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Hagedorn H H, O'Connor J D, Fuchs M S, Sage B, Schlaeger D A & Bohm M K. The ovary as a source of α-ecdysone in an adult mosquito. *Proc. Nat. Acad. Sci. USA* 72:3255-9, 1975.
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Insect physiologists had long thought that the gonads of insects did not produce hormones. This paper was the first to show that the ovary of the mosquito produced ecdysone, otherwise known as the molting hormone, and further showed that the ecdysone stimulated vitellogenin (yolk protein) synthesis by the fat body. [The *SCI*® indicates that this paper has been cited in over 225 publications.]

Ecdysone Production by Insect Ovaries

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The formation of the insect egg provides many problems of interest to the physiologist, for example, the movement of macromolecules along electrical gradients between the nurse cells and oocyte, the synthesis and uptake of vitellogenin by receptor-mediated endocytosis (which was first discovered in the mosquito), and the construction of the chorion. However, by 1975 very little was known about the hormonal control of egg development, except for the common observation that removal of the source of juvenile hormone somehow interfered with the process. In most cases, how juvenile hormone affected egg development was not understood.[1] Since, for the most part, insects chosen for physiological work are large, it is noteworthy that work on the tiny mosquito opened new doors in this field. Despite its size, the mosquito has a major advantage for this work—the blood meal initiates egg development, thus synchronizing the growth of the eggs in the experimental animals.

The paper under consideration was a collaboration between three laboratories, each of which provided a vital link to complete the story. One of these links was the development of a radioimmunoassay for ecdysone in J.D. O'Connor's laboratory.[2] The other two links were physiological studies that came to the same conclusion from quite different lines of investigation. Work done in M.S. Fuchs's laboratory showed that sclerotization of the eggshell was under the control of dopa decarboxylase. Since the enzyme was known to be regulated by ecdysone in other insects, they had started to look for ecdysone in the female mosquito during oogenesis.[3] In my laboratory we had found that the ovary was required for vitellogenin synthesis by the fat body, and we had some evidence that the ovarian factor was ecdysone.[4]

The collaboration was put together at a meeting of the American Society of Zoologists, where I met O'Connor and told him of my interest in finding out whether ecdysone was made by the ovaries. Since he was already working with Fuchs, he suggested a three-way collaboration, to which Fuchs readily agreed. The next months were very exciting as the outlines of the story began to fall into place and the significance of the findings became evident. We found that the titers of ecdysone rose after the blood meal, that the ovary did indeed produce ecdysone, and that the ecdysone stimulated vitellogenin synthesis *in vitro*. Not only had we overturned the dogma that insect gonads do not produce hormones, we also discovered a function for the hormone. Several years later this paper became the focus of a vigorous controversy about the role of ecdysone in vitellogenin synthesis in the mosquito, a controversy that has been apparently resolved recently.[5]

Soon after the publication of our paper it became clear that several other laboratories were independently coming to the same conclusion—that the ovaries of insects made ecdysone. In some insects the ecdysone was found to be stored in the egg, where it is apparently used to regulate molting of the embryo, and in other insects it may be involved in the regulation of juvenile hormone titers, but in most cases its role is still unclear.[6] In several Diptera, however, ecdysone seems to regulate vitellogenin synthesis, and the mosquito remains the best studied example of this situation.

1. **Hagedorn H H & Kunkel J G.** Vitellogenin and vitellin in insects. *Annu. Rev. Entomol.* 24:475-505, 1979. (Cited 205 times.)
2. **Borst D W & O'Connor J D.** Trace analysis of ecdysone by gas liquid chromatography, radioimmunoassay and bioassay. *Steroids* 24:637-56, 1974. (Cited 125 times.)
3. **Schlaeger D A, Fuchs M S & Kang S H.** Ecdysone-mediated stimulation of dopa decarboxylase activity and its relationship to ovarian development in *Aedes aegypti*. *J. Cell Biol.* 61:454-65, 1974. (Cited 55 times.)
4. **Fallon A M, Hagedorn H H, Wyatt G R & Laufer H.** Activation of vitellogenin synthesis in the mosquito *Aedes aegypti* by ecdysone. *J. Insect Physiol.* 20:1815-23, 1974. (Cited 90 times.)
5. **Borovsky D, Thomas B R, Carlson D A, Whisenton L R & Fuchs M S.** Juvenile hormone and 20-hydroxyecdysone as primary and secondary stimuli of vitellogenesis in *Aedes aegypti*. *Arch. Insect Biochem. Physiol.* 2:75-90, 1985. (Cited 20 times.)
6. **Hagedorn H H.** The role of ecdysteroids in reproduction. (Kerkut G A & Gilbert L I, eds.) *Comprehensive insect physiology, biochemistry and pharmacology. Volume 8. Endocrinology II*. Oxford, England: Pergamon Press, 1985. p. 205-62. (Cited 40 times.)