

*Summary.* The administration of sodium chloride to adult adrenalectomized rats in amounts varying from 650 mg to 1 g daily prevents the urinary sodium wastage and potassium retention which characterizes adrenalectomized animals.

## 11502 P

**Oxidation of Tyrosine by Ultraviolet Light in its Relation to Human Pigmentation.**

STEPHEN ROTHMAN. (Introduced by G. F. Dick.)

*From the Department of Medicine, Section of Dermatology, and the Department of Pharmacology, University of Chicago.*

In the skin of mammals tyrosinase never has been conclusively demonstrated. It has been assumed<sup>1</sup> that the immediate precursor of melanin in mammalian skin is 3-4 dihydroxy-phenylalanin ("dopa") which becomes oxidized to melanin by an intracellular specific oxidase present only in normal functioning melanoblasts. The question has remained unsettled from where this dopa may originate; whether it is formed from tyrosine in the blood<sup>2</sup> or in the skin.

Arnow<sup>3</sup> demonstrated the formation of dopa by exposure of tyrosine solutions to ultraviolet radiation. As shown in our laboratory, this process needs a strikingly long irradiation time, namely 8-30 times as much as necessary for slightest pigmentation of human skin. In the presence of ferrous salts, however, the formation of dopa from tyrosine by ultraviolet irradiation is accelerated to such a degree that it may serve as a model of the biologic formation of dopa in human skin.

Samples containing mixtures of tyrosine and ferrous salts, irradiated with 1-3 "threshold erythema doses" yield measurable amounts of dopa but no melanin. When such irradiated samples are kept in the dark, progressively increasing amounts of precipitated melanin are formed after 16-24 hours. In this way the latent period of pigment formation in human skin is simulated by the *in vitro* experiments.

The late formation of melanin occurs for the greatest part at the

---

<sup>1</sup> Bloch, Br., *Jadassohn's Handb. d. Haut. u. Geschlkr.*, 1927, **1**, 434.

<sup>2</sup> Rothman, S., *Z. f. d. ges. exp. Med.*, 1923, **36**, 398.

<sup>3</sup> Arnow, L. E., *J. Biol. Chem.*, 1937, **120**, 151.

expense of dopa which has been formed during the radiation. However, in a few instances a slight decrease of tyrosine and a transitory increase of the dopa concentration could be observed within 1-2 hours after irradiation. This "after effect" of irradiation may be due to formation of rather stable peroxides by ultraviolet rays.

In tyrosine-ferrous salt mixtures the dopa concentration increases with continued irradiation to a certain maximum. If 50 mg % tyrosine solutions are irradiated this maximum amounts to about 5 mg %. Later, in spite of continued irradiation, the dopa concentration remains unchanged because dopa formation and oxidation of dopa to melanin keep balance with each other. Or, the dopa concentration decreases because more melanin than dopa is formed.

In long-lasting irradiation experiments it was found that in spite of a steady decrease of the tyrosine concentration the amount of melanin produced does not exceed a certain maximum. This is due to a decomposition of melanin into lighter colored, soluble products by the continued irradiation.

For clinical actinotherapy this finding indicates that after maximal pigmentation has been reached, continued irradiation does not produce a static but a dynamic equilibrium in which pigment formation and decomposition are kept in balance. Some clinicians have claimed that ultraviolet light treatment should be administered intermittently in order to assure an optimum therapeutic effect by "depigmentation periods." The experimental results, however, seem to obviate the necessity of such a procedure, and it appears justified to continue sunshine treatment in patients who already are tanned to a maximum, because biologic action of the rays continues.

Ultraviolet radiation acts on tyrosine in presence of ferrous salts similarly to tyrosinase in every detail. This fact supports the assumption that in mammals too, in which tyrosinase is not present, the primary precursor of melanin is tyrosine. The formation of dopa may occur in the skin by the action of ultraviolet rays if non-specific oxidation catalysts are present.

*Summary.* The oxidation of tyrosine to melanin by exposure to ultraviolet light in presence of ferrous salts serves as a model of pigment formation by sunshine in human skin. Continued irradiation of tyrosine-ferrous salt mixtures leads to a dynamic equilibrium in which formation and decomposition of melanin are kept in balance.