certain prolongation of the last instar; however, it was statistically insignificant.

Contrary to this, a statistically significant delay of pupation was noted only when the drug in the dose of 125 µg/g b.wt was applied 3 times: on the 1st, 3rd and 5th day of the 7th stage (figure 1). Some differences in the percentage of newly-formed pupae were visible on the 9th and 12th day after the last larval ecdysis ($p < 0.05$, figure). On the 9th day, the percentage of new pupae was 0 in treated insects, whereas, in the control group-injected with saline, it reached about 37, and about 21 in untreated insects. On the 12th day, the percentage of pupae increased in all groups, and it attained about 42 in tranquillized insects, about 83 in those injected with saline, and about 64 in normal ones. During the period between the 9th and 12th days, the greatest and statistically most significant retardation was noted ($p < 0.001$, figure).

The percentage of pupae in both control groups permanently increased, attaining 34-54 on the 10th day and 54-73 on the 11th, whereas in the tranquillized group it was 0 all along. In the latter group, the pupation had only started on the 12th day. In both control groups, pupation proceeded parallel. The minimal differences between them were statistically insignificant for the whole period analyzed. These results showed that neither application of saline, nor the injury due to injection, retarded pupation. Almost complete pupation in both control groups was reached around the 16th day. On the contrary, on the same day pupation in the tranquillized group did not even exceed 80%.

Reserpine is retained for a long time in the insect organism[11,12], as well as in other animals[13-15]. As just mentioned, this drug evoked accumulation of neurosecretory granules in the neurosecretory cells of *G. mellonella* brain probably inhibiting, the release of neurosecretory material. Then, 3-fold reserpine administration (on the 1st, 3rd and 5th day) gave a cumulative effect, inhibiting release of neurosecretory material during the whole last larval instar. Therefore, in our experiments pupation started with a certain delay, probably when the neurosecretum had been released in consequence of diminished action of reserpine. Hence, the most effective dose of the drug, applied to larvae of the last stage, was 125 µg/g b.wt when it was injected repeatedly.

It is very interesting to speculate whether such a large drug dose, being sublethal, caused only retardation of larval-pupal ecdysis, or whether it caused some disturbances in other processes of metamorphosis. This problem will be the subject of our next studies.

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Atypical mast cell degranulation and focal hydropic degeneration of venular endothelium in diffuse fibrosing alveolitis

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Summary. Atypical scroll-like and tubular degranulation of mast cells closely associated with focal endothelial hydropic degeneration is reported in human lung from 4 patients with diffuse fibrosing alveolitis in which the predominant abnormality was hyperplasia and desquamation of type 2 pneumocytes.

Detailed electronmicroscopy study was carried out in 13 patients with diffuse fibrosing alveolitis (diffuse interstitial pulmonary fibrosis). Lung tissue obtained at thoracotomy was fixed immediately with either combined aldehyde or gluteraldehyde fixative. Multiple sections from at least 3 blocks of tissue were examined in each case.

In 8 patients the main finding was moderate or severe interstitial fibrosis with minimal hyperplasia and desquamation of the type 2 pneumocytes. In the remaining 5 patients the predominant abnormality was marked hyperplasia and desquamation of the type 2 pneumocytes with variable fibrosis. In these cases the mast cells were increased in number and in 4 the granules within the mast cells assumed a scroll-like appearance (figure 1). In some sections the granules showed a tubular morphology (figure 1). In the cases with this scroll or tubular type of degranulation, the mast cells were adjacent to areas of focal hydropic degeneration of endothelial cells of venules of the microcirculation (figure 2). Aberrant degranulating mast cells and/or abnormalities of the venular endothelium were not seen in the 8 patients with minimal hyperplasia and desquamation of type 2 pneumocytes.

The association of atypical mast cell degranulation and focal hydropic endothelial degeneration does not appear to have been reported previously in pulmonary diseases nor have we noted this finding in 22 other open lung biopsies. Similar scroll-like mast cell degranulation has previously been described in normal human bronchi and lung[2]. The significance of this type of mast cell degranulation is not known, bit it is important that this ultrastructural change is recognized since it may be confused with viral inclusions, particularly those with morphology similar to rhabdo

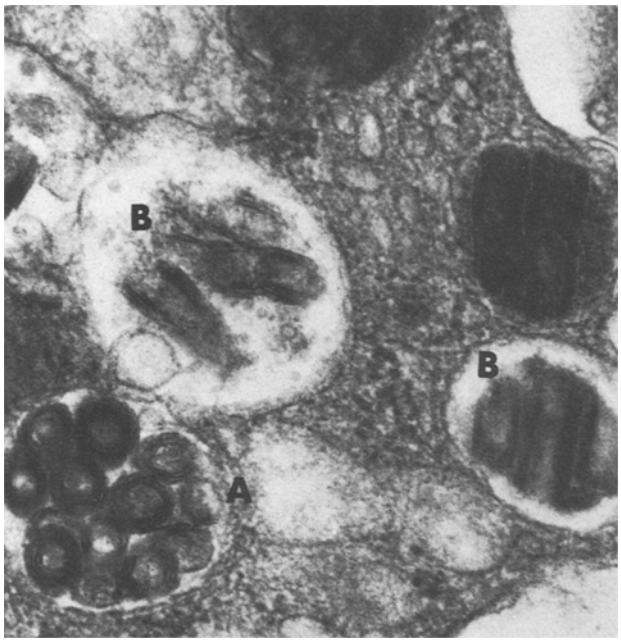

Fig. 1. Electronmicrograph of cytoplasm of a mast cell showing unusual forms of degranulation with scroll (A) and tubular (B) configurations. Tubular configurations may represent longitudinal sections through scrolls. Uranyl acetate and lead citrate. × 36,500.

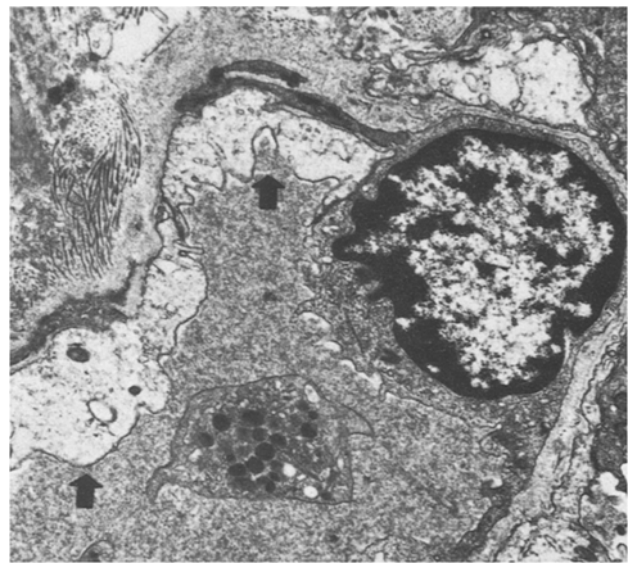

Fig. 2. Electronmicrograph of a pulmonary interstitial venule showing gross hydropic degeneration (arrows). Uranyl acetate and lead citrate. × 8,000.

viruses[3]. Endothelial changes in venules have been reported previously in secreting carcinoid tumours of the stomach[4]. Localized endothelial changes might result from local release of vasoactive factors from mast cells and argentaffin cells.

The association of atypical mast cell degranulation and hydropic endothelial degeneration in patients with marked hyperplasia and desquamation of type 2 pneumocytes leads to speculation that these reactions might have a pathogenic role in some forms of diffuse fibrosing alveolitis. The present findings are reported to focus attention on an unusual morphological association in this enigmatic pulmonary disorder in the hope that it will be confirmed by other diagnostic electron microscopists.

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DPH-induced macrocytosis in the 14-day rat foetus

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Summary. Phenytoin injected in the pregnant rat induces in the 14-day-old foetus macrocytosis of the primitive red blood cells which is sometimes linked with limb haemorrhages. The action of the drug is possibly the result of a blood circulation disturbance.

It is well known that epileptic patients can develop megaloblastic anaemia during long-term treatment with diphenylhydantoin (DPH)[1]; moreover, folate deficiency has sometimes been shown in these patients[2]. Nevertheless, the action of anticonvulsant drugs on folate metabolism is not yet clearly understood. Several explanations have been proposed, including inhibition of intestinal folate conjugase[1], increased hepatic degradation of folic acid during enzyme induction by anticonvulsants[3], and intestinal malabsorption of pteroylmonoglutamates[4].

Teratogenic effects of DPH in humans have been reported and reviewed by several authors[5]. The drug is also teratogenic in rodents[6-10]. The primary defect seems to be cleft palate, but many other skeletal defects have been observed. Several authors obtained the same types of abnormalities in foetal mice and rats by using a folic acid deficient diet[11,12], or by administration of folate analogs and antagonists[13,14]. More recently, several authors obtained similar results by using aminopterin[15] and methotrexate[16]. Although folic acid deficiency is certainly responsible for the teratogenicity of DPH, the processes leading to congenital malformations still remain unknown. Pyrimethamine, another antifolic drug, injected in pregnant rats, induced in foetuses both macrocytosis of the nucleated red blood cells and severe haemorrhages resulting in necrosis of the limbs during the following days[17]. This experiment shows for the first time the existence of a relationship between the presence of foetal blood macrocytosis and the induction of