During the 3 h of starvation, the distribution of radioactive material spread as the cell length increased (Figure 3a). A similar picture was given by electron microscopic observation of *E. coli* 15 T⁻ undergoing thymine deprivation[11]. During recovery, we observed that the number of grains migrating towards the end of the filament is so small that the presence of original DNA in the small cell is uncertain (Figure 3b). Anyway, after this first abortive division an extra cell division is needed to generate a complete living cell, suggesting that damage caused by thymine starvation has been repaired.

*Résumé.* Dans un milieu dépourvu de thymine, des bactéries (*E. coli*) exigeant la thymine pour leur croissance s'allongent, sans qu'il ait cependant de relation directe entre la longueur atteinte et le taux de mortalité. Toutes les cellules dont la synthèse d'ADN reprend après addition de thymine ne donnent pas obligatoirement de colonies, suggérant ainsi que la mort par carence en thymine n'est pas la conséquence du blocage définitif de la synthèse d'ADN. Pour certains filaments, ce n'est qu'à la seconde division que se forme une cellule contenant de l'ADN néoformé capable de se multiplier activement.

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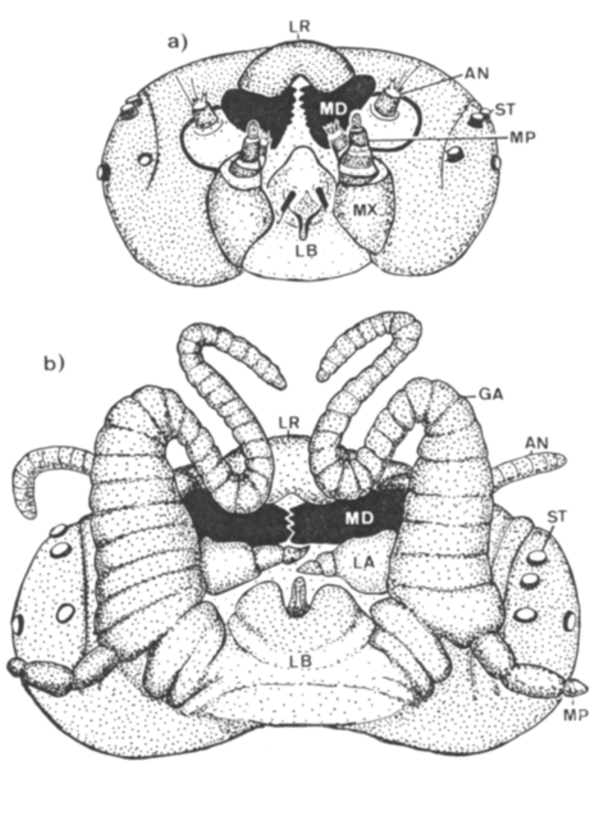
## Homoeötic Transdetermination Caused by Juvenoid in Larvae of *Pieris brassicae* L.[1]

In the course of normal development of insects, all cells become 'determined', i.e. committed to form a given pattern, organ or part of it. During this process the cells or organs change from a stage of high morphogenetic potency, when they are still capable of 'regulation', to the 'mosaic' state with a narrowly restricted morphogenetic potency. Determination takes place in an orderly sequence, and long before the growth and differentiation processes put the morphogenetic plan into effect, some cells being determined at an early, others at a later stage of ontogenesis. However, determination is not always absolute. Under experimental conditions, transdetermination is possible; i.e. one cell type can be transformed into another[2,3]. A familiar example of transdetermination is homoeösis or 'heteromorphous' regeneration, i.e. the replacement of an appendage by one belonging to another region of the body, e.g. regeneration of a leg in the place of a burnt or amputated antenna[4,5]. As WIGGLESWORTH[6] points out, transdetermination is a natural phenomenon at metamorphosis of the Hemimetabola, when the epidermal cells lay down a different cuticle and form different structures in the absence of juvenile hormone[7]. It is commonly believed that the transdetermination of a cell consists in the activation of new sets of genes.

Experiments on the action of juvenoids applied topically to last instar larvae of *Pieris brassicae* have been described in a recent publication[8]. In the course of those experiments a large number of treated larvae underwent an abortive supernumerary larval moult[9]. These insects were not able to ecdyse the old head capsule properly. However, it could be removed with forceps.

The head appendages of all individuals had more or less differentiated in the pupal/adult direction, as shown in Figure 1b. Though the mandibles had maintained their larval character, the antennae were much longer than the larval antennae and of different shape (compare with Figure 1a). The most characteristic feature of these




[1] Ro 20-3600 = isomere mixture of 6,7-epoxy-3,7-dimethyl-1-[3,4-(methylenedioxy)-phenoxy]-2-nonene. The author thanks Hoffmann-La Roche Ltd., Basle for a sample of the juvenoid.

[2] E. HADORN, Rev. suisse Zool. *71*, 99 (1964); Devel. Biol. *13*, 424 (1966); Scient. Am. *219*, 110 (1968).

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[6] V. B. WIGGLESWORTH, *The Principles of Insect Physiology*, 7th edn. (Chapman and Hall, London 1972).

[7] V. B. WIGGLESWORTH, *Insect Hormones* (Olivier and Boyd, Edinburgh 1970).

[8] G. BENZ, Experientia *29*, 1437 (1973).

[9] For details concerning rearing of insects and application of juvenoid the reader is referred to the afore mentioned paper[8].

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Fig. 1. a) Head and mouth parts of normal 5th instar larva of *Pieris brassicae*. b) Same of abnormal 6th instar larva with large maxillae (long galeae and relatively large laciniae and palpi) and elongated antennae. Magnification in a) and b) is the same. AN, antennae; GA, galea; LA, lacinia; LB, labium; LR, labrum; MD, mandible; MP, maxillary palpus; MX, maxilla; ST, stemmata (larval eyes).

insects, however, were the elongated galeae of the maxillae. Since in the normal adult the galae form the proboscis, the strong elongation of the galeae in 6th instar larvae must be regarded as a development in the direction of proboscis differentiation. It is interesting to note that this developmental trend of the galeae could in no case be fully suppressed during $L_5/L_6$ moults of *Pieris*, not even when high doses of juvenoids were applied at a very early stage (during or shortly before the preceding $L_4/L_5$ moult) nor when the head capsule was shed normally. Thus perfect $L_6$ of *Pieris* have never been obtained. They all died of starvation, because their abnormally shaped maxillae prevented proper feeding.

A number of the $L_6$ who could not get rid of the old head capsules showed, at the extremities of the galeae, heavily sclerotized mandible-like structures (Figure 2). Thus the appendages of the maxillary segment had produced structures which normally are restricted to the mandibular segment. This phenomenon must be regarded as a case of homoeösis and involves transdetermination of the cells situated in the apical region of the galeae. It indicates that the juvenoid Ro 20–3600, if applied at the right time and in proper concentration, can activate the genes responsible for mandibular differentiation in cells in which these genes normally would never be activated.

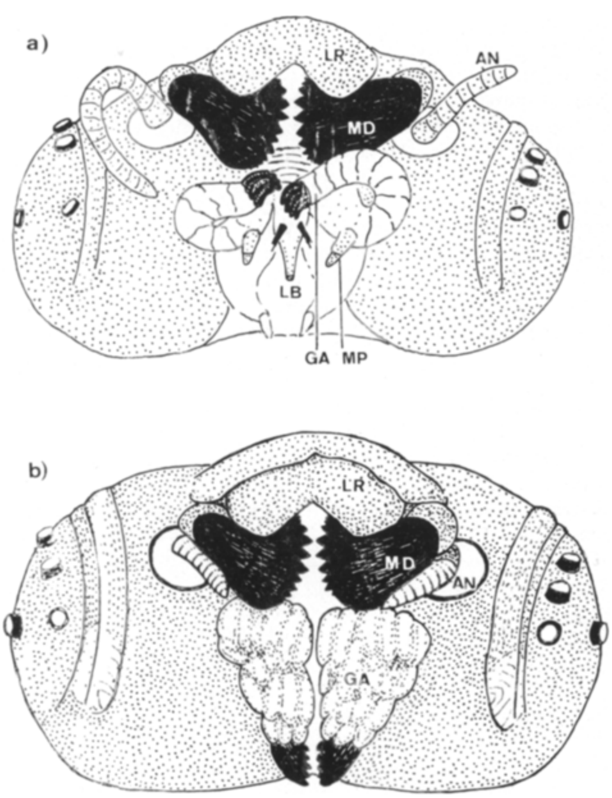


Fig. 2. Two examples of $L_6$ similar to the one shown in Figure 1b, but with less strongly developed galeae bearing mandible-like structures at their extremities. Same symbols as in Figure 1.

It is probable that the effect is not specific for Ro 20–3600, but that the application of the juvenoid leads to an abnormal state of relatively high concentration of juvenile hormone. In normal ontogenesis, the titer of juvenile hormone becomes low in the 5th larval instar. Under this condition the mandibles disintegrate and the maxillae, especially the galeae, elongate during the next moulting process. The larvae with abortive $L_5/L_6$ ecdysis demonstrate that it is easy to prevent the loss of the mandibles, and that it is difficult to prevent the pupal outgrowth of the galeae by the topically applied juvenoid. This may indicate that a relatively low titer of juvenile hormone is sufficient to maintain the formation of mandibular structures, but that a high titer of the hormone is needed in last instar larvae in order to maintain the larval character of the maxillae during a further moult. In the few individuals in which the differentiation of mandibular structures on the maxillae had been induced, the juvenoid was obviously present in an intermediate concentration, i.e. a concentration high enough to maintain mandibular structures, but not high enough fully to prevent differentiation of the galeae in pupal direction, yet sufficiently high to induce the genes in the cells of the apical region of the galeae to furnish the information needed to produce strongly sclerotized organs of mandible-like shape. This probably indicates that juvenile hormone, if acting during a period in which it would normally be absent or present at a lower titer, can activate certain genes which would not become active in normal development and that a specific titer of juvenile hormone is crucial for the realization of each step and each stage of differentiation.

*Zusammenfassung*. Topicale Behandlung des letzten Larvenstadiums von *Pieris brassicae* mit einem Juvenoid[1] ergibt Raupen, die eine abortive zusätzliche Larvenhäutung zum $L_6$ durchmachen, wobei sie die alte Kopfkapsel nicht abstreifen können, weil die Antennen und besonders die Galeae der Maxillen stark verlängert werden. In einigen Individuen wurden an den Enden der Galeae mandibelartige Strukturen ausdifferenziert. Es wird angenommen, dass diese homöotische Transdetermination der apicalen Galeazellen durch den abnormen, intermediären Juvenilhormonspiegel bewirkt wurde.

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## The Mode of Action of Four Anthelmintics

From pharmacological experiments with isolated tissue, Van Neuten[1] concluded that the broad spectrum anthelmintic levamisole (1-2, 3, 5, 6-tetrahydro-6-phenylimidazo[2,1-b] thiazole hydrochloride) causes contraction of mammalian muscle by nerve ganglion stimulation. He suggested that the contraction of *Ascaris lumbricoides* caused by levamisole could also be due to ganglion stimulation as the contraction was less pronounced, but not inhibited, in the presence of hexamethonium, and because it has been reported that levamisole causes a reduced membrane potential of *A. lumbricoides* muscle cell bellies[2].

[1] J. Van Neuten, in *Comparative Biochemistry of Parasites* (Ed. H. Van den Bossche; Academic Press, New York 1972), p. 101.

[2] J. Aceves, D. Erlij and R. Martinez-Maranon, Br. J. Pharmac. *38*, 602 (1970).