Cell Turnover in Pulmonary Tissues

In recent years considerable interest has been shown in the turnover of epithelial cells, particularly those in the gastro-intestinal tract[1,2]. These investigations have been facilitated by the introduction of autoradiographic techniques and the use of tritium-labelled thymidine. This is incorporated specifically by the nuclei of cells in pre-mitosis, at which time synthesis of deoxyribonucleic acid (DNA) is occurring[3].

Bertalanffy and Leblond[4] reported their findings in an investigation of cell turnover in the lung in the albino rat, in which they used the technique of mitotic counting after colchicine arrest; but extensive search of the literature has not revealed any other studies on the pattern of cell turnover in pulmonary tissue.

This communication records the findings of an investigation into turnover of the cells in mouse lung using tritium-labelled thymidine and autoradiography. It has been assumed that the labelled cells behave in the same way as normal cells although it is possible that the use of tritium-labelled substances may result in modification of the DNA molecule[5].

18-day albino mice were used. 100 μc. of tritium-labelled thymidine (Atomic Energy Research Establishment, Harwell; 100 mc./m*M*) in 0·2 ml. saline were injected intraperitoneally into each animal at 11 a.m. on the first day of the experiment. Afterwards the animals were maintained in free-run cages with full access to chow and water. Paired animals were killed by ether anæsthesia at intervals of 1, 6, 24, 48, 72 and 96 hr. after injection and further pairs after 1 week, 10 days and 3 weeks respectively.

The trachea and lungs were dissected immediately and fixed in 10 per cent formalin solution. Paraffin-embedded sections of whole lungs were cut to include parts of the main bronchi and autoradiographs were prepared using stripping-film technique (Kodak; *AR*10). After exposure for one month, and developing, the sections were stained with neutral red. All the slides were examined by light microscopy.

1 hr. following injection it was found that only scattered epithelial cells in the large bronchi showed nuclear labelling. The labelled cells were situated mainly, but not exclusively, in the basal layer of the bronchial epithelium. The superficial cells showing labelling at 1 hr. were no longer present at 3 days.

Over the three-week period of observation the labelled cells in the basal layer showed migration towards the surface of the epithelium. Very occasional labelled cells, however, were still present at the end of this time. In the small bronchi and respiratory bronchioles only scattered, labelled epithelial cells were seen at 1 hr. Turnover was faster than in the large bronchi and no labelled cells were present at 10 days.

With the techniques used it was clear that the scattered, labelled cells seen in the walls of pulmonary alveoli were macrophages. It was impossible, however, accurately to differentiate histologically between the vacuolated and non-vacuolated forms described by Bertalanffy and Leblond[4].

At 7 days the labelled cells showed an abrupt decrease, but thereafter the appearances remained roughly constant with, at 3 weeks, very occasional cells still showing labelling. There was no evidence of shedding of labelled cells into alveolar spaces in any of the sections.

In the pleural tissues scattered mesothelial cells showed labelling at 1 hr. While occasional cells still showed labelling at 10 days, none was evident at 3 weeks.

It is apparent, therefore, that unlike the widespread uptake of tritium-labelled thymidine shown by gastro-intestinal epithelium, the uptake by respiratory epithelium is limited to scattered cells. This low degree of mitotic activity and slow turnover of cells may be related to the fact that, under normal conditions, respiratory epithelium is not exposed to significant amounts of trauma, nor is it called on to secrete large quantities of enzyme, as is the situation, for example, in the small intestine. It is also of interest to find that, contrary to orthodox opinion, mitosis is not confined to cells in the basal layer of bronchial epithelium but also occurs in the intermediate and superficial layers.

From our observations we have concluded that the turnover time for epithelial cells in the small bronchi and respiratory bronchioles is 7–10 days. In the large bronchi it was apparent that the superficial cells showing labelling at 1 hr. had a shorter life-span (3 days) than the overall figure of 3 weeks while occasional basal cells had a longer life-span, since labelling was still present at 3 weeks. These epithelial cells with greater and lesser life-span did not differ histologically from those epithelial cells with a turnover time of 3 weeks.

In the pulmonary alveoli, despite the failure to make a histological differentiation between vacuolated and non-vacuolated macrophages with the techniques used, the marked decrease in labelled cells at 7 days indicated that the majority of these macrophage cells had a life-span of approximately 7 days. It is considered that these probably corresponded to non-vacuolated macrophage cells which were estimated by Bertalanffy and Leblond[4], using mitotic counting, to have a life-span of 8 days. The alveolar cells showing labelling after 7 days later proved to have a life-span in excess of 3 weeks. These probably represented vacuolated macrophages which Bertalanffy and Leblond[4] estimated to have a life-span of 29 days.

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ANATOMY

Significance of Arachnoidal Cell Clusters in Man

Since the early part of this century arachnoidal cell clusters in man have generally been accepted as a manifestation of advancing age. They were first described by Meyer[1] as a post-mortem finding in the meninges of patients suffering from mental disease. It has since become evident that they occurred not only in man but also in various laboratory animals[2,3]. Their association with advancing age can be attributed largely to the work of Weed[4], who, in a series of cats of