboratory of London and the Eugenics Record Office at Cold Spring Harbor, Long Island, as follows:

"The English school has leaned backward in its devotion to the inductive method of accumulating inheritance data, ostensibly without prejudice for or against any particular theory but in reality with an ill-concealed bias against anything savoring of Mendelism. The American school recognizing in Mendelism a great advance and an important instrument for the discovery of new truth, has ignored the possibility that other undiscovered laws of heredity may exist and has cast aside as superfluous the valuable biometric tools wrought with such patient toil by Galton and Pearson. It will be the part of wisdom for students of genetics to imitate the hostile attitude of neither school but to utilize the positive results of both." In discussing "disharmonies" said to result from race-crossing (124) in the light of his own work with rabbits, he said: "So far as a biologist can see, human race problems are not biological problems any more than rabbit crosses are social problems.—The sociologist who is satisfied with human society as now constituted may reasonably decry race crossing. But let him do so on social grounds only. He will wait in vain if he waits to see mixed races vanish from any biological unfitness."

In the article "Eugenics" for the *Encyclopaedia Britannica* supplementary volume of 1926 (136) he referred to claims that feeble-mindedness, insanity, epilepsy, and violent temper were inherited as single Mendelian traits: "Possibly some of these and other results published by the Eugenics Record Office have been put into too simple and too rigid categories and a strictly Mendelian statement of results has been adopted oftener than is justified by present knowledge of genetics." It should be remembered that the Director of the Record Office was C. B. Davenport, the former teacher of Castle and the man to whom he had dedicated his textbook. The encyclopedia article ended with five criticisms from "those who decry or look with disfavor on the modern eugenic movement," the last being that its basic philosophy was wrong. Finally in 1930 (151) he attacked the work of Davenport and Steggerda on Negro-white race-mixture in Jamaica, accusing these authors and H. S. Jennings of overstatements and misinterpretation of data in the following words: "The honestly made records of Davenport and Steggerda tell a very different story about hybrid Jamaicans from that which Davenport and Jennings tell about them in broad sweeping statements. The former will never reach the ears of eugenics propagandists and Congressional committees; the latter will be with us as the bogeymen of pure-race enthusiasts for the next hundred years." In the last edition of his textbook (154) he gave, as usual, both sides of such controversial questions, ending his discussion of eugenics with these words: "Practically, therefore, we are limited to such eugenic measures as the individual will voluntarily take in the light of present knowledge of heredity. It will do no good, but only harm, to magnify such knowledge unduly or to conceal its present limitations."

It is apparent from reading Castle's published work (and in the absence of correspondence of which he seems not to have kept copies, this is our chief source of information) that he was determined to meet the obligations which were increasingly being placed upon scientists to speak out on public questions, but it is equally clear that he intended to speak only as a scientist, and within the limits of his scientific competence. Only twice did he step outside this bound, once to plead for retention of research direction within the universities (70) and once for calendar reform (206, 207). This meant that in general he spoke chiefly to his fellows and published only in journals devoted to science. A few articles appeared in *Popular Science Monthly* and its successor *Scientific Monthly*.

He was devoted to science as an individual activity and not as an organized collective effort. He wrote to me in 1943 as follows:

"I should be greatly alarmed over the Kilgore bill, if I thought there was the barest possibility of its being passed by Congress. Bureaucratic regimentation of science would in my judgment be deadly to its highest interests which rest in the independence and initiative of individuals. When any bureau head is authorized to *direct* what questions shall be investigated and how, the spontaneity, inventiveness and value of research will be lost.

"Even as mild a form of bureaucracy as the National Research Council has, I think, limited usefulness and has resulted in waste of talent rather than its utilization. The one thing of value which it has accomplished is to provide research opportunities for a certain number of talented young men who had attained Ph.D. status but had no job. They were enabled to keep going for 2 or 3 years longer as prospective investigators.

"But each year of its history one or more of our top-notch investigators—such as Harrison, F. Lillie, McClung, Cole, et al.—have put aside valuable research activity of their own to warm an office chair in Washington and hold endless committee meetings and compile endless reports. I have received reams of them, not one in a hundred of which got anywhere except to name more sub-committees and designate fields of research without providing means for accomplishment.

"I am all against organizing science and all for fostering the individual scientist who has ideas and enough energy, inventiveness and resourcefulness to give them a try-out.

"Now this is not to criticize in the slightest degree your well meant efforts in *Science* to clarify the situation. Each of us must follow the course which seems best to him.

"But I cannot forbear unbosoming to you a thought which has long been growing in my mind—that the worst thing which could happen to science would be governmental organization of it for war or for peace."

EDITORIAL WORK AND SOCIETIES

Although Castle believed first of all in individual effort as the motive power for scientific advance, he believed also in voluntary cooperation among scientists and participated in the founding of the first American journals and societies devoted to genetics. In his "Beginnings of Mendelism in America" (228) he has given us an account of the founding (1903) and early meetings of the American Breeders' Association. Of its fourth meeting in Lincoln, Nebraska, in January 1906, he wrote: "Its proceedings contain little of present day interest, but resulted in a characteristic American organizational spree, leading to the formation of special committees on breeding of nearly every different crop or breed of animals." The Association ceased to meet after 1909 but began then the publication of the monthly *American Breeders' Magazine,* the first American genetical journal. The magazine, largely through the efforts of Castle and David Fairchild, was replaced in 1913 by the *Journal of Heredity,* which is now completing its fiftieth year. Castle was vice president of the sponsoring organization, the American Genetic Association, and a staunch supporter and editorial adviser of the journal throughout his life.

Castle was a member of the editorial board of the *Journal of Experimental Zoology* from its founding in 1903 until his death in 1962. It was in this journal, of which Ross G. Harrison was managing editor for over fifty years, that many of the key papers by American geneticists were published in the period between 1903 and 1916.

In 1916 Castle joined with ten colleagues to found the journal *Genetics* with George H. Shull as managing editor. He remained a member of the editorial board until his death. When in 1935 I became managing editor of this journal, I wrote to Dr. Castle asking his views about the function of the editor since I knew he would not volunteer any advice. He replied, *inter alia:* "Contributors cannot expect you to rewrite their papers, but only to decide whether *as presented* they are or are not acceptable. The author is the best judge of what in his paper is important and what can be passed over lightly. If he takes too much space for it, you can tell him that for that reason his paper is unacceptable, and put it up to him to do the cutting or seek publication elsewhere. If his ideas are all wrong, *you* are not responsible for them. . . .

"Don't worry over the *poor* papers which come in for *Genetics.* Reject them. Publish the good ones and publish them in full, if they are really good. But if they are too long, even though good, tell the author to boil them down if he wants them accepted."

Castle's purpose was not to allow life and work to become complicated. He apparently did not retain the records of the many editorial consultations in which he was involved nor of the large correspondence with other geneticists in this and other countries. "Finish the talk and get on with the work" seemed to be his motto. His views about scientific writing were reflected in his own writings. It should be simple and clear and so unable to conceal the thought of the author. Mistakes and incompletenesses would thus be the more exposed. Since these were inevitable accompaniments of scientific work, the important thing was to be able to detect and to correct them. This view was clearly expressed in one of his last letters to me (June 10, 1961). Referring to his collected writings, about which I had inquired, he wrote: "I realize that they represent awkward attempts by trial and error to develop a sound theory of genetics, but by such efforts, science progresses."

Although he was far from being an organization man he participated in starting (1922) the Joint Genetics Section of the American Society of Zoologists and the Botanical Society of America (chairman 1924), which in 1932 became the Genetics Society of America. He was interested in the Jackson Memorial Laboratory, Bar Harbor, Maine, founded by his former student, C. C. Little, and as an "honorary trustee" Castle was the guest of honor at its twenty-fifth anniversary celebration in 1954. He saw that laboratory as one "modeled after the Bussey Institution a semi-detached center for research by a small group of competent investigators in intimate daily contact." Such laboratories should act as a foil to increasing centralization but should themselves not get too big. "Great fundamental discoveries are largely the work of men of genius working alone, not in teams. Team work is needed only for verification and utilization of great discoveries. This is the point I tried to make in my paper at Bar Harbor." (Letter, Dec. 31, 1954, W. E. C. to L. C. D.)

Castle never lost, I think, his faith that even though scientific work might become complex and highly organized and big, still simplicity could and should be fostered by the intimate attachment of the research worker to his work as his manner of life. This belief and its practice brought a serenity into his own life that endured to its very end. One of my first views of Castle at home was as a student when upon entering the kitchen of his house on the hill above Belmont, Massachusetts, I found the kitchen range enclosed by a low barrier. This, Mrs. Castle explained, was to confine the guinea pigs, recently collected in the highlands of Peru, to the warmest place in the room until they should become acclimated. In the garden of that house he found space to express his lifelong interest in plants and filled the borders with iris. He was never far from the soil in both the figurative and the literal senses. He published no further observations on plants after his first paper of 1893, but nearly seventy years later, in his tenth decade he was cultivating his garden in Berkeley until a few days before his death.

CHRONOLOGY

1867	Born at Alexandria, Ohio, October 25
1889	A.B. Denison University, Granville, Ohio
1889-1892	Professor of Latin, Ottawa University, Ottawa, Kansas
1892	Admitted to senior class, Harvard College
1893	A.B. Harvard; Phi Beta Kappa; first scientific paper published
1894	A.M. Harvard
1895	Ph.D. Harvard
1895-1896	Instructor in Zoology, University of Wisconsin
1896	Married Clara Sears Bosworth, August 18
1896-1897	Instructor in Zoology, Knox College
1897	Instructor in Zoology, Harvard College
1900	Member of American Academy of Arts and Sciences
1903	Assistant Professor, Harvard; first six papers on genetics published; editorial board, *Journal of Experimental Zoology*
1904	Research Associate, Carnegie Institution of Washington; Vice President, American Society of Zoologists
1908	Professor of Zoology, Harvard
1910	Member of American Philosophical Society
1911	Publication of *Heredity in Relation to Evolution and Animal Breeding* (New York, D. Appleton & Co.)
1915	Member of National Academy of Sciences
1916	Founding member of Editorial Board of the journal *Genetics;* first edition of *Genetics and Eugenics* (Cambridge, Mass., Harvard University Press)
1919	President, American Society of Naturalists
1921	Sc.D. University of Wisconsin; LL.D. Denison University
1936	Emeritus Professor of Genetics, Harvard University; Research Associate in Mammalian Genetics, University of California
1940	Publication of *Mammalian Genetics* (Cambridge, Mass., Harvard University Press)
1955	First recipient of Kimber Genetics Award of the National Academy of Sciences
1962	Died at Berkeley, California, June 3

BIBLIOGRAPHY

KEY TO ABBREVIATIONS

Am. Breeders' Mag. = American Breeders' Magazine

Am. J. Phys. Anthropol. = American Journal of Physical Anthropology

Am. Naturalist = American Naturalist

Arch. Entwicklungsmech. Organ. = Archiv fuer Entwicklungsmechanik der Organismen, Wilhelm Roux'

Bibliographia Genet. = Bibliographia Genetica

Bull. Museum Comp. Zool. = Bulletin of the Museum of Comparative Zoology at Harvard College

Carnegie Inst. Wash. Publ. = Carnegie Institution of Washington Publication

Harvard Graduate Mag. = Harvard Graduate Magazine

J. Abnormal Psychol. = Journal of Abnormal Psychology

J. Exp. Zool. = Journal of Experimental Zoology

J. Genet. = Journal of Genetics

J. Heredity = Journal of Heredity

J. Morphol. Physiol. = Journal of Morphology and Physiology

J. Wash. Acad. Sci. = Journal of the Washington Academy of Sciences

Pop. Sci. Monthly = Popular Scientific Monthly

Proc. Am. Acad. Arts Sci. = Proceedings of the American Academy of Arts and Sciences

Proc. Am. Breeders' Assoc. = Proceedings of the American Breeders' Association

Proc. Nat. Acad. Sci. = Proceedings of the National Academy of Sciences

Sci. Monthly = Scientific Monthly

Trans. Kansas Acad. Sci. = Transactions of the Kansas Academy of Science

Z. Induktive Abstammungs-Vererbungslehre = Zeitschrift fuer Induktive Abstammungs und Vererbungslehre

1893

1. A list of flowering plants and ferns collected in Franklin County, Kansas. Trans. Kansas Acad. Sci., 13:80-89.

1894

2. On the cell lineage of the ascidian egg. A preliminary notice. Proc. Am. Acad. Arts Sci., 30:200-16.

1895

3. With C. B. Davenport. Studies in morphogenesis. III. On the acclimatization of organisms to high temperatures. Arch. Entwicklungsmech. Organ., 2:227-49.

1896

4. The early embryology of *Ciona intestinalis,* Fleming (L.). Bull. Museum Comp. Zool., 27:201-80.

1900

5. The metamerism of the Hirudinea. Proc. Am. Acad. Arts Sci., 35:283-303.
6. Some North American fresh-water Rhynchobellidae, and their parasites. Bull. Museum Comp. Zool., 36:15-64.

1903

7. The heredity of sex. Bull. Museum Comp. Zool., 40:187-218.
8. Mendel's law of heredity. Proc. Am. Acad. Arts Sci., 30 (Jan.):543-48.

8a. Mendel's law of heredity. Science, 18 (Sept. 25): 396-406. (A part of this paper had been published in Jan. 1903; cf. #8.)

9. Note on Mr. Farabee's observations. Science, 17:75-76.
10. The heredity of angora coat in mammals. Science, 18:760-61.
11. With G. M. Allen. The heredity of albinism. Proc. Am. Acad. Arts Sci., 38:603-22.
12. The laws of heredity of Galton and Mendel, and some laws governing race improvement by selection. Proc. Am. Acad. Arts Sci., 39:223-42.

1904

13. Experimental studies of heredity in small mammals. Annual reports in Year Books of Carnegie Institution of Washington, Vols. 3-38, 40.
14. Sex determination in bees and ants. Science, 19:389-92.

1905

15. Heredity of coat characters in guinea-pigs and rabbits. Carnegie Inst. Wash. Publ., 23. 78 pp. 6 pl.
16. Review of *The Evolution Theory,* by August Weismann. Science, 21:668-70.
17. Recent discoveries in heredity and their bearings on animal breeding. Proc. Am. Breeders' Assoc., 1:120-26; also in Pop. Sci. Monthly, 66; also in Die Umschau, 9 (Dec. 9).

1906

18. With F. W. Carpenter, A. H. Clark, S. O. Mast, and W. M. Barrows. The effects of inbreeding, cross-breeding, and selection upon the fertility and variability of Drosophila. Proc. Am. Acad. Arts Sci., 41:729-86.
19. Inbreeding, cross-breeding and sterility in Drosophila. Science, 23:153.
20. With Alex Forbes. Heredity of hair-length in guinea-pigs and its bearing on the theory of pure gametes. Carnegie Inst. Wash. Publ., 49:1-14.
21. The origin of a polydactylous race of guinea-pigs. Carnegie Inst. Wash. Publ., 49:17-29.
22. Yellow mice and gametic purity. Science, 24:275-81.

1907

23. On a case of reversion induced by cross-breeding and its fixation. Science, 25: 151-53.
24. Experimental evolution in Lawrence Hall. Harvard Graduate Mag., 16.
25. The production and fixation of new breeds. Proc. Am. Breeders' Assoc., 3:34-41.
26. Color varieties of the rabbit and of other rodents: their origin and inheritance. Science, 26:287-91.

27. With H. MacCurdy. Selection and cross-breeding in relation to the inheritance of coat-pigments and coat patterns in rats and guinea-pigs. Carnegie Inst. Wash. Publ., 70. 50 pp. 2 pl.

1908

28. Color variation among domesticated animals. Proc. Am. Breeders' Assoc., 4:172-80.
29. A new color variety of the guinea-pig. Science, 28:250-52.

1909

30. The behavior of unit-characters in heredity. In: *Fifty Years of Darwinism,* pp. 143-59. New York, Henry Holt.
31. On some laws of heredity. Ill. Med. J., 15: 406-12; also in Chicago Medical Recorder, Feb., pp. 119-26.
32. A Mendelian view of sex-heredity. Science, 29:395-400.
33. With J. C. Phillips. A successful ovarian transplantation in the guinea-pig, and its bearing on problems of genetics. Science, 30:312-13.
34. With C. C. Little. The peculiar inheritance of pink eyes among colored mice. Science, 30:313-15.
35. In collaboration with H. E. Walter, R. C. Mullenix, and S. Cobb. Studies of inheritance in rabbits. Carnegie Inst. Wash. Publ., 114. 70 pp. 4 pl.
36. Review of *Mendel's Principles of Heredity,* by W. Bateson. Science, 30:481-83.

1910

37. The effect of selection upon Mendelian characters manifested in one sex only. J. Exp. Zool., 8:185-92.
38. Heredity. Pop. Sci. Monthly, 77:417-28.
39. Russo on sex-determination and artificial modification of the Mendelian ratios. Am. Naturalist, 434-39.
40. With C. C. Little. On a modified Mendelian ratio among yellow mice. Science, 32:868-70.
41. The nature of unit characters. Harvey Lectures, 6:90-101.

1911

42. Double mating of silk-worm moths. Science, 34:15-21.

43. With J. C. Phillips. On germinal transplantation in vertebrates. Carnegie Inst. Wash. Publ., 144:1-26.
44. On sex-chromosomes in hermaphroditism. Am. Naturalist, 45:425-30.
45. On "Soma influence" in ovarian transplantation. Science, 34:113-15.
46. *Heredity in Relation to Evolution and Animal Breeding.* New York, D. Appleton & Co., 184 pp.

1912

47. On the origin of an albino race of deer-mouse. Science, 35:346-48.
48. On the origin of a pink-eyed guinea-pig with colored coat. Science, 35:508-10.
49. Are horns in sheep a sex-limited character? Science, 35:574-75.
50. The inconstancy of unit-characters. Am. Naturalist, 46:352-62.
51. On the inheritance of tricolor coat in guinea-pigs, and its relation to Galton's law of ancestral heredity. Am. Naturalist, 46:437-40.
52. Some biological principles of animal breeding. Am. Breeders' Mag., 3:270-82.
53. The method of evolution. In: *Heredity and Eugenics,* pp. 39-61. Chicago, University of Chicago Press.
54. Heredity and sex. In: *Heredity and Eugenics,* pp. 62-82. Chicago, University of Chicago Press.

1913

55. With Q. I. Simpson. A family of spotted Negroes. Am. Naturalist, 47:50-56.
56. Simplication of Mendelian formulae. Am. Naturalist, 49: 170-82.
57. Reversion in guinea-pigs and its explanation. Carnegie Inst. Wash. Publ., 179:3-10.
58. With J. C. Phillips. Further experiments on ovarian transplantation in guinea-pigs. Science, 38:783-86.

1914

59. The cytological time of mutation in tobacco. Science, 39:140.
60. Multiple factors in heredity. Science, 39:686-89.
61. Review of *Controlled Natural Selection,* by J. C. Nottram. Science, 39:944-45.
62. Some new varieties of rats and guinea-pigs and their relation to problems of color inheritance. Am. Naturalist, 48:65-73.
63. An apple chimera. J. Heredity, 5:200-2.
64. Pure lines and selection. J. Heredity, 5:93-97.
65. Yellow varieties of rats. Am. Naturalist, 48:254.
66. Nabour's grasshoppers, multiple allelomorphs, linkage and misleading terminologies in genetics. Am. Naturalist, 48: 383-84.
67. The theoretical distinction between allelomorphs and close linkage. Am. Naturalist, 48:503-4.
68. Review of *Problems of Genetics,* by W. Bateson. Science, 40:241-45.
69. Review of *Vorträge über Deszendenztheorie,* by A. Weismann. Science, 40:245-46.
70. Research establishments and the universities. Science, 40: 447-48.
71. With J. C. Phillips. Piebald rats and selection: an experimental test of the effectiveness of selection and of the theory of gametic purity in Mendelian crosses. Carnegie Inst. Wash. Publ., 195. 54 pp. 3 pl.
72. The nature of size factors as indicated by a study of correlation. Carnegie Inst. Wash. Publ., 196:51-55.
73. Size inheritance and the pure line theory. Z. Induktive Abstammungs-Vererbungslehre, 12:225-37.
74. Variation and selection: a reply. Z. Induktive Abstammungs-Vererbungslehre, 12:257-64.

1915

75. With P. B. Hadley. The English rabbit and the question of Mendelian unit-character constancy. Proc. Nat. Acad. Sci., 1:39-42; also in Am. Naturalist, 49:22-27.

76. Mr. Muller on the constancy of Mendelian factors. Am. Naturalist, 49:37.
77. With H. D. Fish. The black-and-tan rabbit and the significance of multiple allelomorphs. Am. Naturalist, 49:88-96.
78. Selection, sugar beets and thrips. Am. Naturalist, 49:121-22.
79. Bateson's address: Mendelism and mutation. Science, 41: 94-98.
80. Review of *Heredity and Environment,* by E. G. Conklin. Science, 42: 162-63.
81. With S. Wright. Two color mutations of rats which show partial coupling. Science, 42: 193-95.
82. Review of *Feeble-mindedness: Its Causes and Consequences,* by H. H. Goddard. J. Abnormal Psychol., Aug.-Sept., pp. 3-7.
83. Some experiments in mass selection. Am. Naturalist, 49: 713-26.

1916

84. Is selection or mutation the more important agency in evolution? Sci. Monthly, 2:91-98.
85. Variability under inbreeding and cross-breeding. Am. Naturalist, 50:178-83.
86. Can selection cause genetic change? Am. Naturalist, 50:248-56.
87. An expedition to the home of the guinea-pig and some breeding experiments with material there obtained. Carnegie Inst. Wash. Publ., 241:1-58.
88. Further studies of piebald rats and selection, with observations on gametic coupling. Carnegie Inst. Wash. Publ., 241:163-87.
89. Size inheritance in guinea-pig crosses. Proc. Nat. Acad. Sci., 2:252-64.
90. New light on blending and Mendelian inheritance. Am. Naturalist, 50:321-34.
91. Tables of linkage intensities. Am. Naturalist, 50:575-76.
92. *Genetics and Eugenics.* Cambridge, Mass., Harvard University Press. 346 pp.

1917

93. Piebald rats and multiple factors. Am. Naturalist, 51:102-14.
94. The role of selection in evolution. J. Wash. Acad. Sci., 7:369-87.

1919

95. Is the arrangement of the genes in the chromosome linear? Proc. Nat. Acad. Sci., 5:25-32.
96. The linkage system of eight sex-linked characters of *Drosophila virilis* (data of Metz). Proc. Nat. Acad. Sci., 5:32-36.
97. Piebald rats and the theory of genes. Proc. Nat. Acad. Sci., 5:126-30.
98. Are genes linear or non-linear in arrangement? Proc. Nat. Acad. Sci., 5:500-6.
99. Inheritance of quantity and quality of milk production in dairy cattle. Proc. Nat. Acad. Sci., 5:428-34.
100. Siamese, an albinistic color variation in cats. Am. Naturalist, 53:265-68.
101. Piebald rats and selection, a correction. Am. Naturalist, 53:370-75.
102. Does evolution occur exclusively by loss of genetic factors? Am. Naturalist, 53:555-58.
103. Studies of heredity in rabbits, rats, and mice. Carnegie Inst. Wash. Publ., 288. 56 pp. 3 pl.

1920

104. Linked genes in rabbits. Science, 52:156-57.
105. Genetics of the Dutch rabbit—a reply. J. Genet., 10:293-99.
106. The measurement of linkage. Am. Naturalist, 54:264-67.
107. Review of *Orthogenetic Evolution in Pigeons,* by C. O. Whitman. Am. Naturalist, 54:188-92.
108. Model of the linkage system of eleven second chromosome genes of Drosophila. Proc. Nat. Acad. Sci., 6:73-77.
109. *Genetics and Eugenics.* 2d revised ed. Cambridge, Mass., Harvard University Press. 390 pp.

1921

110. A new type of inheritance. Science, 53:339-42.
111. Genetics of the Chinchilla rabbit. Science, 53:387-88.
112. With W. C. Wachter. Genetics of Hereford cattle. J. Heredity, 12:36-39.
113. On a method of estimating the number of genetic factors concerned in cases of blending inheritance. Science, 54:93-96.
114. An improved method of estimating the number of genetic factors concerned in cases of blending inheritance. Science, 54:333.
115. More linked genes in rabbits. Science, 54:634-36.

1922

116. Genetics of the Vienna white rabbit. Science, 55:269-70.
117. Genetics of the Vienna white rabbit. II. Science, 55:429-30.
118. Genetic studies of rabbits and rats. Carnegie Inst. Wash. Publ., 320. 55 pp. 2 pl.
119. The y-chromosome type of sex-linked inheritance in man. Science, 55:703.

1923

120. Further data on webbed toes (in man). J. Heredity, 14:209-10.
121. The relation of Mendelism to mutation and evolution. Am. Naturalist, 57:559-61.

1924

122. The genetics of multi-nippled sheep, an analysis of the sheep-breeding experiments of Dr. and Mrs. A. G. Bell at Beinn Bhreagh, N. S. J. Heredity, 15:75-85.
123. Some varieties of white rabbits. J. Heredity, 15:211-19.
124. Biological and social consequences of race crossing. J. Heredity, 15:363-69.
125. Does the inheritance of differences in general size depend upon general or special size factors? Proc. Nat. Acad. Sci., 10:19-22.
126. Genetics of the Japanese rabbit. J. Genet., 14:225-29.

127. Linkage of Dutch, English, and Angora in rabbits. Proc. Nat. Acad. Sci., 10:107-8.
128. The Japanese rabbit and gametic purity. Proc. Nat. Acad. Sci., 10:222-24.
129. On the occurrence in rabbits of linkage in inheritance between albinism and brown pigmentation. Proc. Nat. Acad. Sci., 10:486-88.
130. With W. L. Wachter. Variations of linkage in rats and mice. Genetics, 9:1-12.
131. *Genetics and Eugenics.* 3d revised ed. Cambridge, Mass., Harvard University Press. 434 pp.

1925

132. The hare-rabbit, a study in evolution by hybridization. Am. Naturalist, 59:280-82.
133. Heredity in rabbits and guinea-pigs. Bibliographia Genet., 1:419-56.
134. Heredity: the general problem and historical setting. In: *Our Present Knowledge of Heredity,* pp. 17-38. Philadelphia, Pa., W. B. Saunders Co.

1926

135. Reviews of some new books on genetics. Science, 64:18-20.
136. Eugenics. In: *Encyclopaedia Britannica.* Suppl. Vol. I.
137. Studies of color inheritance and of linkage in rabbits. Carnegie Inst. Wash. Publ., 337:1-47. 8 pl.
138. Biological and social consequences of race-crossing. Am. J. Phys. Anthropol., 9:145-56.
139. The explanation of hybrid vigor. Proc. Nat. Acad. Sci., 12:16-19.
140. On the pattern of the Dutch rabbit, a discussion of the results of Punnett and Pease. J. Genet., 16:189-96.
141. A sex difference in linkage in rats and mice. Genetics, 10:580-82.

1928

142. The fate of unborn rabbit embryos. Am. J. Anat., 42:399-401.

143. With G. Pincus. Hooded rats and selection, a study of the limitations of the pure-line theory. J. Exp. Zool., 50:409-39.

144. Genetics. In: *Nelson's Looseleaf Encyclopedia,* Vol. V.

1929

145. A mosaic (intense-dilute) coat pattern in the rabbit. J. Exp. Zool., 52:471-80.

146. The rex rabbit. J. Heredity, 20:192-99.

147. Linkage studies on Castorrex rabbits. Z. Induktive Abstammungs-Vererbungslehre, 52:53-60.

148. A further study of size inheritance in rabbits with special reference to the existence of genes for size characters. J. Exp. Zool., 53:421-54.

149. With P. W. Gregory. The embryological basis of size inheritance in the rabbit. J. Morphol. Physiol., 48:81-93.

150. Review of *Scientific Papers of William Bateson,* ed. by R. C. Punnett. Science, 69:428-31.

1930

151. Race mixture and physical disharmonies. Science, 71:603-6.

152. The significance of sexuality. Am. Naturalist, 64: 481-94.

153. The quantitative theory of sex and the genetic character of haploid males. Proc. Nat. Acad. Sci., 16:783-91.

154. *Genetics and Eugenics.* 4th revised ed. Cambridge, Mass., Harvard University Press. 474 pp.

155. *The Genetics of Domestic Rabbits.* Cambridge, Mass., Harvard University Press. 31 pp. 39 figs.

1931

156. With P. W. Gregory. Further studies on the embryological basis of size inheritance in the rabbit. J. Exp. Zool., 59:199-210.

157. With P. W. Gregory. The effects of breed on growth of the embryo in fowls and rabbits. Science, 73:680-81.

158. Size inheritance in rabbits: the backcross to the large parent race. J. Exp. Zool., 60:325-38.

1932

159. Body size and body proportions in relation to growth rates and natural selection. Science, 76: 259-60.
160. Green's studies of linkage in size inheritance. Am. Naturalist, 66:82-87.
161. English and Dutch spotting and the genetics of the Hotot rabbit. Carnegie Inst. Wash. Publ., 427:3-13; 6 pl.
162. Growth rates and the racial size in rabbits and birds. Science, 76:365-66.
163. Three views of evolution. J. Heredity 23:405-6.

1933

164. With C. E. Keeler. Blood group inheritance in the rabbit. Proc. Nat. Acad. Sci., 19:93-98.
165. With C. E. Keeler. Tests for linkage between the blood-group genes and other known genes of the rabbit. Proc. Nat. Acad. Sci., 19:98-100.
166. The furless rabbit. J. Heredity, 24:81-86.
167. With C. E. Keeler. A further study of blood groups of the rabbit. Proc. Nat. Acad. Sci., 19:403-11.
168. Dice on geographic variation in Peromyscus. Am. Naturalist, 67:267-78.
169. The incompleteness of our knowledge of heredity in mammals. Journal of Mammalogy, 14:183-88.
170. The linkage relations of yellow fat in rabbits. Proc. Nat. Acad. Sci., 19:947-50.
171. With H. Nachtsheim. Linkage interrelations of three genes for rex (short) coat in the rabbit. Proc. Nat. Acad. Sci., 19:1006-11.
172. The gene theory in relation to blending inheritance. Proc. Nat. Acad. Sci., 19:1011-15.

1934

173. Possible cytoplasmic as well as chromosomal control of sex in haploid males. Proc. Nat. Acad. Sci., 20:101-2.
174. Size inheritance in rabbits: further data on the back-cross to the small race. J. Exp. Zool., 67:105-14.

175. With C. E. Keeler. Blood group incompatibility in rabbit embryos and in man. Proc. Nat. Acad. Sci., 20:273-76.
176. Review of *Vererbungslehre,* by L. Plate. J. Heredity, 25:65-67.
177. With C. E. Keeler. The influence of pregnancy upon the titre of immune (blood-group) antibodies in the rabbit. Proc. Nat. Acad. Sci., 20:465-70.
178. Genetics of the Dutch coat pattern in rabbits. J. Exp. Zool., 68:377-91.
179. Charles Darwin's Diary—a review. J. Heredity, 25:440-44.
180. Body size of reciprocal hybrids in rabbit crosses. Proc. Nat. Acad. Sci., 20:621-25.

1935

181. With H. D. King. Linkage studies of the rat (*Rattus norvegicus*). Proc. Nat. Acad. Sci., 21:390-99.

1936

182. Further data on linkage in rabbits. Proc. Nat. Acad. Sci., 22:222-25.
183. With L. W. Law. Satin, a new hair mutation of the rabbit. J. Heredity, 27:235-40.
184. Size inheritance in mice. Am. Naturalist, 70:209-17.
185. With W. H. Gates and S. C. Reed. Studies of a size cross in mice. Genetics, 21:66-78.
186. With S. C. Reed. Studies of inheritance in lop-eared rabbits. Genetics, 21:297-309.
187. With W. H. Gates, S. C. Reed, and L. W. Law. Studies of a size cross in mice. II. Genetics, 21:310-23.
188. Superior influence of the mother on body size in reciprocal hybrids. Science, 84:627.
189. With W. H. Gates, S. C. Reed, and G. D. Snell. Identical twins in a mouse cross. Science, 84:581-82.
190. A simplified explanation of Bellamy's experiments concerning sex determination in tropical fishes. Proc. Nat. Acad. Sci., 22:679-82.

1937

191. With H. D. King. Linkage studies of the rat (*Rattus norvegicus*) II. Proc. Nat. Acad. Sci., 23:56-60.

1938

192. The relation of albinism to body size in mice. Genetics, 23: 269-74.
193. Sex and genes. Sci. Monthly, 46:344-50.

1939

194. On a method for testing for linkage between lethal genes. Proc. Nat. Acad. Sci., 25:593-94.

1940

194a. With H. D. King. Linkage studies of the rat (*Rattus norvegicus*) III. Proc. Nat. Acad. Sci., 26:578-80.
195. *Mammalian Genetics.* Cambridge, Mass., Harvard University Press. 169 pp., illus.
196. *Manual for a Laboratory Course in Genetics.* 20 pp., with tables of probable error after R. A. Emerson. Cambridge, Mass., Harvard University Press.
197. The genetics of coat color in horses. J. Heredity, 31:127-28.
198. Genetics of horns in sheep. J. Heredity, 31:486-87.

1941

199. Influence of certain color mutations on body size in mice, rats and rabbits. Genetics, 26:177-91.
200. With H. D. King and Amy L. Daniels. Linkage studies of the rat (*Rattus norvegicus*) IV. Proc. Nat. Acad. Sci., 27: 250-54.
201. With H. D. King. Linkage studies of the rat (*Rattus norvegicus*) V. Proc. Nat. Acad. Sci., 27:394-98.
202. Size inheritance. Am. Naturalist, 75:488-98.
203. With P. B. Sawin. Genetic linkage in the rabbit. Proc. Nat. Acad. Sci., 27:519-23.

1942

204. Genetics of the Palomino horse. The Western Horseman, July-Aug., pp. 12-13.

205. Size genes of mice. Proc. Nat. Acad. Sci., 28:69-72.
206. Calendar reform and the National Academy of Sciences. Science, 95:195.

1943

207. Calendars and calendar reform. Sci. Monthly, 56:163-68.

1944

208. With H. D. King. Linkage studies of the rat (*Rattus norvegicus*) VI. Proc. Nat. Acad. Sci., 30:79-82.
209. Linkage of waltzing in the rat. Proc. Nat. Acad. Sci., 30: 226.

1945

210. Dr. Osborn's experiments with mink mutations. American Fur Breeder, 17(9):18.

1946

211. Genes which divide species or produce hybrid vigor. Proc. Nat. Acad. Sci., 32:145-49.
212. Genetics of the Palomino horse. J. Heredity, 37:35-38.
213. With Larry Moore. Mutations of mink under domestication. J. Heredity, 37:137-45.
214. Mutation mink varieties, a correction. J. Heredity, 37:215.
215. Linkage in the albino chromosome of the rat. Proc. Nat. Acad. Sci., 32:33-36.

1947

216. With F. L. King. The albino in Palomino breeding. The Western Horseman, 12(6):24-25, 68.
217. The domestication of the rat. Proc. Nat. Acad. Sci., 33: 109-17.
218. With Helen D. King. Linkage studies of the rat. VII. Shaggy, a new dominant gene. J. Heredity, 38:341-43.
219. With Helen D. King. Linkage studies of the rat. VIII. Fawn, a new color dilution gene. J. Heredity, 38:343-44.

1948

220. The ABC of color inheritance in horses. Genetics, 33:22-35.

220a. (Revised and simplified version also in The Cattleman, Sept.)
221. With Helen D. King. Linkage studies of the rat. IX. Cataract. Proc. Nat. Acad. Sci., 34:135-36.

1949

222. With Helen D. King. Linkage studies of the rat. X. 1. Fawn linked with agouti in linkage Group V. 2. Further evidence of linkage between red-eyed yellow and waltzing. Proc. Nat. Acad. Sci. 35:545-46.

1950

223. Albinism is indispensable in Palomino breeding. The Western Horseman, 15(12):30.
224. Are mosaic genes semi-allelic? Am. Naturalist, 84:497-98.

1951

225. Dominant and recessive black in mammals. J. Heredity, 42:48-49.
226. With F. L. King. New evidence on the genetics of the Palomino horse. J. Heredity, 42:61-64.
227. Variation in the hooded pattern of rats, and a new allele of hooded. Genetics, 36:254-66.
228. The beginnings of Mendelism in America. In: L. C. Dunn (ed.), *Genetics in the 20th Century,* pp. 59-76. New York, Macmillan.
229. Winge on inheritance in dogs (a review). J. Heredity, 42: 297-98.
230. Simplified mink genetics (a review of Shackelford's *Genetics of the Ranch Mink).* J. Heredity, 42:189-90.
231. Genetics of the color varieties of horses. J. Heredity, 42: 297-98.

1952

232. Genetic linkage in the common rat. Virginia Journal of Science, 3:95-100.

1953

233. What to expect in chinchilla mutations. American Fur Breeder, 26(2):14.

234. Silver dapple, a unique color variety among Shetland ponies. J. Heredity, 44:139-45.
235. Silver, a new mutation of the rat. J. Heredity, 44:205-6.
236. The "why" of sorrel and silver dapple colors in Shetland ponies. American Shetland Pony Journal, July, pp. 8-10.

1954

237. Coat color inheritance in horses and in other mammals. Genetics, 39:35-44.
238. The part of mammalian genetics in founding the Jackson Memorial Laboratory. J. Nat. Cancer Inst., 15:595-606.

1955

239. With Everett R. Dempster and Harriet C. Shurrager. Three new mutations of the rat. J. Heredity, 46:9-14.
240. Further studies of linkage in the third chromosome of the rat. J. Heredity, 46:84-86.

1957

241. Viewing Shetlands with a geneticist. American Shetland Pony Journal, Dec.

1958

242. Genetics of coat color in horses and ponies. American Shetland Pony Journal, Dec.

1960

243. With W. R. Singleton. Genetics of the "brown" horse. J. Heredity, 51:127-30.
244. Fashion in the color of Shetland ponies and its genetic basis. J. Heredity, 51:247-48.

1961

245. Genetics of the claybank dun horse. J. Heredity, 52:121, 128.
246. With W. R. Singleton. The Palomino horse. Genetics, 46: 1143-50.