Perspectives

Anecdotal, Historical and Critical Commentaries on Genetics

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Harvard, Agriculture, and the Bussey Institution

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The genes are units useful in concise descriptions of the phenomena of heredity. Their place of residence is the chromosomes. Their behavior brings about the observed facts of genetics. For the rest, what we know about them is merely an interpretation of crossover frequency. In terms of geometry, chemistry, physics, or mechanics we can give them no description whatever. E. M. EAST (1926)

GENETICS had its first influence in agriculture and first achieved independent status in agricultural colleges. The main training ground was the Bussey Institution of Harvard University.

By his will of 1835, BENJAMIN BUSSEY left his extensive farm (now the Arnold Arboretum) to Harvard to be held forever as a Seminary for "instruction in practical agriculture, in useful and ornamental gardening, in botany, and in such other branches of natural science, as may tend to promote a knowledge of practical agriculture, and the various arts subservient thereto and connected therewith." The government of the University is also "to cause courses of lectures to be delivered there . . . and also to furnish gratuitous aid . . . to such meritorious persons as may resort there for instruction."

The bequest did not become available until 1861, and the school did not open until 1871, following the construction of a suitable building. The initial appointments included, as instructor of farming, BUSSEY's grandson-in-law, THOMAS MOTLEY, who came with the farm; FRANCIS STORER, brother-in-law of Harvard's President ELIOT, as professor of agricultural chemistry and dean; and FRANCIS PARKMAN, the famous historian, as professor of horticulture.

The resources for the school were seriously depleted when a number of Bussey estate rental properties were destroyed in the Great Boston Fire of November 9–10, 1872. The meager income was augmented by growing vegetables, cutting firewood, and boarding horses. The school never did come up to Harvard undergraduate standards, which were not all that high, at best.

From a movement led by the physicist WALLACE SABINE, a Graduate School of Applied Science was organized in 1906 to replace the undergraduate Lawrence Scientific School. As part of the reorganization in 1908, "Bussey" became a graduate school for advanced instruction and research in scientific problems that relate and contribute to practical agriculture and horticulture—this just at the time when the claims of genetics could no longer be ignored. In recommending to President ELIOT that W. E. CASTLE's work be transferred from Cambridge to the Bussey Institution, Dean SABINE wrote, "The University has Professor Castle to start with; to lose him will be to lose the best man in the country in genetics." So instead of going to Wisconsin or Yale, CASTLE moved his animals to Forest Hills, soon to be joined by the noted plant geneticist EDWARD MURRAY EAST from the Connecticut Agricultural Experiment Station. CASTLE and EAST have been the subjects of recent *Perspectives* (SNELL and REED 1993; NELSON 1993); see also the biographies by WRIGHT (1963) and JONES (1944).

WILLIAM MORTON WHEELER, an erudite scholar who rated artistry in taxonomy above all his other powers, left Texas in 1908 to join the Bussey as Professor of Economic Entomology. He was appointed dean in 1915 when the Bussey was separated from the other schools of applied sciences, but in 1929 he resigned in favor of the more congenial atmosphere of the Museum of Comparative Zoology. IRVING W. BAILEY, who came to the Bussey from the defunct School of Forestry, acted as secretary. Between 1912 and 1939, 44 doctorates in genetics were awarded.

Animal genetics had its roots in liberal arts, not agriculture, with Johns Hopkins University as the early leader. E. B. WILSON, the cytologist (Ph.D. 1881), T. H. MORGAN (Ph.D. 1890), E. G. CONKLIN (Ph.D. 1891), and R. G. HARRISON (Ph.D. 1894), ostensibly students of the morphologist W. K. BROOKS, came under the influence of the physiologist H. NEWELL MARTIN and, except for CONKLIN, furthered their studies in Europe. (MORGAN, who retained his interest in embryology, was the only one to become a member of the Genetics Society of America.)

At Harvard, C. B. DAVENPORT (Ph.D. 1892) and W. E. CASTLE (Ph.D. 1895) were students of EDWARD L. MARK, whose doctorate in 1876 from the University of Leipzig was under RUDOLPH LEUCKART, an early proponent of the need to combine morphology and physiology. Their theses, based on morphological studies, were published in the *Bulletin of the Museum of Comparative Zoology*. Both DAVENPORT and CASTLE had farm backgrounds and later worked with laboratory and farm animals. DAVENPORT, with a B.S. degree in civil engineering, brought quantitative methods to biology but turned his attention to eugenics and administration. CASTLE, who assisted DAVENPORT as a student and succeeded him at Harvard when DAVENPORT departed in 1899, had little interest in eugenics and none in administration, but they remained close friends, and DAVENPORT, through control of Carnegie funds, provided assistance to CASTLE at the Bussey. Both men were interested in heredity even before 1900, so their grasp of Mendelism, after its rediscovery in 1900, was not immediate because they carried a considerable baggage of seemingly conflicting evidence.

After the rediscovery of MENDEL's laws, there ensued lively debate about the extent to which the laws applied to animals, including man. Naturally it was the conspicuous characters that attracted attention at first, but, as the inheritance of more and more characters was shown to behave according to simple Mendelism or one of its easily understood modifications, attention shifted to the materials in their own right—on one hand, as sources for new problems; on the other, as a new approach to the solution of old problems, such as the limits of selection or the consequences of inbreeding.

From 1901 to 1905, CASTLE, with the cooperation of four students in successive years, followed the effects of inbreeding in *Drosophila melanogaster* through 59 generations of brother-sister mating. After the move to the Bussey, no one used *Drosophila* for thesis research, but it became the favorite material for Harvard undergraduate teaching in Cambridge, so the graduate students were familiar with its usefulness. They kept abreast of developments and some, notably E. C. MACDOWELL, L. C. DUNN, and S. C. REED, later used *Drosophila* for research.

Although he emphasized the importance of laboratory animals in the study of inheritance, CASTLE retained an interest in farm animals. Between 1940 and 1961 (after retiring to Berkeley) he published 17 papers on coat colors in horses, and while at the Bussey he published on inheritance in sheep and dairy cattle and on various aspects of animal breeding.

After graduation, a number of CASTLE's students and two of EAST's worked with economic animals. JOHN DETLEFSEN worked with rats, mice, and cattle at Illinois. SEWALL WRIGHT went to the Bureau of Animal Industry, while L. C. DUNN went to the Connecticut Agricultural Experiment Station at Storrs, where he worked with poultry. TAGE ELLINGER from Denmark became a plant

breeder, whereas H. C. MCPHEE (EAST's student) became Chief of the Animal Husbandry Division of the U.S. Bureau of Animal Industry. P. W. GREGORY went to Davis, where he investigated the genetics of cattle, including size inheritance, and also worked with rats. EDWARD LIVESAY became professor of animal husbandry at West Virginia. NELSON WATERS went on to a career in poultry research. Four of CASTLE's 23 doctoral candidates spent their entire careers after graduation working with economic species; four others were so engaged over a period of years. EAST's student, W. R. SINGLETON, studied coat color inheritance in horses in collaboration with CASTLE. The first generation of geneticists were able to pursue problems in pure and/or applied research.

CASTLE's own favorite species was the rat. He had come to distrust the concept of gametic purity on finding that the Mendelizing guinea pig characters, polydactylism, long hair, and rough coat were not exactly the same when extracted from crosses. To test his hypothesis, he undertook a selection experiment with hooded rats and by 1914 had reared and studied the color pattern of over 25,000 rats. With great persistence he defended his hypothesis in the face of mounting criticism—some rather heated. EMERSON and EAST's classic paper on maize, showing that quantitative characters are inherited in Mendelian fashion, appeared in 1913, a year before the completion of CASTLE and PHILLIPS' monograph (1914). The concept was debated in Bussey seminars, with CASTLE and EAST holding opposing views. CASTLE was not convinced until he performed the critical experiments suggested by WRIGHT. His retraction appeared in the *American Naturalist* in 1919 (CASTLE 1919). In L. C. DUNN's words, "Castle cured himself of disbelief in the integrity of the gene the hard way—by 15 years of arduous experimentation."

It is noteworthy that both CASTLE and EAST considered it the function of the professor to provide space, materials, encouragement, and little else, with course work in diverse areas only sufficient to broaden the students' perspective. CASTLE's first graduate students, JOHN A. DETLEFSEN, who arrived in 1908 and worked with guinea pigs, and EDWIN CARLETON MACDOWELL, who arrived a year later and worked with rabbits, received their doctorates in 1912. They did not share CASTLE's skepticism concerning the multiple-factor theory, and MACDOWELL's thesis, published as a monograph (1914), carried a prefatory note by CASTLE: "While not entirely sharing his views, I have tried not to bias his judgment either for or against the multiple-factor hypothesis which he adopts in this paper. But to avoid misunderstanding, I wish to say that in my own opinion the theory of the purity of the gametes has not been established." CASTLE was aware that the top signer of the thesis is not the only or even the chief source of guidance. He himself had been influenced more by C. B. DAVENPORT than by his professor, E. L. MARK.

The only students to use rats exclusively for doctoral thesis research were H. W. FELDMAN on sterility and

fertility, GREGORY PINCUS on cytological studies, and LIVESAY on hybrid vigor, while DUNN and W. L. WACHTER worked on linkage in rats and mice. CLYDE KEELER's thesis was on rodless retina in mice, but he published 18 papers between 1940 and 1949 on rats. LAURENCE SNYDER published on the effects of X-rays on rats while at the Bussey, but his doctoral thesis was on blood groups in man, and he remained a human geneticist. With great persistence himself and tolerance on the part of others, CASTLE continued to collect and study mutants in the rat, even after moving to California in 1936.

Rabbits and guinea pigs were natural choices at the turn of the century because both species thrive under ordinary laboratory conditions. CASTLE assembled and studied a number of traits before the Bussey was reorganized, but about the only ones to stick mainly to one species were SEWALL WRIGHT with guinea pigs and PAUL SAWIN with rabbits. C. C. LITTLE, founder of The Jackson Laboratory, was the first graduate student to work with mice, but eventually most of CASTLE's students adopted the mouse, as did WRIGHT's. W. H. GATES' thesis was on the Japanese waltzing mouse, later shown by T. S. PAINTER to involve a chromosome deletion. In the 1930s, SHELDON REED worked on harelip, FRANK CLARK on hydrocephalics, siderocyte anemia and brachyury, SUMNER BURHOE on waved coat, and LLOYD LAW on size inheritance. It became increasingly evident that the mouse would serve as a model for human diseases. At Columbia University DUNN picked up work on the mouse where he had left off as a student (having published on black-and-tan in 1916, on yellow in 1919, and on sable and white spotting in 1920). He brought the much debated role of modifying genes to a satisfactory state by his thorough analysis of "sub-threshold alleles" that modify spotting. He early perceived that the *t*-complex was uniquely fitted for intensive study of gene action, while the discovery of *t* mutants in feral populations led to studies in population genetics and distorted segregation ratios.

Even though their attendance at the Bussey Institution was separated by 10 years, the careers of DUNN (S.D. 1920) and GEORGE D. SNELL (S.D. 1930) were strikingly similar. Both became interested in genetics under the influence of JOHN H. GEROULD at Dartmouth College; both had experience with mice before attending the Bussey, and their dissertations involved linkage in rodents; both later came to concentrate on a very small segment of a mouse chromosome, and in the process each developed stocks that are highly prized. In 1980, GEORGE SNELL, age 77, shared the Nobel Prize in Physiology or Medicine for his work on histocompatibility genes. Similarities between the HLA system in humans and the major histocompatibility complex in mice have reinforced the fundamental nature of SNELL's painstaking efforts over many years.

E. M. EAST was trained as a chemist, but as assistant to C. G. HOPKINS at Illinois he became interested in plant

breeding with emphasis on maize. (His doctoral research was on the potato.) In 1905 EAST joined the Connecticut Agricultural Experiment Station where he remained until the call to Harvard in 1909.

Relations between EAST and his student, R. A. EMERSON (S.D. 1913), were unusual in that EMERSON, 6 years older than EAST, was already an established investigator at the University of Nebraska. The two remained close friends and collaborators.

Although EMERSON was the first to earn the doctorate degree in plant genetics at the Bussey, he was not EAST's first graduate student. That distinction goes to H. K. HAYES, who joined the Connecticut Station as assistant to EAST on July 1, 1909. EAST had already accepted the offer from Harvard but remained at the Connecticut Station until the fall. With the Harvard master's degree in 1911, HAYES did not submit his doctoral thesis until 1921, using data on wheat and corn from the University of Minnesota, the institution he joined in 1915.

As successor to HAYES, DONALD JONES (S.D. 1918) was the sole geneticist at the Connecticut Station from 1915 until 1921, when PAUL MANGLES DORF came as his assistant. With materials left behind by EAST and HAYES, prior experience in practical horticulture, and friendly relations with EAST and E. H. JENKINS, JONES was in a particularly favorable position. With an undiminished passion for gardening and plant breeding, JONES became involved in theoretical genetics—the theory of heterosis, cytoplasmic male sterility, fertility-restoring genes, somatic segregation, and sex differentiation—but he is best known as the inventor of the double-cross method of corn breeding and as co-author with EAST of *Inbreeding and Outbreeding* (EAST and JONES 1919). For further information on EAST, EMERSON, and JONES, see NELSON (1993).

Before mechanization, the horse was the unit of power, animal husbandry was in the driver's seat, and vocational subjects prevailed. Consequently, even though he majored in chemistry and physics, R. A. BRINK's degree from the Ontario Agricultural College was not accepted by Cornell University. So he went to Illinois, where he became a botanist, obtained a master's degree, and was recommended to the Bussey by DETLEFSEN.

At the time, EAST's experimental work was confined almost exclusively to studies on self sterility in tobacco. J. B. PARK (S.D. 1916), and EDGAR ANDERSON (S.D. 1922) before BRINK and E. R. SEARS (S.D. 1936) after, worked on different aspects of the problem. BRINK's assignment was the physiology of pollen. That the matching of problem and student was not a perfunctory matter is evident from EAST to SEARS (June 14, 1937): "I am sorry that, with the amount of work you have gone through, there are so many negative results . . . You begin to see how difficult it is to set out problems for graduate students where the problem is worth while and results can be more or less guaranteed inside of three years." The thesis problem was by no means an end in itself, and most

Bussey students pursued quite different lines of research in later life. BRINK's distinguished career at Wisconsin, with contributions to plant breeding and theoretical genetics, is described by OWEN and NELSON (1986).

KARL SAX (S.D. 1922) and PAUL MANGLES DORF (S.D. 1925) channeled their research to conform to Harvard directions. On appointment in 1928 as Associate Professor of Plant Cytology at the Arnold Arboretum, SAX abandoned work with wheat, dividing his efforts between horticulture and comparative chromosomal studies. Later he turned his attention to radiation cytology, a line followed by a number of his graduate students. In 1940, when MANGLES DORF returned to Harvard, he made the transition from practical breeding to study of the ancestry of corn, an interest he acquired at Texas A and M.

RALPH SINGLETON (S.D. 1936), like SAX, received his B.Sc. and M.Sc. from Washington State College and was steered to the Bussey by E. F. GAINES. His doctoral thesis was on tetraploid hybrids in tobacco. As senior geneticist (1948–1955) at the Brookhaven National Laboratory, he studied induced mutations in growing plants laid out in concentric circles around a central cobalt-60 source.

E. R. SEARS and HAROLD SMITH (Ph.D. 1936) were among the last of the Bussey students. (J. D. BEASLEY's Ph.D. was awarded in 1939.) SMITH ended up as Professor of Plant Genetics at Cornell, while SEARS spent his entire career after graduation at the University of Missouri. Picking up where SAX left off, SEARS launched a research program in wheat cytogenetics that remained at the cutting edge throughout his lifetime. He developed the complete series of wheat aneuploids, nullisomic through tetrasomic, for all 21 chromosomes. Also, combining a number of techniques, including X-irradiation, he was able to transfer disease resistance to wheat from a wild relative.

EDGAR ANDERSON's career was unlike that of any other Bussey graduate student. Shy, precocious, introspective, independent, disliked by Bussey classmates, but a favorite of EAST's—whom he admired but with reservations—ANDERSON was fitted to break new ground in a field eschewed by other students from agricultural colleges. Since the secrets of inheritance had come from artificially cultivated forms, it is not surprising that geneticists were unsympathetic to the methodologies of taxonomy. ANDERSON used genetics as a tool rather than an end in itself and was primarily a naturalist. Of graduate school he said, "My thesis [the genetic behavior of cross sterility in *Nicotiana*] was not particularly interesting; the topic was largely a question of what was available. I don't think it did me any harm and it did give me an insight into a certain field" (ROE 1952, p. 98). After graduation, ANDERSON spent his entire professional career attached to the Missouri Botanical Garden in St. Louis (1922–1931 and 1935 on) and the Arnold Arboretum (1931–1935).

Staking out for himself the much neglected classification of weeds and cultivated plants, ANDERSON made contributions to methodology, theory, and teaching methods. Impressed by the rarity of hybrids under natural conditions in contrast to the survival of hybrid swarms in "hybridized habitats," he emphasized the role of introgressive hybridization in plant evolution. His closest friend, G. L. STEBBINS, with similar interests, was never connected directly with the Bussey, although KARL SAX was on his thesis committee.

At the Sixth International Congress of Genetics held in Ithaca, New York, in 1932, there were 399 participants from the United States, including CASTLE, EAST, and 32 of their students (Figure 1). T. H. MORGAN, from Cal Tech, was president of the Congress, but former Bussey student C. C. LITTLE was chairman and general secretary, L. C. DUNN was secretary of the council, E. M. EAST was chairman of the program committee, and D. F. JONES was chairman of the publications committee. Because the conference was held at Cornell, with R. A. EMERSON as chairman of the local committee, the selection of Bussey men is not surprising, but it is significant that this carried over to the organization of the Genetics Society of America later in the same year.

Up through 1931 genetics was affiliated with the American Society of Zoologists and the Botanical Society of America. Because a number of geneticists were members of neither Society, it was decided in 1931 to reorganize the Joint Genetics Sections as an independent society. A cordial invitation was tendered to "geneticists interested in agriculture" to apply for membership. R. A. BRINK was chosen to organize symposia of interest to agriculturists, but "Geneticists Interested in Agriculture" was discontinued as a separate group. The first seven presidents of the Society had Bussey connections:

Year	President	Location
1932	L. C. DUNN	Columbia University
1933	R. A. EMERSON	Cornell University
1934	SEWALL WRIGHT	University of Chicago
1935	D. F. JONES	Connecticut Agricultural Experiment Station
1936	P. W. WHITING	University of Pennsylvania
1937	E. M. EAST	Harvard University
1938	L. J. STADLER	University of Missouri

(WHITING was a research worker at the Bussey in 1927, STADLER in 1925–1926.)

At the Seventh International Congress held in London, Cambridge, and Edinburgh in 1939, the Bussey was again well represented. In addition to nine holders of the Bussey doctorate, the program included presentations by 12 Bussey visiting scientists, most of whom had spent 1 or 2 years there.

To declare financial exigency as the reason for closing an institution is like saying the candidate lost because he didn't get enough votes. The tide in the affairs of men began in earnest in 1924, the year that Harvard failed to

FIGURE 1.—A group picture of attendees at the 1932 International Congress of Genetics at Cornell University who had been associated with the Bussey Institute. Its influence is apparent. *Front row:* KARL SAX, L. C. DUNN, P. W. WHITING, C. C. LITTLE, O. E. WHITE, Mrs. W. E. CASTLE, Mrs. KARL SAX, E. M. EAST, N. F. WATERS, F. H. CLARK, D. W. DAVIS, R. A. EMERSON. *Second row:* G. G. PINCUS, E. C. MACDOWELL, R. B. GOLDSCHMIDT, W. E. CASTLE, H. W. FELDMAN, L. H. SNYDER, H. C. MCPHEE, G. L. SLATE, E. F. GAINES, R. A. BRINK, E. N. WENTWORTH. *Third row:* A. MARSHAK, J. BEN HILL, HAIG DERMEN, L. J. STADLER, P. C. MANGELSDORF, S. C. REED, EDGAR ANDERSON, J. B. PARK, G. D. SNELL, J. I. KENDALL, D. F. JONES. *Back row:* M. R. IRWIN, W. R. SINGLETON, S. H. YARNELL, H. P. RILEY, T. W. WHITAKER, L. C. STRONG, WILLIAM GATES, P. W. GREGORY, C. R. BURNHAM, P. B. SAWIN, R. C. ROBB.

respond to the Rockefeller Foundation's willingness to invest up to \$20,000,000 as an endowment for a broadly conceived program of fundamental biological research. Although the Bussey lingered on until 1936, the final paroxysm occurred in September 1929 when, by a vote of 10 to 9, the Board of Overseers turned down the Harvard Corporation's decision to appoint RAYMOND PEARL as dean of the Bussey Institution.

Joining the University of California in 1936 as research associate in mammalian genetics, CASTLE became the first recipient of the Kimber Genetics Award of the National Academy of Sciences in 1955 and continued to work almost up to his death in 1962.

On April 20, 1937, WILLIAM MORTON WHEELER collapsed on the Harvard Square subway and died within a few minutes. On November 8, 1938, RALPH W. WETMORE spent the evening with EAST in the hospital where EAST's operation was scheduled for the following morning. Recalling events of his career in genetics and grasping WETMORE's hand in both of his, EAST said, "Tomorrow it will be all over." It was.

LITERATURE CITED

- CASTLE, W. E., 1919 Piebald rats and selection, a correction. *Am. Nat.* **53**: 370-375.
- CASTLE, W. E., and J. C. PHILLIPS, 1914 Piebald rats and selection. Publication No. 195, Paper No. 21. Carnegie Institution of Washington, Washington, D.C.
- EAST, E. M., 1926 The concept of the gene. *Proc. Int. Congr. Plant Sci.* **1**: 889-895.
- EAST, E. M., and D. F. JONES, 1919 *Inbreeding and Outbreeding*. J. B. Lippincott, Philadelphia.
- EMERSON, R. A., and E. M. EAST, 1913 The inheritance of quantitative characters in maize. *Bull. Nebraska Agric. Exp. Sta.* **2**: 1-120.
- JONES, D. F., 1944 Edward Murray East (1879-1938). *Biogr. Mem. Natl. Acad. Sci.* **23**: 217-242.
- MACDOWELL, E. C., 1914 Size inheritance in rabbits. Publication No. 195, Paper No. 22. Carnegie Institution of Washington, Washington, D.C.
- NELSON, O. E., 1993 A notable triumvirate of maize geneticists. *Genetics* **135**: 937-941.
- OWEN, R. D., and O. E. NELSON, 1986 ROYAL ALEXANDER BRINK, 1897-1984. *Genetics* **112**: 1-10.
- ROE, A., 1952 *The Making of a Scientist*. Dodd, Mead & Co., New York.
- SNELL, G. D., and S. REED, 1993 WILLIAM ERNEST CASTLE, pioneer mammalian geneticist. *Genetics* **133**: 751-753.
- WRIGHT, S., 1963 WILLIAM ERNEST CASTLE, 1867-1962. *Genetics* **48**: 1-5.