•15• Albino animals - use and misuse

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The main aim of this chapter is to show that albino animals are far from always good models. Many important enzyme systems are abnormal in albino animals, and these animals should not be used uncritically. The choice of the correct animal model is essential for Refinement.

Albino animals have had and continue to have very extensive use as experimental animals. Unfortunately they are occasionally used uncritically and without taking into consideration that they may not represent the optimal model. Albino animals are available in most of the usual research animal species. They can of course be excellent models for the study of albinism, but this is appropriate in only a very limited number of experiments. In most experiments, the albino animal model is used to represent general biological processes or phenomena or normal pigmented humans or animals.

If albino animals are just normal animals that happen to be white, then it would not have been a problem, but the albino model has its clear limitations. There are in fact a series of important differences in addition to colour that separate albino animals from the pigmented. It is important to be aware of these differences such that informed decisions can be made between albino and pigmented strains for use in experiments. There are ever increasing claims that pigmented animals rather than albino animals are more often the optimal model for most objectives in biomedical research.

Many features of albino animals are different from pigmented animals. Important differences can especially be observed in metabolism, the neurosensory system and behaviour. C-locus albinism is characterized by a lack of tyrosinase, an enzyme that is necessary for the synthesis of the pigment melanin. Accordingly, all metabolic pathways that involve tyrosine and tyrosinase are altered. Many chemical substances, including some comparatively common medicaments, bind to melanin and can be stored in pigmented tissue for long periods. This applies particularly to polycyclic drugs. Streptomycin, clindamycin, nicotine, chloroquine, pilocarpine, serotonin, adrenaline, noradrenaline and dopamine are reported to bind to melanin. Such drugs will have a significant tendency to accumulate in melanin-rich tissues such as the skin, eyes, the inner ear and some parts of the brain. Many of the named drugs can cause cellular damage in melanin-containing tissue because of accumulation and prolonged binding. The malarial drug chloroquine, for example, is reported to cause a toxic effect on the retina and in the ear. The drug will in addition cross the placenta and accumulate in melanin-containing tissues for up to 90 days. Foetal injury has been demonstrated in pigmented animals. If the drug was tested in albino animals (that lack melanin), the medicament would have an altered pattern of distribution and would not give the same harmful effect. Prolonged use of the phenothiazine sedatives such as chlorpromazine in high doses results in accumulation in the iris, cornea and lens in a high proportion of pigmented patients. In some cases, a general chlorpromazine-induced melanosis with pigment deposition in the kidneys, myocardium and liver can occur. Similar effects will not be observed in albinos where accumulation of the drug does not occur.

It is less well accepted that a series of other enzyme systems are also affected, including cytochrome P-450, glutamine synthetase and glucuronyl transferase. Morphological deviations in the liver's endoplasmic network in albino animals result in microsomal changes. Anaesthetic period, lethal dose and microsomal enzyme response of the liver are significantly different in albino animals compared with pigmented animals. The cytochrome P-450 system localized in the endoplasmic network is central to oxidative metabolism and detoxification of many drugs in the liver. The activity of this system is different in albino animals compared with pigmented animals. The P-450 system is operative in newborn pigmented mice, but cannot be demonstrated in newborn albino mice. After the administration of alcohol or pentobarbital, which are metabolized by the P-450 system, albino mice or rats will have a longer anaesthetic period than pigmented animals. The lethal dose of these drugs is lower in albino rats than in pigmented rats. Drugs such as DDT or eucalyptol have been shown to give stronger induction of microsomal liver enzymes in albino stock than in pigmented animals. Ultrastructural changes have also been demonstrated in the Golgi apparatus and the nuclear membrane in albinos. Newer research can however indicate that the differences demonstrated are probably not linked directly to the albino gene. Nevertheless, it is still important to know that many albino strains show significant deviations in the P-450 system.

Defects in visual and auditory senses are correlated with albinism and hypopigmentation in a number of mammals including Man, the mouse, rat, guinea pig, rabbit and cat. The connection between albinism and neurosensory defects is the result of a common embryonic origin (neural crest). Possibly the most classical functional defect in association with albinism is vision. A lack of pigment in the retina not only gives the animals red eyes, but also gives much poorer protection against light-induced injury to the retina. Specific optic fibres are reduced in number in albino animals. Structural differences in the eye result in dissimilarities in electroretinography (ERG) between nonpigmented and pigmented animals. Similar defects have also been demonstrated in the auditory system and anatomical changes in the cerebral cortex have been described. Experiments have shown that melanin has a direct significance for the uptake of retinol and transfer of the drug to and from the photoreceptor cells.

Albino rats were initially preferred by researchers because they were generally less aggressive than their pigmented counterparts, so it should not be surprizing that albino animals often show behavioural deviations from pigmented animals. However, the reduced aggression of nonpigmented animals is not connected to the albino gene itself. A number of behavioural differences have been demonstrated in tests for evaluating visual learning. Some of these can be connected to differences in the animal's visual senses. Albino rats have been shown to learn more slowly than pigmented rats.

The concentration of many serum proteins, such as albumin, transferrin and alpha-fetoprotein are significantly different in albino animals compared with pigmented animals of the same species. In addition to the usual form of albinism resulting from the genotype cc, other mutations are also found that give complete or partial albinism. These hypopigmented animals often have structural, functional and metabolic defects in addition to a melanin deficiency. For example, animals with Chediak-Higashi syndrome, a type of partial albinism, have defects in phagocytes, thrombocytes, NK cells and tubule cells in the kidneys.

A related theme is drugs that bind to pigmented cells in brain tissue and that produce an illness similar to Parkinson's disease. Such a drug is MPTP that binds to neuromelanin, especially in the substantia nigra of the mid-brain. Primates and amphibians have neuromelanin in their nerve cells and therefore are highly sensitive to the toxic effects of MPTP. Rodents in general, and not just albino animals, have little or no neuromelanin, and can therefore be less suited as models for Parkinson's disease.

Conclusion

Many more substantial differences can be found between albino and pigmented animals than the colour of their fur. These differences can have significance for your experiment. If you do not have a special reason to choose an albino strain, why not consider using a pigmented animal? One should especially investigate whether the following factors can be significant for the experiment:

1. Drugs that have affinity for melanin will have an altered distribution and therefore often different effects in albino animals.
2. Many important enzyme systems, e.g. tyrosinase, are abnormal in albino animals.
3. One should be aware of differences in the sensory apparatus and behaviour.

Perform literature searches and/or pilot studies to investigate whether these factors are of significance for your experiment, if you wish to use albino models.

References

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