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# 5-HYDROXYTRYPTAMINE IN THE DEVELOPING CHICK BRAIN: ITS NORMAL AND ALTERED DEVELOPMENT AND POSSIBLE CONTROL BY END-PRODUCT REPRESSION*†

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IT now appears to be generally accepted that the biosynthesis, tissue levels and metabolism of 5-hydroxytryptamine (5-HT) may play an important role in brain function (EIDUSON, GELLER, YUWILER and EIDUSON, 1964). Although WEISS (1955) clearly pointed out the importance of the developmental dynamism of the growing organism, few observations have been made on the normal developmental appearance of serotonin in the developing brain and almost none on the consequences of its relatively long-term alteration (KARKI, KUNTZMAN and BRODIE, 1962; HSIA, NISHIMURA and BRENCHLEY, 1963; BOURNE, 1965). In addition, there is little information to suggest the manner in which the biosynthesis of this presumed important biogenic amine is regulated in the brain (or elsewhere). In the course of our experiments, it became evident that our data suggested the possibility of regulation of the biosynthesis of 5-HT by way of end-product repression and (or) inhibition. There appear to be only a few examples in the literature of this type of control mechanism in animal tissues (DEMARS, 1958; WYNGAARDEN and ASHTON, 1959; WALKER, 1960; UMBARGER, 1964).

We chose to study regional parts of the developing chick brain because we found the chick to be a very suitable organism especially since, in the embryonic stages, it is encased in its shell and thus virtually a closed system but one which could be entered at will without destroying the organism. Accordingly we first studied the changing levels of 5-HT in distinct regional parts of the normally developing brain. We then altered the normal appearance of 5-HT in the brain by making available to the embryo quantities of the precurser material, 5-HTP. Further, a study of the developing activities of some of the enzymes involved in the biosynthesis and metabolism of 5-HT led to suggestions concerning possible regulation of serotonin in the brain. The observations we have made during the course of these studies serve as the subject matter of this report.

## EXPERIMENTAL PROCEDURE

### *Materials*

L-5-Hydroxytryptophan was obtained from Calbiochem and used directly without further purification; [*carboxy*-$^{14}$C]5-hydroxytryptophan was obtained from ChemTrac Division of Baird-Atomic; kynuramine dihydrobromide was obtained from Regis Chemical Co.; New Hampshire Red Eggs (fertilized) were obtained from Redwing Hatcheries, Los Angeles, California.

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*Abbreviations used:* 5-HTP, 5-hydroxytryptophan; MAO, monoamine oxidase; DOPA, 3-4-dihydroxyphenylalanine.