(*3*). Doubtless polarity, which is basic in the elaboration of many patterns of growth and differentiation in both unicellular and multicellular forms (*4*), is another factor. It may control the orderly distribution of cytoplasmic material and various substances. Finally, as in the cells here described, there may be specific, qualitative alterations in the reactivity systems of the cells, due to permanent changes in the genetic make-up of the cytoplasm itself.

References

1. Baumgärtel, O. *Ber. dtsch. Bot. Ges.*, 1917, 35, 603.
2. Billingham, R. E., and Medawar, P. B. *Nature, Lond.*, 1947, **159**, 115.
3. Bloch, R. *Amer. J. Bot.*, 1937, 24, 279; *Bot. Rev.*, 1941, 7, 110; *Amer J. Bot.*, 1944, **31**, 71.
4. Bloch, R. *Bot. Rev.*, 1943, 9, 261; *Chron. Bot.*, 1943, 7, 297.
5. Bloch, R. *Amer. J. Bot.*, 1946, 33, 544.
6. Darlington, C. D. *Nature, Lond.*, 1944, **154**, 164.
7. Rhoades, M. M. *Proc. nat. Acad. Sci., Wash*, 1943, **29**, 327.
8. Scott, F. M. *Bot. Gaz.*, 1942, **103**, 225.
9. Sinnott, E. W. *Amer. Nat.*, 1942, **76**, 253.
10. Sinnott, E. W., and Bloch, R. *Proc. nat. Acad. Sci., Wash.*, 1939, 25, 248; *Amer. J. Bot.*, 1946, 33, 587.
11. Spiegelman, S., and Kamen, M. D. *Science*, 1946, **104**, 581.
12. Wright, S. *Physiol. Rev.*, 1941, **21**, 487; *Amer. Nat.*, 1945, **79**, 289.

Separate Localization in the Medulla Oblongata of the Vagal Inspiratory and Expiratory Reflex Centers

Oscar A. M. Wyss

Institute of Physiology,
University of Geneva, Switzerland

Stimulation of the afferent vagus nerve acts upon respiration in two different ways. With low stimulus frequency corresponding to the low rate of afferent impulses elicited by lung deflation or small lung volume, the effect on respiratory posture and breathing movements is mainly inspiratory, whereas with higher stimulation rates corresponding to the higher afferent impulse frequencies produced by lung inflation or great lung volume, breathing becomes predominantly expiratory. It must be emphasized, however, that there is no hard, clear-cut line between the low-rate inspiratory effect and the high-rate expiratory effect, and that they both exist simultaneously over a wide range of intermediate frequencies. Thus, within physiological limits, a dual control of respiration is accomplished by these two antagonistic vagal tendencies, inspiratory and expiratory, the former prevailing with a decrease, and the latter with an increase, of the frequency of centripetal impulses emerging from the pulmonary stretch receptors. From this statement it may be inferred that posture as well as movement of the respiratory effector system, which is mainly or even exclusively an inspiratory one, results at any moment of the breathing act from the combined influence of the two opposite vagal drives, excitatory and inhibitory. Perhaps only in the extreme conditions of the vagus nerve artificial stimulation, with adequately chosen rates and intensities of stimuli, may pure inspiratory or expiratory effects be obtained, appearing then as inspiratory or expiratory standstill of breathing.

In order to determine whether separate reflex centers for inspiratory and expiratory effects, respectively, can be distinguished at the level of the medulla oblongata, small circumscribed lesions have been made by means of nonstimulating high-frequency coagulation, in the region of the bulbar respiratory center. It was first observed that suitable lesions situated at a more cranial level can destroy only the expiratory drive without any weakening of the inspiratory one. On the other hand, a somewhat lower, *i.e.* more caudally located lesion, abolishes only the inspiratory component of the vagal respiratory reflex, leaving the expiratory effect intact. Thus, the existence of two different central pathways involved in vagal respiratory reflexes and corresponding to the two antagonistic reflex components has been proved and has later on found further and more detailed anatomical confirmation.

Selective elimination of either the inspiratory or expiratory effect of vagal stimulation demands a small destruction lying in the tractus solitarius, its nucleus, and the adjacent dorsal part of the lateral reticular formation. For the expiratory component, this critical lesion occupies the tractus solitarius system at a more cranial level, *i.e.* just caudal to the entrance of the vagal respiratory fibers. But this expiratory lesion does not interfere with all the descending fibers of the tractus solitarius, unless the inspiratory effect be also abolished, and "central vagotomy" ensues. Some lateral portion of the solitary system, including mainly tractus fibers, must be spared, which seems to indicate that impulses mediating the inspiratory effect are conveyed in those descending fibers. For the inspiratory component of the vagal respiratory reflex, the region responsible lies in the caudal part of the tractus solitarius system, at a distance of about 2 or 3 mm. This inspiratory lesion is much less critical than the expiratory one, involving the entire transverse section of the solitary complex.

The related experimental findings lead to the following anatomical considerations: All the afferent respiratory fibers of the vagus nerve enter the medulla oblongata through the cranial portion of the vagus root and join the tractus solitarius, running down into the latter, but leaving it again at a higher level to form the expiratory and, at a lower level, the inspiratory reflex pathways. Assuming that these fibers leaving the tractus solitarius terminate mostly in its nucleus and the adjacent part of the reticular formation, where they come in synaptic contact with internuncial neurones, the column of gray matter accompanying the tractus solitarius may be considered as the locus proper of the vagal respiratory reflex centers. It is worth noting that central lesions affecting one or the other of the two antagonistic components of vagal respiratory control include besides, or perhaps rather than the tractus solitarius itself, these adjoining cellular structures. There is reason to believe that the above-described selective interruptions of the intrabulbar reflex pathways are located at those places where afferent fibers, or fiber collaterals, converge toward an interneuronic relay station, and that no selection would be obtained by the destruction of fiber tracts only. The same may be true with regard to the continuing fiber pathways, whether they be regarded as further intracentral connections of the afferent system or as the descending efferent paths of the "reflex arc." In this latter case, which appears the most likely, the selective suppression of central reflex transmission would thus be located at the origin of the internuncial neurones acting on the respiratory motoneurones of the spinal level. Definite conclusions, however, will have to be postponed until further anatomical and experimental studies have been made.

As far as our present state of knowledge permits inferences concerning the central mechanism and structural arrangement underlying the vagal respiratory reflexes, we may consider the nuclear column adjoining the tractus solitarius as the common interneurone pool for these reflexes, with a cranial part of expiratory, *i.e.* inspiratory-inhibitory, and a caudal part of inspiratory-excitatory, internuncial neurones. It is suggested that these solitary interneurones are controlling the inspiratory motoneurones directly, in an excitatory as well as in an inhibitory way. But a higher reflex integration involving the autonomous divisions of the respiratory center also exists, for it alone could account for some particular features of the vagal control of breathing.

References

Adrian, E. D. *J. Physiol.*, 1933, **79**, 332.

Andereggen, P., Oberholzer, R. J. H., and Wyss, O. A. M. *Helv. physiol. Acta*, 1946, **4**, 213.

Bartorelli, C., and Wyss, O. A. M. *Boll. Soc. ital. Biol. sper.*, 1941, **16**, 219.

Beer, T., and Kriedl, A. *Pflüg. Arch.*, 1896, **62**; 156.

Hering, E., and Breuer, J. *Sitzgsber. Akad. Wiss. Wien, Math.-naturwiss. Kl.*, 1868, **57**, 672; 1868, **58**, 909.

Hess, W. R. *Pflüg. Arch.*, 1930, **226**, 198; 1936, **237**, 24.

Oberholzer, R. J. H., Andereggen, P., and Wyss, O. A. M. *Helv. physiol. Acta*, 1946, **4**, 495.

Wyss, O. A. M. *Pflüg. Arch.*, 1939, **242**, 215; 1940, **243**, 457; *Schweiz. med. Wschr.*, 1941, **71**, 290; *Helv. physiol. Acta*, 1943, **1**, 301; 1945, **3**, 437; *Exper.*, 1946, **2**, 381.

Wyss, O. A. M., Andereggen, P., and Oberholzer, R. J. H. *Helv. physiol. Acta*, 1946, **4**, 443.

Wyss, O. A. M., and Croisier, M. *Helv. physiol. Acta*, 1943, **1**, 89.

A New Disease of the Variegated Cutworm, *Peridroma margaritosa* (Haw.)

Edward A. Steinhaus

Laboratory of Insect Pathology, Division of Biological Control, College of Agriculture, University of California, Berkeley

In February 1947 we received from F. H. Wymore, of the Union Oil Company insectary at Anaheim, California, several diseased specimens of the variegated cutworm, *Peridroma margaritosa* (Haw.). This species was being reared in a small insectary room to obtain eggs on which ovicidal tests were being run. In the accompanying correspondence Wymore wrote that the disease had been causing an extremely heavy mortality among the older caterpillar population for a period of about four or five weeks. Only a small percentage of the caterpillars ever reached pupation, and only about 50 per cent of the eggs produced by the moths which later emerged proved fertile.

Microscopic examination of the cutworms revealed the presence of bacteria in the blood and a pathology of the fat tissues characterized by the presence of large numbers of small, granular inclusions in the cytoplasm of the fat cells. The nuclei of the fat cells were usually hypertrophied and in a state of degeneration. The bacteria, possibly secondary invaders, were gram-negative small rods which, for the most part, did not ferment lactose.

Additional diseased as well as normal caterpillars were kindly furnished by Mr. Wymore, and with this material infection experiments were conducted which provided the following information.

Healthy variegated cutworms may be infected by direct inoculation into the body cavity, and through the mouth by means of contaminated food. (There is also some evidence that the infecting agent may pass from one generation to the next through the egg.) After two or three days the infected insects begin to eat less food; they may remain slightly smaller in size than normally developing insects, have a somewhat languid appearance, and, in the cases so far observed, usually die before pupating. The fragility of the integument and the marked internal liquefaction of tissues, so characteristic of polyhedroses, is absent. The larvae are flaccid, but the body wall remains relatively firm.

Upon dissecting a diseased larva, one immediately notices an opaque whiteness of the fat tissue which may be solidly white or, in lighter infections, of the normally clear appearance except that it is flecked with opaque, white areas. Under a compound microscope these opaque areas may be seen to consist of nodules of hypertrophied fat cells filled with large numbers of minute (0.4–0.6 μ) granules. Suspended in an ordinary wet mount the infected cells break down rather rapidly, liberating the contained granules until eventually the entire preparation consists of millions of discrete granules together with some cellular debris. The granular inclusions are nearly spherical, are not as refringent as are polyhedral bodies, possess a very slight cream coloration when seen *en masse*, and are readily visible with an ordinary light microscope. When ordinary stained preparations are attempted, these bodies lose much of their distinct granular aspect and appear as lightly stained amorphous particles, frequently coalesced. They do not have the characteristic attributes of bacteria and are not cultivable on the usual bacteriological media.

Sections of the diseased cutworms show a characteristic histopathology of the fat tissue. The nuclei of the fat cells appear either as considerably enlarged, densely staining masses or as disintegrated particles of chromatin material scattered over an area which represented the originally hypertrophied nucleus. The cytoplasm of these cells is packed with large numbers of the granular inclusion bodies. Sometimes the cell membranes are broken down so that the contents of several cells are enclosed in a single area the size of several cells.

The exact nature of the granular inclusions has not been determined. Whether or not they themselves represent the causative agent, probably a virus or agglomerates of a virus, or a peculiar type of granular degeneration, is not known. A few filtration experiments have shown the filtrates from Mandler filters of coarse porosity to be infectious but, so far, not those from Mandler filters of medium or fine porosity. The granular inclusions characteristic of this disease have points of similarity with those described by Paillot (*2*) in the case of *pseudograsserie 1* of another cutworm, *Euxoa segetum* Schiff., and possibly with those briefly described by Graham (*1*) in the case of a disease of the spruce budworm, *Archips fumiferana* (Clem.). It is possible that these agents are representatives of a distinct group of virus diseases of insects, the other two groups being the well-known polyhedroses and those infections (e.g. sacbrood) characterized by the absence of inclusion bodies of any kind.

References

1. Graham, K. *Bi-monthly Prog. Rep., Forest Insect Invest., Dominion Dept. Agric.*, 1947, **3**, No. 2, 3.
2. Paillot, A. *C. R. Acad. Sci., Paris*, 1934, **198**, 204-205; *Ann. Epiphyt. Phytogénét.*, 1936, **2**, 341-379.