

fashion and a tracheal papilloma. Alone I_2 did not induce any respiratory tract tumors, but given in combination with B(a)P induced 2 papillomas of the larynx and 19 papillomas in the trachea. These papillomas were composed of a fibrous stalk covered by proliferating epithelium. The 1st papillomas were seen in this group in an animal that died 8 weeks after the start of the treatment. Alveolar epithelial proliferation was also common, although the condition was not always of a neoplastic nature. Benign epithelial growth in the bronchiolar region resulted in tumors composed of small cuboidal cells arranged in a glandular fashion. Peripheral adenomatoid lesions were common, along with adenosquamous lesions, 2 adenomas and 2 squamous cell carcinomas of the lung were seen. In B(a)P/ $FeCl_3$ treated animals, an activating effect of the dust was noticed, although not as strongly as with B(a)P/ I_2 . $FeCl_3$ alone was ineffective, but in combination with B(a)P induced 6 tracheal papillomas. Tumor distribution is given in table 2.

The carcinogenic polycyclic aromatic hydrocarbons are relatively inert as far as reactions with cellular components are concerned. The specific chemical binding of hydrocarbons with biological macromolecules^{6,7} - probably the 1st essential step in cancer induction - requires that the compounds be activated by cellular hydroxylating enzymes¹. Several hydroxylases require transitional metals (iron is the most commonly found) for enzymic activity², and this suggests that metals play a role of prime importance in the hydroxylation reaction. A covalent binding of B(a)P and other carcinogenic hydrocarbons to nucleic acids⁸ is also produced by I_2 , hydrogen peroxide, hydrogen peroxide plus ferrous ion.

Previous studies have mainly involved the physical characteristics of the dust. One of the main functions of the carrier agent was considered to be an increased retention time of the dust, compared to B(a)P alone^{9,10}. Chemical activation by metals of polycyclic hydrocarbons has been reported in experiments in mouse skin¹¹. Since atmospheric pollution may contain, and cigarette tobacco tars do contain, both various metal ions and aromatic hydrocarbons, the results presented here, may be relevant to the etiology of pulmonary cancer in man.

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Pigment granules in choroidal melanophores of the albino goldfish¹

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Summary. Pigment granules in choroidal melanophores of the albino goldfish contained fine particulate materials which were in various degrees aggregated in clumps. Tyrosinase was considered to be present in an inhibited state in these pigment granules.

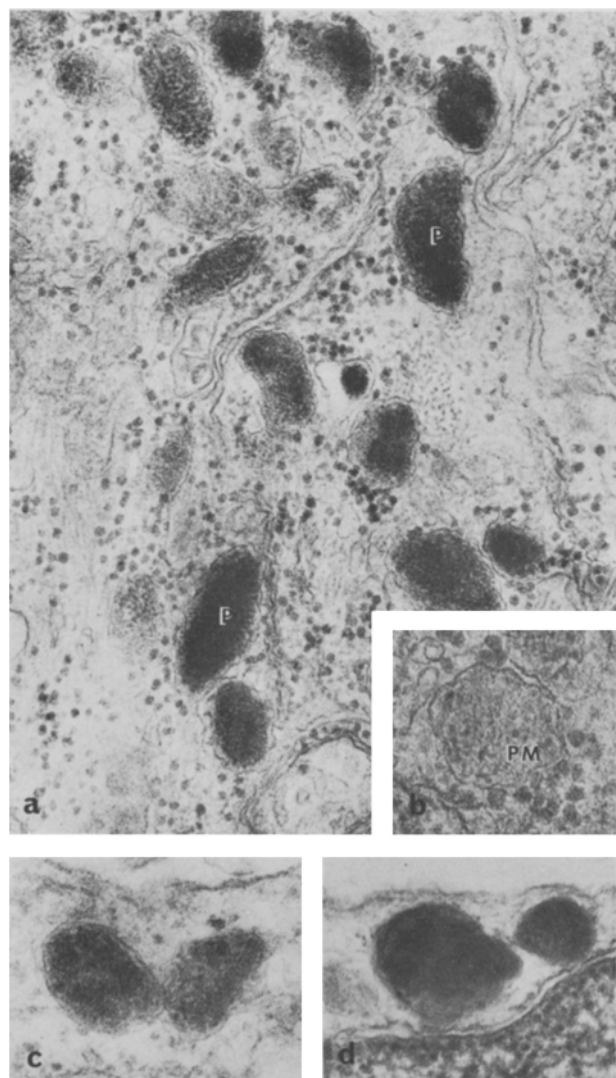
In the melanin-synthesizing cells of many vertebrate species, melanin pigments are synthesized and stored in pigment granules called 'melanosomes'. In higher vertebrates, premelanosomes, the unpigmented precursors of melanosomes, have a highly organized internal structure composed of numerous coiled filaments, which are arranged parallel to each other and oriented along the long axis of the granule³. This internal structure of the premelanosome has also been reported in dermal melanophores and retinal pigment cells of some species of Reptilia⁴, Amphibia^{5,6}, and Pisces⁷. Recently, however, we have reported that the premelanosomes in melanophores of the guppy and retinal pigment cells of the goldfish contained only fine particulate materials^{8,9}. On the other hand, Turner et al.¹⁰ claimed that the premelanosomes in melanophores of the goldfish are multivesicular-type in their inner structure. To clarify this, pigment granules in choroidal melanophores of the albino goldfish were examined electron microscopically in the present study. The albino mutant is known to show complete or incomplete absence of melanin synthesis in melanosomes, and is very suitable material to study the premelanosome inner structure¹¹.

From the adult goldfish (*Carassius auratus*) of the albino strain (gene symbol, *pp,cc*⁹), the eyes were removed intact and immersed in a Karnovsky's solution. In this solution,

choroidal layers of the eyes were dissected out and cut into small pieces. Fixation and embedding into epoxy resin were according to the same method indicated in the previous paper¹².

Cytoplasm of choroidal melanophore was filled with numerous pigment granules. Most of these granules were ellipsoidal in shape, about 0.2 μ m in diameter and 0.4 μ m in length, and contained fine particulate materials which were in various degrees aggregated in clumps (figure, a). However, no granules whose cores had been completely occupied with these materials were encountered. These observations indicated that melanization was only partially stopped in these pigment granules. Pigment granules were sometimes found in which fine particulate materials were only lightly deposited. This type of granule was always smaller in size than the densely pigmented one (figure, b). Thus, it was considered to be the precursor of the densely pigmented one, that is, the goldfish premelanosome. Granules with a multivesicular-type core were not found in the present study.

For the detection of tyrosinase activity, the tissues were first incubated with Dopa according to the method described by Ide¹³. This treatment resulted in no ultrastructural changes in the pigment granules (figure, c). Secondly, the tissues were incubated with Dopa and iodoacetamide according



a Pigment granules in choroidal melanophore of the albino goldfish (P). $\times 50,000$. b Premelanosome (PM). $\times 90,000$. c Pigment granules after incubation with Dopa. $\times 47,000$. d Pigment granules after incubation with Dopa and iodoacetoamide. $\times 47,000$.

to Hishida et al.¹⁴ with the slight modification, namely, that the incubation time was shortened from 24 h in their method to 3 h, to avoid the autoxidation of Dopa. This treatment produced full melanization in most of the pigment granules (figure, d). These results indicated that tyrosinase is present in an inhibited state in these pigment granules^{14,15}. In several animal species, the albinism has been attributed in part to the inhibition of melanin formation caused by the presence of tyrosinase inhibitor¹².

As described briefly in the previous paper, the particulate or granular type of premelanosome inner structure has recently been reported in the melanocytes of certain skin-color mutants of the mouse and of mammalian melanomas⁸. Additionally, this type of premelanosome was reported in the melanophores of the melanomatous xiphophorus fish¹⁶ and in the melanocytes in café-au-lait spots of neurofibromatosis¹⁷ and in lentigines of Leopard syndrome¹⁸ in man. The albino goldfish seems to be a suitable material for studying the formation of these unusual premelanosomes.

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Histochemical localization of cholinesterases in the neural tissue of the pineal in the rhesus monkey¹

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Summary. The neural tissue of the monkey pineal contains both acetyl and butyryl cholinesterases. Acetylcholinesterase was localized in the cisternae of the nuclear membrane, rough endoplasmic reticulum, on the plasma membrane of the neurones, and on the axolemma of both non-myelinated and myelinated fibres. The enzyme was not found in the axosomatic or axo-dendritic synapses. It is therefore suggested that the pineal neurones have a cholinergic function rather than a cholinceptive one.

The pineal of the rhesus monkey is distinguished by the presence of a distinctive and substantial mass of neural tissue comprising neurones, axons, dendrites and glial cells^{2,3}. Ultrastructural and experimental studies have shown that the pineal-neurones and their dendritic processes are innervated by nerve fibres originating from, or coursing through the habenula³. The present studies were carried out to determine the distribution of cholinesterases in the neural tissue of the pineal with a view to understanding its functional role.

14 healthy, adult female rhesus monkeys, each weighing 5–6 kg, were used in the present studies. The pineals of 6 monkeys were processed⁴ for studying the distribution of specific (acetyl) and nonspecific (butyryl) cholinesterases by optical microscopy. The pineals from the remaining 8 monkeys were processed⁵ for studying the ultrastructural