SPECIAL ARTICLES

A LETHAL MUTATION IN THE RABBIT WITH STIGMATA OF AN ACROMEGALIC DISORDER

A DWARF mutation in the rabbit was described in a previous paper.[1] In that instance the symptom-complex of affected animals suggested a diminished function of the growth-promoting hormone of the pituitary combined with basophilic over-activity and secondary disturbances of other endocrine glands. A contrasting abnormality of hereditary origin has also been found in the rabbit. When this affection was first seen, it was studied as a condition probably arising from a disturbance of thyroid function, and therapeutic tests, which were inconclusive, seemed to lend some support to this assumption. But it was later pointed out to us by Dr. H. M. Evans that the distinctive feature of the condition corresponded closely with the cutaneous overgrowth which Stockard[2] first recognized as a characteristic manifestation of acromegalic disorders.

This peculiar abnormality appeared several years ago in some hybrid stock derived from an inbred line of Dutch rabbits. It was traced back to a Dutch female, and unsuccessful attempts were made to fix the character for further study. Animals presenting the abnormality in typical form were comparatively rare, and these died at an early age. The few hybrids seen were more vigorous than the pure Dutch stock, and it was assumed that in the inbred line individuals of this class were probably lost before characteristic symptoms of the condition developed. Eventually, however, a small male presenting mild but typical symptoms of the abnormality was reared by the use of a foster mother, and breeding experiments were undertaken.

The distinctive features of the abnormality usually develop toward the end of the first or second week of life. A faint redness with an edematous thickening of the skin appears over the nape of the neck, between the shoulders, at the base of the skull, behind the ears or under the chin. This spreads to the whole ventral surface of the body and is particularly noticeable about the genital and anal regions. The condition increases rapidly. In typical cases, the skin of the entire body is thrown into loose, transverse folds. It is at first reddened, thickened and edematous with a glistening surface. Subsequently, the surface of the skin becomes covered with fine white scales and then with thicker crusts, while the skin itself becomes stiff and indurated. The hair is at first normal, but its growth is disturbed and it becomes coarse, sparse and stubby. As a rule, the growth of affected animals is at first rapid, but virtually ceases within a few days after the development of typical symptoms, and the disease progresses to a lethal termination in the course of a week or ten days. Mild and atypical, or "fugitive," cases of this affection also occur, and some of these animals are viable, but few have survived to a breeding age. The chances of survival are increased when affected animals are transferred to a foster mother, and advanced cases may be arrested by this form of treatment.

This abnormality occurs in animals of all sizes (birth weights), but in most instances the animals presenting these symptoms are exceptionally large and well nourished at the time of onset, while the small and wizened appearance of others first suggested the idea of a cretinoid abnormality, and in the end all seriously affected animals present this appearance. The bones have not been studied in detail, but skeletal overgrowth does not occur in all animals; some are large, others are small, and there is additional evidence that cutaneous and skeletal changes are to some extent separable and that one may occur independent of the other.

Breeding experiments based largely on the small Dutch male mentioned above have shown that the F_1 progeny from unrelated females is essentially normal. So far, attempts to reproduce the character in an F_2 generation, from animals obtained in this manner, have been unsuccessful. Only a few F_1 males have been tested, but none of these has transmitted the character. Still when certain F_1 females are back crossed to their male parent, typical cases of abnormality appear, while others, on repeated tests, have produced only normal young. Matings between the male referred to and F_1 daughters derived from unrelated females and known to be transmitters have given 15 typically affected and 44 normal young, exclusive of a few cases of mild or atypical abnormality, which is a close approximation to a 3:1 ratio.

These tests show that the male in question is heterozygous, despite the fact that he exhibited typical symptoms of abnormality in early life. He was derived from a mating of parents both of which were proven transmitters and, so far, all known male transmitters have been obtained in this fashion. Results from the reciprocal cross are uncertain. Only one female presenting definite symptoms of abnormality has been raised to breeding age and, in this case, repeated matings proved to be infertile. This animal also came from pure Dutch stock and from parents

[1] H. S. N. Greene, C. K. Hu and W. H. Brown, SCIENCE, 79: 2056, 1934.

[2] C. R. Stockard, "The Physical Basis of Personality," W. W. Norton and Co., New York, 1931. Herbert M. Evans, *Jour. American Medical Association*, 101: 425, 1933.

both of which were heterozygous. In this connection, it is of interest to note that this female was also of the small or dwarf type and that the male under consideration has shown a variable fertility with periods of diminished secondary sex characters and complete sterility. It has been found, however, that matings between heterozygous females and normal males produce only normal young, as in the case of affected male × normal female. No homozygous animal of either sex has been encountered among those tested.

The condition described is unquestionably inherited, and it is evident that in the F_1 generation the character is completely recessive. On the other hand, it is known that in matings between heterozygous parents the abnormality may be expressed in heterozygous males as well as in homozygous individuals, and that the homozygous form is apparently lethal. Until this situation is cleared up, ratios of normal to affected individuals can not be interpreted with certainty.

The disease described appears to fit into the syndrome which, at present, is associated with over-activity of the growth-promoting hormone of the pituitary. The apparent disturbance of thyroid function in certain cases may likewise be attributed to a pituitary abnormality affecting the thyrotropic hormone. In this instance, however, there is some evidence of an appreciable degree of differentiation, or separation, of cutaneous and skeletal manifestations of functional disorder. But further experiments will be necessary to determine the etiology of the condition as well as the precise mode of its inheritance.

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THE MODE OF PENETRATION OF PEAR AND APPLE BLOSSOMS BY THE FIRE-BLIGHT PATHOGEN[1]

A STUDY of the mode of penetration of the fire-blight pathogen into pear and apple blossoms has revealed some facts which seemingly are significant from a point of view of possible control measures. Histological studies of both natural and artificial infections, which will be fully illustrated by photomicrographs and drawings in a later paper, reveal the following.

There is a well-defined cuticle covering the nectarial region of both pear and apple blossoms.[2]

The nectar, instead of exuding from naked cells, as commonly assumed, passes out through stoma-like openings, the openings seemingly being regulated by guard cells, as in true stomata. For these nectar-exuding structures the writer proposes, for convenience, the name "nectarthodes." They have previously been noted in nectarial regions of other blossoms by various authors.

In the nectarial region of pears and apples, the fire-blight pathogen gains entrance into the interior by means of these nectarthodes, though entrance through these is apparently not nearly as common on apple blossoms as on pear. The reason for this difference rests essentially in the narrow, elongated, tightly covered calyx cup, characteristic of apple blossoms during nectar flow, contrasted with the broad, open and shallow calyx cup, characteristic of pear blossoms.

In addition to penetration through nectarthodes, *Erwinia amylovora* has no difficulty penetrating the following: First, the stigmatic surfaces of both pear and apple gynoecia, the large glandular naked cells of these surfaces making penetration under suitable conditions a relatively simple matter. The manner of such penetration will be fully illustrated elsewhere. Second, the locules of the anthers, with a seeming passage into filaments. The passage from anther to filament has not been fully confirmed.

These common methods of penetration of pear and apple blossoms are additional to those which the writer and other investigators have previously reported, and which include penetration through stomata of calyx lobes and outer receptacle walls, as well as through petals.

If floral infections of apples depended entirely on nectarial penetration, what chance would there be of controlling blossom infection by depositing a germicidal spray with ordinary spray-equipment in such tightly covered plant parts?

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[1] Research Paper 352 Journal Series, University of Arkansas.

[2] Professor L. H. MacDaniels, of Cornell University, has confirmed and amplified the writer's findings concerning cuticular covering of nectarial regions of pear and apple blossoms.

BOOKS RECEIVED

BRANSON, E. B. and others. *The University of Missouri Studies.* Vol. VIII. No. 4. Pp. 265–349. Illustrated. University of Missouri. $1.25.

COOPER, LANE. *Aristotle, Galileo, and the Tower of Pisa.* Pp. 102. Cornell University Press. $1.50.

FERREE, C. E. *Studies in Physiological Optics.* Vols. I and II. Johns Hopkins University School of Medicine.

LADD, HARRY S. *Geology of Vitilevu, Fiji.* Pp. 263. 11 figures, 44 plates. Bernice P. Bishop Museum, Honolulu. $3.00.

MILLS, CLARENCE A. and JAMES T. HEADY. *Living With the Weather.* Pp. 206. Caxton Press, Cincinnati. $1.50.

Report of the First Scientific Expedition to Manchoukuo. Sections I, IV, V. Waseda University, Tokyo.

SHERMAN, HENRY C. *Food and Health.* Pp. x + 296. Macmillan. $2.50.