pramine the potentiation of NE effect was of similar intensity and lasted for 3 h.

It is but a fraction of free NE, released by stimuli or in the process of normal turnover, which exercises a physiological effect[5]. Another fraction is carried away by the blood stream or is inactivated by catechol-*o*-methyltransferase (COMT). Most of the released free NE is inactivated by reentry into the storage pools[4]. It is this process which is inhibited by the thymoleptic agents[4], as also evidenced by the presented results.

The prolonged vasoconstricting effect of NE below the threshold doses in the imipramine and in the desipramine pretreated rats is indirect but strong evidence that the thymoleptic drug itself as well as its metabolic product, desipramine, prevents the reentry of free (and probably the injected) NE into the storage pools. To this free NE, protected by the 2 thymoleptic drugs, the injected NE provides an additional amount, resulting in effective and prolonged inhibition of the histamine-induced vascular response. The fact that imipramine and desipramine pretreatment resulted in the same potentiation of NE effect, without differences in time-course and intensity, suggests that both the drug and its metabolic product have similar effects on the histamine-induced vascular alterations[6].

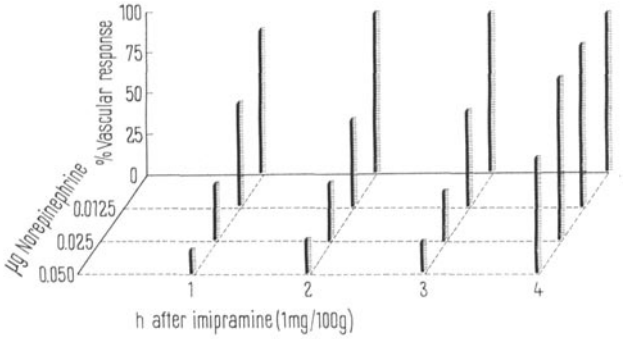

Fig. 2. % vascular response to intradermal injection of 20 µg histamine and increasing doses of l-norepinephrine bitartarate administered at different time intervals after intramuscular treatment with a constant dose of 1 mg/100 g imipramine. Each column represents the average readings of 8 rats.

Résumé. Les résultats rapportés nous autorisent à postuler l'hypothèse que la norépinéphrine est un inhibiteur hormonal naturel dans les premières phases de la réaction inflammatoire et que l'imipramine et la désipramine, qui empêchent l'accumulation de la norépinéphrine dans les réserves, augmentent et prolongent l'action de la norépinéphrine sur le réseau capillaire. En aucune façon les effets de l'imipramine sur le réseau capillaire se sont montrés différents de ceux causés par la désipramine.

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Experimental Studies on Embryonic Development of *Dendrocoelum lacteum* O. F. Müller

The embryonic development of *Tricladida* takes place within a cocoon consisting of a hard non-transparent tunic. Nevertheless, the course of development processes can be observed in vivo if, immediately after the cocoon of *Planaria torva* is laid, its content is sucked out by means of a capillary tube, spread on a cover-slip and protected against drying[1]. The span of life of such a culture is, however, limited. The embryos die early, when the syncytium becomes surrounded by the cells of provisional ectoderm. By aid of the method described above SEILERN-ASPANG[1] could state that the deformation (flattening) of the embryonic buds (embryonic area) caused by the conditions of culture results in polyembryony. Since, in the course of normal embryonic development of *Dendrocoelum lacteum*, undisturbed by any experimental factor, polyembryony was observed[2], it seemed to be of interest to study the behaviour of the embryos of this species under experimental conditions, i.e. raised on cover-slips.

The content of a newly laid coccoon of *D. lacteum* was spread all over a cover-slip of a moist chamber by means of a glass pipette. The moist chamber consisted of 2 cover-slips separated by a 3 mm thick vinidur ring whose diameter was 20 mm. A small tampon of wet cotton was inserted into the moist chamber. The edges of the slides were tightened with sterile vaseline. The cocoons, before being punctured, were put into penicillin and streptomycin solution for 5–10 min. The pipettes, slides, ring, cotton etc. were sterilized by means of UV-radiation. The temperature of the culture was 20–25 °C.

A few hours after the cocoon content is spread on the cover-slip of the moist chamber, some vitelline cells encircle the egg-cell and form a compact layer. After 24 h, when the dissolving vitelline cells form syncytia, the germs become more or less flat, depending on the thickness of the mass of cells spread all over the cover-slip. In such a flattened syncytium one can clearly distinguish a more granulous external part and a more homogeneous inner part containing the blastomeres (Figure 1). After 3 days the embryo assumes a spherical shape, and sometimes if the layer of the spread mass of cells is sufficiently thin, it bulges over the surface. On 1 pole of the spherical embryo one can easily see the formation of embryonic pharynx. The embryo containing an embryonic pharynx is, strictly speaking, a specific larva which is able to

[1] F. SEILERN-ASPANG, Zool. Anz. *159*, 193 (1957).

[2] B. KOŚCIELSKI, J. Embryol. exp. Morph. *12*, 633 (1964).

swallow up the vitelline cells. In the course of the swallowing process, the larva performs some uniform rotatory movements. According to METSCHNIKOFF[3], the embryo of *Planaria polychroa* at the larval stage, being covered with cilia, is able to perform some movements. On the other hand, MATTIESEN[4] states that the provisional ectoderm is not equipped with cilia and at this stage the embryo does not move. Similarly, other authors[5–7] have not confirmed the presence of cilia at the larval stage. According to my observations, the larva equipped with embryonic pharynx performs some rotatory movements. So far, however, the factor responsible for these movements is unknown. The author, like the scientists mentioned above, has not confirmed the presence of cilia in provisional ectoderm, either in cytological preparations[8] or in observations conducted in vivo (although they could be conducted for an arbitrarily long time). It is possible that the rotation is caused by the contractions performed by the pharynx, and by the currents of liquid resulting from these contractions. It seems that this movement plays an important role in swallowing vitelline cells. If the larva remained immobile within a cocoon, it would have at its disposal merely a certain amount of vitelline cells lying near its pharynx. The swallowing of vitelline cells lasts for about 6 h. With the end of this process, the provisional intestine, being filled with the swallowed vitelline cells, takes up almost the entire interior of the larva (Figure 4). The rotatory movements performed by the larva gradually cease. During the next few days, the larva's body becomes flattened and somewhat elongated. 10 days later the embryo has already developed into a juvenile form which, being equipped with cilia, floats actively among the vitelline cells (Figure 5). The anterior end of the animal is widened.

The development described above takes place in cultures, where the spread cellular mass forms a sufficiently thick layer. If the content of the cocoon forms a thinner layer, the resulting syncytia are much flattened. The fate of such syncytia is different and depends on the degree of flattening. In the least deformed embryos, a spherical larva bulges from the large oval syncytium and, performing rotatory movements, swallows up the granular mass of the syncytium (Figure 4). Such larvae develop into normal ciliated forms. In more flattened syncytia, the inner part containing the blastomeres divides into 2, 3 or sometimes into 4 areas that contain a few or several blastomeres (Figure 2). The manner of division of the

[3] E. METSCHNIKOFF, Z. wiss. Zool. *38*, 331 (1883).
[4] E. MATTIESEN, Z. wiss. Zool. *77*, 274 (1904).
[5] B. FULIŃSKI, Bull. int. Acad. pol. Sci. Lett. 147 (1914).
[6] B. FULIŃSKI, Zool. Anz. *47*, 380 (1916).
[7] R. CARLÉ, Z. Morph. Ökol. Tiere *29*, 527 (1935).
[8] B. KOŚCIELSKI, Zoologica Pol. *16*, 83 (1966).

The microphotographs represent living embryos of *D. lacteum* raised on cover slip.

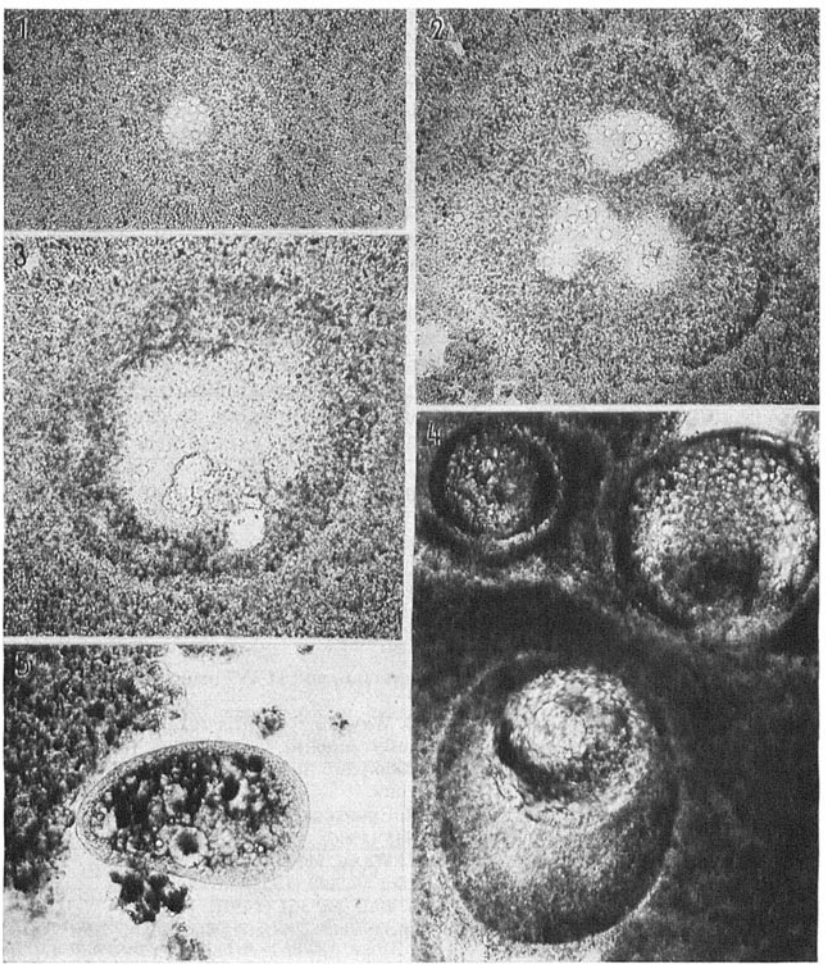

Fig. 1. Flattened syncytium of *D. lacteum*. Blastomeres seen in its inner part.

Fig. 2. More flattened syncytium of *D. lacteum*. The inner part of the syncytium has been previously divided into two parts, of which one (the lower on the microphotograph) continues its division. In the upper, as well as in the right lower embryonic areas, some blastomeres are differentiating into the embryonic pharynx.

Fig. 3. Most flattened syncytium. On one of its poles (in lower part of the microphotograph) one sees the pharynx pumping the granular mass into the syncytium. An empty light space seen below the pharynx indicates the spot from which the trophic material was taken out.

Fig. 4. The larval stage. In the upper right corner one sees an immobile larva filled entirely with the swallowed vitelline cells. Below a larva rotating within the oval syncytium.

Fig. 5. A 10-day-old juvenile form of *D. lacteum* raised on a cover slip.

embryonic area of *D. lacteum* raised on a cover-slip is different from that of *Planaria torva*[1], being rather similar to the division observed in natural polyembryony[2]. The divided syncytia of *D. lacteum*, like those of *P. torva*[1], do not develop into larvae. It seems that the factor which induces polyembryony (sufficiently thin layer of the cocoon content spread all over the cover-slip) makes, in turn, both separation and rounding of the buds difficult. Nevertheless, the beginning of the differentiation of the blastomeres into the embryonic pharynx could be observed in the separated areas (Figure 2). In the most flattened syncytia, neither is part of the syncytium surrounded by the cells of provisional ectoderm, nor does the division of the inner part of the syncytium take place. Nevertheless, some blastomeres differentiate into the embryonic pharynx (Figure 3) and are able to perform normal functions.

Summing up, it should be stated that the embryonic development of *D. lacteum*, starting from an egg-cell, to a form in which the differentiation of germ-layers takes place, can be investigated in vivo on cover-slip cultures. This method allows a deeper experimental analysis of the development of *Tricladida*.

Résumé. En culture entre lamelles de verre, on a examiné expérimentalement le développement embryonnaire de *Dendrocoelum lacteum* et observé le phénomène de la polyembryonie expérimentale analogue à la polyembryonie naturelle.

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Department of General Zoology of the Zoological Institute, University of Wroclaw (Poland), April 4, 1966.

Pharmacogenetic Factor in the Convulsive Responses of Mice to Flurothyl

The existence and the importance of genetically-determined variations in sensitivity to drug action is emphasized in the new subject of pharmacogenetics as defined and reviewed by KALOW[1] and MEIER[2]. Among the reports of differing drug responses between inbred strains of mice there are several involving drugs affecting the central nervous system, but few dealing with convulsants. MEIER et al.[3] determined the reactivity of 4 strains to pentylenetetrazol in an attempt to correlate this convulsive response with strain-characteristic 'arousal levels' as reflected in locomotor activity. Of these 4, the DBA/2 mice had the shortest latency and longest duration of convulsions with intraperitoneal pentylenetetrazol, while C57BL/6 mice had by far the longest latency. Similarly, we have reported that DBA/2 mice differed considerably from the C57BL/6 strain and from 2 lines of random-bred albino Swiss mice, having the lowest latency for myoclonic jerk and clonic seizure in response to the volatile convulsant ether flurothyl[4]. In the present research we sought to confirm these earlier observations and further test the correlation of convulsive and locomotor responses using certain of the same strains as in the studies cited above.

Measurements of the convulsive response to flurothyl (hexafluoordiethyl ether, Indoklon[5]) were conducted by the continuous inhalation method of TRUITT et al.[6], with the exception that a 15% rather than a 10% concentration of flurothyl in ethanol was used. Latencies (in sec) for first myoclonic jerk, for first sustained (3 sec) clonic seizure and for tonic extensor seizure were recorded while adding 0.05 ml of flurothyl every 30 sec. Measurements of locomotor activity were made upon groups of 4 mice placed without injection or other treatment into photocell-type actometers (Woodard Research Corp., Herndon, Virginia). Total counts for a 30 min period were recorded for 6 groups from each strain.

Inbred mice of the C57BL/6, DBA/2, C3H/An, CBA and BALB/c strains were obtained from Cumberland View Farms (Clinton, Tenn.). A random-bred Swiss-Webster albino strain (NLW) was obtained from the National Laboratory Animal Co. (Creve Cœur, Mo.). All mice were received at 30 days of age and were convulsed at 38–45 or 49–56 days of age. Others tested for locomotor activity were between 6 and 12 weeks old.

Responsiveness of the 6 strains to flurothyl was determined twice, using 20 different mice of each strain in each of the 2 replications. Tests were confined to a 3 h time span (08.30–11.30) to avoid circadian variation[7]. The results (Figure) show considerable differences between strains that were rather consistent between replications. There was significant heterogeneity among variances for the different strains: the C3H strain showing a particularly low variance while the BALB/c strain was at the high extreme. The data were transformed to reduce the heterogeneity in order to permit analysis of variance. For the myoclonic jerk latencies the transformation used was $\log(x - 50)$, and for the remaining data the transformation was $\log(\times - 100)$. As variances were still slightly short of the desired degree of homogeneity by the test of DAVID[8], an α-level of 0.01 rather than 0.05 has been used in the analyses of variance and intergroup comparisons in accord with the recommendation of MCNEMAR[9].

Variance analyses which were conducted across the 2 replications for each of the 3 convulsive response criteria revealed highly significant differences between treatments (strains + replications) and among strains ($p < 0.005$, Table I). There was one significant replication effect but no significant interactions (strain × replication). The Duncan multiple range test[10] was applied to the means of combined replications for all strains at each of the 3 response criteria. Significant ($p < 0.01$) differences among the 6 strains are indicated in Table II.

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