Letters

Melatonin and Puberty

Gina Kolata's Research News article "Puberty mystery solved" (20 Jan., p. 272) incorrectly leads the reader to believe that a major new discovery has established the role of the pineal gland and melatonin in puberty and that "the case is closed."

Two elements of the article concern me. First, the central theme is overstated, and second, the substance is faulted.

The central theme is that a decrease in serum melatonin during development triggers puberty. The new evidence is a recently published finding (*1*) that nocturnal levels of circulating melatonin decrease 75 percent during early stages of human development. But many physiological parameters change during puberty. Proof that they, not melatonin, control puberty is no better or worse; neither melatonin nor pinealectomy has been experimentally shown to either trigger or block puberty.

The substance of Kolata's article is a review of the history of work in this area. Several important points should be clarified.

1) It is incorrectly indicated that Otto Huebner, a German physician, reasoned that the pineal gland of children might produce a substance that actively suppresses puberty. As reviewed in detail by the pineal historian Ariëns-Kappers (*2*), Huebner was only the first to describe a boy both showing premature puberty and suffering from a pineal tumor. Marburg (*3*) wrote that the human pineal gland was an endocrine organ which inhibited the function of the hypothalamus and, thus, the development of the reproductive system (*2*).

2) The article incorrectly indicates that sensitive methods were not available to measure melatonin in the 1960's, and that synthesis of this compound had to be studied indirectly by measuring an enzyme involved in melatonin synthesis, hydroxyindole-*O*-methyltransferase. In fact, a sensitive fluorometric method to measure melatonin directly was used in 1964 in the first report of a day-night pineal melatonin rhythm (*4*).

3) The reader might believe that melatonin production is regulated in a simple manner—that is, that light depresses it and darkness increases it. This is not the case. Melatonin production is regulated by a self-sustaining circadian clock in the brain, specifically the suprachiasmatic nucleus (SCN). The SCN turns melatonin production on and off with 24 (±0.5)–hour rhythmicity, even in constant darkness. Light acts on the system to reset the clock each day, ensuring that it is entrained to environmental lighting schedules. Light can also block SCN stimulation of the pineal gland at night (*5*), but darkness during the day cannot increase melatonin production.

4) The article states incorrectly that constant light shortens the reproductive cycle of the rat. In fact, constant light causes the rat to become reproductively acyclic, a well-known condition described as persistent estrus. This is reported to be independent of the pineal gland (*6*).

5) The reader might come away with the wrong impression that the daily rhythm in melatonin in humans was discovered by Lynch *et al.* (*7*). This discovery was made by Pelham *et al.* in 1973 (*8*).

6) The article implies that melatonin inhibits gonadal function. However, current research from investigators on several continents has convinced many in this field to reject the old melatonin-is-antigonadotrophic concept in favor of a role of the compound as a controller of seasonal rhythms. Melatonin appears to mediate photic-regulated seasonal physiological changes, including coat color and reproduction. The mechanism is gradually becoming understood; a key characteristic is that the duration of the dark period of the night is translated into a biochemical signal—the duration of elevated night melatonin levels. Physiologically, long periods of elevated melatonin at night appear to inhibit reproduction in hamsters but promote reproduction in sheep (*9*).

7) The article glosses over published work on the same topic, including one report that described high levels of daytime blood melatonin early in human development (*10*). A second human study found that, although total melatonin metabolite excretion was constant, a marked decrease in rate per kilogram body weight or volume did occur during development (*11*), suggesting serum concentrations of melatonin are higher at early ages. Both reports raised the possibility that melatonin plays a role in puberty. Other reports find no evidence of marked changes in blood melatonin during development or in precocious puberty (*12*).

Last, the article heralds some unpublished work on sleep-inducing effects of melatonin as opening a new chapter, yet overlooks a 1981 report that a 1-milligram intranasal dose of melatonin produces sleep within 30 minutes in some human subjects (*13*).

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Erratum: The former affiliation of Bernard Goldstein, the new assistant administrator at the Office of Research and Development at the Environmental Protection Agency (News and Comment, 20 Jan., p. 262) was incorrectly reported. He was chairman of envirionmental health and community medicine at the University of Medicine and Dentistry of New Jersey's Rutgers Medical School.

Erratum: In the report "The structure of abelsonite" by C. B. Storm *et al.* (9 Mar., p. 1075), the second full paragraph in column three should have begun, "The multiplets at 4 and 5 (Fig. 3A) are immediately recognizable. . . ."