Terminology for the Anterior Pituitary Hormones

Josephine Stewart and C. H. Li [*Science* **137**, 336 (1962)] have made what they apparently consider an appeal to reason for the acceptance of *-tropin* and *-tropic* endings in connection with anterior pituitary hormone terminology. It must be pointed out that this particular coin does have another side and that an equally good, if not better, case can be made for the acceptance of the *-trophin* and *-trophic* endings. Preference, according to Stewart and Li, has a geographic or personal basis, and they imply that a multitude of biochemists and endocrinologists have no knowledge or awareness of the derivation and meaning of the suffixes *-tropin* and *-trophin*. I would like to suggest that the opposite is actually true; that *because of* the continued use of both endings, practically everyone who is aware of this duality of terminology is well versed in the etymologic basis for both usages and is cognizant of the equivocal nature of the problem. The somewhat facetious, tongue-in-cheek statement of the editors of *Hormones in Blood* would seem merely to emphasize this point.

While I agree wholeheartedly with Stewart and Li in regard to the *desirability* of universal acceptance of one or the other type suffix, I do not agree with their contention that *-tropin* and *-tropic* should be adopted on the basis of "signification." They are willing to take a few linguistic liberties in proving the signification of *-tropin* but are really puristic in what they consider the verb *nourish* implies. In their report they state, "Thus, terminology with this suffix [*-tropic*] implies the stimulating effect of the hormone on its target organ which is characteristic of all these adenohypophyseal hormones." This statement would seem to involve an undue extension of pituitary-gonadal reciprocity, since the term *gonadotropic* ought to imply that the gonad, not the "tropic" hormone, is the stimulating agent. What this terminology actually indicates, and properly so, is the fact that the adenohypophyseal hormones turn toward or are directed toward, or have affinity for, their target organs. On the other hand, it is held by many that the pituitary "trophic" hormones do, in fact, *nourish* the target glands, if not in the restricted sense of supplying carbohydrates, fats, and proteins, certainly in the general sense of supplying "hormonal nourishment" which

somehow fosters, supports, and stimulates the subordinate glands. Furthermore, one of the significant effects of the anterior pituitary hormones is the production of an increased blood flow through the target glands, and this must also make for better nutrition (in the restricted sense of the word) of the glandular cells, indirectly at least.

Finally, I would suggest that, in addition to legitimacy and signification, priority and volume of usage be considered in the eventual resolution of this question. The terms *gonadotroph* and *thyrotroph* were suggested as suitable functional designations for the particular basophils which produce the gonadotrophic and thyrotrophic hormones, respectively. Although originally used by H. D. Purves and W. E. Griesbach of New Zealand [*Endocrinology* **49**, 224 (1951)], these terms have found almost universal acceptance among the cytologists of the world, and, in fact, cytologists in the United States have since added the following names for other specific cell types: "corticotroph" for a cell type thought to be the producer of ACTH [M. G. Farquhar, *Anat. Record* **127**, 291 (1957)] and "luteotroph" for the acidophil which produces Luteotrophin (E. G. Rennels, *Endocrinology*, in press). Obviously, acceptance of the *-tropin* and *-tropic* endings would demand also a change to the suffix *-trope* for the various cell types. Such a universal change is not likely to be dictated by the wishes, whims, or preferences of any one laboratory or any one journal. Any eventual agreement and unification of usage must be the result of an arbitrary decision among either the leading endocrinologists of the world or the several journals which publish endocrinologic papers. I would favor acceptance of the endings *-trophic, -trophin,* and *-troph.*

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Thousands of scientists and teachers have wrestled more or less seriously with the etymo-biological problem stated by Stewart and Li in their article concerning the use of *-tropin* or *-trophin* in reference to the adenohypophyseal hormones. From long perusal of the endocrinological literature I note that some investigators have avoided making a firm personal decision in this matter, possibly being influenced by coauthors or other colleagues to use one or the other form at various times. (Perhaps

the rare cases in which both terminologies have appeared in one paper can be ascribed to typographical error.)

In my own case, I took a firm stand in favor of *-trophin* and *-trophic* some 12 years ago—not in response to any endogenous conviction but as a result of reading a compelling argument published several years previously by G. W. Corner [*Endocrinology* **33**, 405 (1943)]. The amazing thing is that Stewart and Li have used a similar approach to reach a conclusion exactly opposite to that reached by Corner, who agreed with J. H. Burns that a *thyrotropic* hormone, for example, would mean one which is attracted *to* the thyroid by some stimulus exerted *by* the thyroid. Said Corner: "The use of -tropic as in gonadotropic therefore reverses and confuses a clear, practical pre-established usage in the broad field of biology. To use it is to countenance the warping and blunting of our scientific terminology, which should be a precision tool."

Anyone for *-trophin*?

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In connection with the hormones of the anterior pituitary, Stewart and Li have proposed that the suffixes *-tropin* and *-tropic* be generally adopted. We believe, however, that a better case can be made for the use of *-trophin* and *-trophic*, both on the basis of current usage and on the basis of etymology.

Widespread use of *-tropic* is relatively recent in this country, and it is now almost wholly restricted to the United States. When I (J.A.R.) was a student at the University of California in the early 1930's, I first became acquainted with the pituitary hormones as "trophic" substances, and in our time at Yale from 1938 to 1950, "trophic" was the preferred usage. *Endocrinology* for 1934 carries only *gonadotrophin* in its index. By 1936 only *gonadotropin* appears, but in later years *Endrocrinology*, like many other journals in this country, has allowed either word according to the usage of the authors. In Europe, *-tropic* seems to have been used first in several languages. However, the *Biochemical Journal* began to use *-trophic* consistently in 1937, and the *Journal of Endocrinology* has used only *-trophic* since its first volume in 1939. Except for those in the United States, publications in English throughout the world—in Britain, Scandinavia, Canada, and Australia—have now for

many years used *-trophic* almost exclusively. In Latin America, only *trophic* seems to be used, with *f* replacing the *ph* in Spanish. In France both forms are used, but that related to *-trophic* is the more common in scientific journals. Thus, those who prefer the early European usage of *-tropic* are now in a minority in the world literature.

Like Stewart and Li, we believe that terminology is closely related to concept and that precision in meaning should be considered more important than popular usage in determining scientific language. We differ from these authors, however, in the meanings we associate with the words in question. Here are some summary definitions from a standard Greek lexicon (Liddell and Hart, ed. 8):

tropē: a turn or turning; solstice; turning about of the enemy, putting to flight, a rout; of wine, turning sour; a turn of speech.

tropikos: of the solstice (i.e. of the apparent turning of the sun, hence modern Tropic of Cancer, (tropical); in rhetoric, figurative.

tropos: a turn, direction, way; manner, guise; of persons, habit, temper.

tropheus: one who rears or brings up; foster father, nurse; breeder, rearer.

trophē: nourishment, food, provisions; livelihood, that which procures sustenance; nurture, rearing, bringing up, education; rearing or keeping of animals.

trophicos: nursing, tending.

trophimos: nourishing; one who finds board, master of the house; foster child; of bodies, healthy, strong; of plants, flourishing.

trophos: feeder, rearer, nurse.

It is evident that the original meanings of the two root words differ not only from each other but from the meanings attributed to them by Stewart and Li. *Tropē* or *tropos* refers literally to a physical turn or turning away, figuratively only to way or manner or turn of speech. *Trophē* refers, not to nutrition in the sense of food per se, but to nurture in the sense of providing sustenance and care, of fostering or making to grow and flourish.

These meanings have been preserved closely in modern usage. In several dictionaries (standard English, medical) *-tropic* is defined as referring to turning or movement toward or away from a focus of heat, light, or other stimulus. No type of "response" other than turning is indicated. A tropometer is an instrument for measuring angle of torsion; the examples given by Stewart and Li, such as *heliotropic* or *isotropic*, all refer to turning movement or to physical direction. *Trophic* is defined as meaning concerned with, or regu-

lating, nutrition of tissues, often with the example "as in *trophic* nerves." Surely the latter usage implies not that nerves furnish food to the muscles they serve, as Stewart and Li appear to believe, but rather that the nerves foster growth and function. Even those who describe the adenohypophyseal hormones as "tropins" admit that in the absence of these substances the target organs become "atrophic" and that excess of the hormones induces "hypertrophy."

From these definitions and uses we conclude that *-tropic* is not well applied in this context but that *-trophic* is apposite. For example, *somatotropic* suggests only turning the body—something to do with orthopedics or gymnastics perhaps—whereas *somatotrophin* can be understood readily as concerned with the nutrition of the body and with its nurture and growth in a broad sense. Our understanding of the meanings of *gonadotropin* and *gonadotrophin* are illustrated in the older fashion by the following cautionary tale.

There once was an Interstitial Cell residing in a Non-American testis. It was a plump and peaceful cell, rich in lipid and productive of testosterone. This benign supporter of the pleasure principle depended for its *nurture* and its *nourishment* on the gentle constant attendance of a swarm of companions from a distant gland, who called themselves gonado*trophins*, or sometimes, playfully, Interstitial-Cell-Stimulating Hormones. Once, during a terrible phase of the late war, the possessor of this Non-American testis nearly starved in a concentration camp. The amiable companions of the Interstitial Cell nearly disappeared, and the cell knew for a time a lonesome dwindling which it recognized as *atrophy*. Happily, the postwar period brought prosperity and good health to the possessor of the Interstitial Cell. All was as before, until, as may befall any man, the owner came to dwell in the United States. For a few months (one may presume a period of cultural lag) all was well, but then the Interstitial Cell perceived that the gentle nurture of its companions was supplanted by rude jostling. Frequent tremors shook its Golgi apparatus, wavelets crisscrossed its endoplasmic reticulum, and the cell, fumbling, and embarrassed, began to produce rather more etiocholanolone than it ought. Then one morning, horribly, its nucleus began to revolve counterclockwise. The cell cried to its erstwhile gentle companions: "What awful change has come

upon you?" The companions in brute chorus replied: "We are *gonadotropins* now, members of the American Adenohypophyseal Turnverein." Said the cell: "I see that you are already much coarsened; you have begun to drop your aitches." "Never mind that," said the hormones, "we are true *tropins*, and you must respond in kind." The poor cell replied: "But I am unaccustomed; I hardly know which way to turn." "It matters not," roared the grinning tropins. "You're in the U.S.A. now. Twist, brother, twist!"

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As Mellen notes, the eminent biologist George W. Corner published an article some 20 years ago on the problem of the suffixes in the terminology of the pituitary hormones, presenting another side of the argument. We have also read with interest Mellen's own arguments and those of Rennels and of Russell and Wilhelmi in favor of the *-trophin* suffix, and since these arguments seem to rest primarily on linguistic grounds, we want to add a linguistic footnote here, at the same time reiterating that the chief concern in all these arguments should be to establish a terminology where the *meaning* is congruent with our best present knowledge of the mechanism of action of the pituitary hormones.

The crux of the arguments on the other side (first stated by J. H. Burn in 1937 and developed fully by Corner) is that a term like *phototropic*, for example, refers to an organism that turns toward the light, or that has light as its orienting stimulus. In this usage, the first or noun portion of the compound designates the stimulus, not the object of the stimulus. On this basis, the argument continues, a term like *gonadotropic* would imply that the gonads act upon the hormone, rather than the reverse; on the other hand, by analogy with our usage, a heliotrope would be a flower that turns the sun!

This argument is an intriguing one, but let us examine it more closely. In the Greek, these compounds consisting of a noun element and a verbal element, as well as the compound adjectives formed from them, are legitimately operative in both directions; that is to say, the verbal element can bear with equal legitimacy either a passive or an active meaning, can imply either "acting" or "acted upon," depending upon the context. To take an example that contains one of the suffixes in question, *kourotrophos* can mean either "nourishing youths" or "nourished by youths." [To be entirely accurate, one should mention that the Greeks usually (although not invariably) made the distinction between the two by the placing of the accent. If the verbal portion of the compound bore an active meaning, the accent was on the antepenult—thus, *kourótrophos*—and if passive, on the penult, *kourotróphos*. When foreign words came into English through the Latin, however, the very strongly regular Latin accent was imposed; thus, any difference in accentuation disappears in the English language]. By the same token, the meaning of *-tropos* could be either "turned upon" or "turning"; and even in the case of the oft-marshaled example *phototropism*, the interpretation "light-turning" (where *light* is the object of the action), rather than "turned by or toward the light" would be perfectly designative in the proper context—say in optics, where an agent could be referred to as bending a light beam. Thus, there is no linguistic precedent in the original Greek that would favor one cause-and-effect order over the other in connection with these compounds.

As to the point that our usage is contrary to a familiar precedent in the field of biology, it is true that there stands established in biological usage a group of words where the noun portion of the compound represents the orienting stimulus and not the thing stimulated. But Corner himself quotes other instances where the reverse is true: *chromotrope*, meaning a dye which changes color under chemical action, or *bacteriotropic*, meaning directed toward bacteria or affecting them in a specific way.

Moreover, if words like *electrotropic*, *phototropic*, and *thermotropic* can be cited, in which the electricity, the light, or the heat is the stimulating agent, the same holds true for the other suffix. Consequently, we can argue that if *phototrophic* means nourished by light and *neurotrophic* means nourished by or through the nerves, then *gonadotrophic* means nourished by the gonads or *thyrotrophic* means nourished by the thyroid. Yet we are certain that no one would insist, except for the sake of argument, that any serious confusion has actually arisen on this ac-

count with either of the suffixes. And furthermore, surely in 1962, nearly three decades after the usage was incorporated into *Webster*, there can be no valid objection to extending the sense of "tropic" from the purely physical sense of "pertaining to a turning," to the figurative "tending to turn or change, esp. . . . in response to a (specified) stimulus." So what we are left with is a difference of opinion about which terminology reflects most accurately the actual mechanism involved in the action of the pituitary hormones on their target organs.

It is interesting that one of the most convincing arguments for the *-trophic* suffix, made by Russell and Wilhelmi, also depends upon a similar extension from the literal to the figurative, from "to nourish" to "fostering growth and development." Their argument that the target organ atrophies if it is not stimulated, and that therefore the hormone fosters growth and development is a good one. We, however, still adhere to our objection to *-trophin* in either of these senses. We feel that the hormone must be viewed, not as an agent which per se fosters the growth and development of the target organ, but rather as an agent that triggers a mechanism in the target organ whereby that gland or organ flourishes and grows. Or it may be seen as a key which *turns* a lock, like an ignition key in a motor car, setting the mechanism into motion. What the mechanism is, we do not know at present. In the next decades we will begin to find out what it is and how it operates, since most of the pituitary hormones have been isolated in pure form and some of them have been synthesized. The mechanism may involve nucleic acids, or it may be something like an interaction between the protein hormone and some subcellular entity or entities in the target gland. At any rate, Corner himself saw that the *-trophin* suffix was "not perfectly apt," but he considered it the lesser of two evils. We strongly believe that, in view of the present concern about hormonal mechanism, the sense of nurture is no longer "sufficiently noncommittal" to render the suffix *-trophin* free from confusion (*1*).

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Note

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