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Introduction

This volume contains review articles that summarize some of the newly described actions of the ubiquitously acting endogenous molecule melatonin. Because some subject areas have been extensively reviewed elsewhere in recent months, summaries of those findings are not included in this volume. For tabulations on the following subjects, computer searches with the appropriate words will uncover the related findings and most recent reviews: melatonin and Alzheimer's disease; melatonin and ischemia/reperfusion injury; melatonin and circadian rhythmicity; melatonin and sleep; melatonin and jet lag; melatonin and apoptosis.

Considering that melatonin was discovered less than 50 years ago, advances in understanding its multiplicity of actions have been remarkable. Although initially linked with circannual and circadian rhythms, its actions far transcend these basic functions, and it is now apparent that melatonin may influence every organ system in the body. Furthermore, the idea that melatonin is exclusively of pineal gland origin is now obsolete. Clearly, any number of cells, widely distributed in the body, have the capability of generating melatonin.

This widespread production of melatonin emphasizes another issue. Melatonin produced in some organs is specifically for the use of cells in that organ, i.e., it is not released into the general circulation. In this context, melatonin not only functions as a hormone, but, in some cases, as an autocoid, a paracoid, a tissue factor, and as an antioxidant and free-radical scavenger. In mammals, the only organ known normally to release substantial amounts of melatonin into the systemic circulation is the pineal gland.

The fact that melatonin is not uniquely produced in the pineal gland should not be unexpected considering its distribution in the animal kingdom. Organisms that lack a pineal gland, e.g., insects and molds, generate melatonin. Furthermore, single-cell organisms, e.g., algae, which by definition have no organs, also produce melatonin. Indeed, this very wide phylogenetic distribution throughout the animal kingdom portends important functions for this remarkable molecule.

Another important feature to remember about melatonin is that, within an organism, melatonin is seemingly not in equilibrium. For example, there is now evidence that certain bodily fluids, i.e., bile, cerebrospinal fluid, and so on, contain much higher concentrations of melatonin than does the blood. This is probably also the case for the cells that produce melatonin. Because of this, it is important to define a physiological level of melatonin relative to a specific fluid or cell type. What may be a physiological level of melatonin in one fluid or cell, may not be physiological in another fluid or cell.

There are many yet to be made discoveries regarding this important molecule. It seems almost certain we are only seeing "the tip of the iceberg" when we consider the current functions of melatonin. The purpose of this special issue of *Endocrine* is to introduce the reader to some of the more recently uncovered data concerning this essential molecule.

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