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prey. Thus, selection is expected to favour uniform warning signals and suppress variation. Nevertheless, warning signal variation is evident across the natural world. The mechanisms maintaining this puzzling variation are still poorly understood, but it is thought that this may arise for various reasons. Some warning signals may serve other purposes, such as intra-specific signalling, or be a response to different selective pressures which would trade-off with the pressure exerted by predators. For example, in the colour polymorphic wood tiger moth (*Parasemia plantaginis*), yellow males are generally better defended from predators. In contrast, under some circumstances, white males are more successful at mating and have higher flying activity, which might help them find emerging females quicker or compensate behaviourally for a less efficient anti-predator colouration. In cold environments, increased black wing pattern elements bring thermoregulatory benefits to these moths, but at the cost of reduced warning coloration (white or yellow). Recently, local predator communities have also been shown to aid in the maintenance of warning signal variation. Hence, it is likely that different properties of warning colouration become costly or beneficial in changing environments. Finally, it cannot be discarded that the variation is not adaptive, but the product of hybridisation or drift.

Are warning signals honest?

According to the 'handicap principle', signals that provide reliable information about an individual's quality should be selected for. Such signals must be costly for the signaller and, thus, unaffordable for low-quality individuals. Warning signals can be honest, if they are reliable indicators of prey unprofitability. Therefore, secondary defences may vary as well, and this variation may by no means be less relevant. For example, in the strawberry poison frog (*Oophaga pumilio*) great variation in toxicity among populations is positively correlated with conspicuousness. Likewise, in the seven-spot ladybird (*Coccinella septempunctata*), the amount of coloured pigments correlates positively with the level of chemical defences. At least for the ladybirds, this correlation seems to depend on resource availability. This means that there can be costs associated with the production of primary or secondary defences, or both, that may affect the effectiveness of aposematism.

Are there cheaters? Yes. When predators learn to avoid a warning signal that is shared among aposematic individuals, organisms of other species may mimic that signal and get protection benefits without investing in secondary defences or predator education. In Batesian mimicry, a palatable organism is protected by its resemblance to an unpalatable one. Thus, Batesian mimics should not be considered aposematic, because they lack a secondary defence. The increase of Batesian mimics in a population decreases the efficacy of the signal, because predators start to ignore it as it becomes less reliable. Maybe the most well known Batesian mimics are hoverflies, which resemble wasps and bees. In Müllerian mimicry, on the other hand, two or more aposematic animals have evolved a similar appearance that is avoided by predators. Textbook examples include the famous *Heliconius* butterflies and dart poison frogs in the *Ranitomeya imitator* complex. In fact, mimicry is one of the first and strongest pieces of evidence for Darwinian natural selection.

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Quick guide

Deaf white cats

Andrej Kral[1] and Stephen G. Lomber[2]

What are deaf white cats? The term 'deaf white cat' is used to describe domestic cats with completely white fur (short-hair or long-hair) that have no functional hearing; they typically have blue eyes (Figure 1A). It is estimated that in the overall cat population, 5% are white, and a subpopulation of these are blue eyed. As early as 1868, Charles Darwin noted in his book *The Variation of Animals and Plants under Domestication* that "white cats, if they have blue eyes, are almost always deaf". This observation has been substantiated in many subsequent studies. Deafness identified in white cats can be bilateral (both ears), or, less frequently, unilateral (one ear) with residual hearing in the opposite ear.

What makes deaf white cats so interesting? Any mammal can fail to develop functional hearing. In many species, such as domestic cats and dogs, there is a higher incidence of deafness in animals with a white coat. The association between white coat and deafness is greatest in white cats with blue eyes. Animals bred for this trait are a natural model for human congenital deafness. Consequently, deaf white cats are ideal for studying the effects of hearing loss on development and function of the auditory system. Furthermore, studies examining this animal model have demonstrated the beneficial effects of hearing restoration with cochlear prosthetics (implants). These experiments were essential for evidence-based recommendations on the treatment of congenital deafness in children. Today, approximately 400,000 hearing impaired individuals world-wide benefit from cochlear implants in their daily life. Given the present rate of implantation, the number of people using cochlear implants is projected to reach one million in 2020. Overall, the cochlear implant is the most successful neuroprosthetic device.

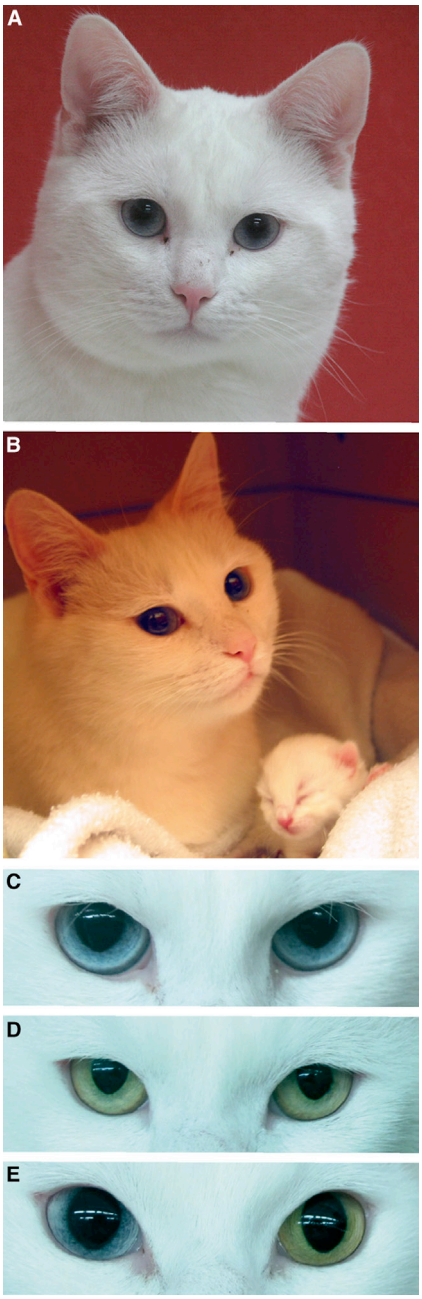

Figure 1. The phenotype of the deaf white cats is characterized by white fur, blue irises and hearing loss.
(A) Photograph of a congenitally deaf cat with blue eyes. (B) Congenitally deaf queen with a young pup a few days old. The eyes of the pup have not yet opened. (C–E) Examples of iris colors from three white cats in the deaf white cat colony in Hannover: (C) two blues eyes; (D) both amber eyes; and (E) a heterochromy (one blue and one amber eye). Photo credits: B. Tiemann (Universitätsklinikum Hamburg-Eppendorf) and A. Burghard (Hannover Medical University).

Why are deaf white cats deaf? There are three general forms of hearing loss: conductive, sensory or neuronal. Conductive hearing loss refers to the inability of acoustical vibrations to reach the cochlea (the inner ear) and stimulate hair cells, the sensory receptors. In contrast, sensory hearing loss refers to the inability to transduce the vibrations into neuronal excitation caused by the loss of sensory hair cells. Finally, neuronal hearing loss is due to damage anywhere along the auditory pathway that prevents the transmission of excitation from the cochlea to cortex.

In deaf white cats, the reason for the hearing loss is sensory in nature. These cats show an inherited degeneration in the cochlea with a cascade of deleterious events resulting in the loss of inner and outer hair cells. Supporting cells in the organ of Corti are partially preserved and the spiral ganglion (auditory nerve) degenerates very slowly with age.

The inheritance of deafness is autosomal, non-Mendelian, but more similar to recessive than dominant patterns. The involvement of several genes in the deaf phenotype is likely. The genetic background is related to the W-locus and possibly involves the encoded growth factor receptor known as c-Kit. In colonies of white cats bred for deafness, about 70% of the offspring are deaf if deaf parents are mated.

How is deafness confirmed? Even in white cat colonies bred for deafness, not all animals are born deaf. As a rule, pigmentation of kittens safely excludes non-white deafness; however, to confirm deafness, screening procedures of hearing are required. One of the less invasive objective methods applicable in cats is the measurement of auditory-evoked brainstem responses. This method detects small changes in the electrical field evoked by stimulation of the auditory pathway by sound and can be performed under sedation using small silver electrodes placed subcutaneously. Similar methods have been introduced to screen Dalmatian pups for deafness where, again, hearing loss is associated with whitish fur. Such screening has to be performed early in life. In humans, similar newborn hearing screening procedures have been introduced in many countries to identify and treat neonatal hearing loss.

***Are all cats born deaf*?** Yes, they are all born deaf; cats are altricial animals whose sensory systems (eyes and ears) become functional sometime after birth (Figure 1B). Typically, hearing onset in cats takes place during the second week of life, with first responses in the auditory pathway to stimuli below 100 dB SPL at 10 days after birth. In contrast, the somatosensory and olfactory systems are functional at birth, allowing the newborn cats to find the papillae and orient in the first days of life in the nest. The standout advantage of the use of altricial animals in developmental neuroscience is the ability to control the hearing status from its onset onward.

Are deaf white cats albino or Siamese? A popular misconception is that deaf white cats are albino; however, albino cats have pink 'unpigmented' eyes, whereas deaf white cats have blue or (less frequently) amber eyes (Figure 1C–E). White cats have different amounts of melanin, while albino cats are devoid of melanin. No relation between hearing loss and albinism has ever been demonstrated. Another misconception is that the deaf white cats have Siamese traits; however, Siamese cats have unusual visual systems that include an abnormal retinogeniculate pathway. No such findings have been reported for deaf white cats that are not related to Siamese cats. Deaf white cats also have the same visual acuity as non-white cats.

Are all white cats deaf? No. The proportion of hearing-impaired animals in the colony differs with respect to the breeding strategy. If deaf white cats are mated, the majority of offspring (about 70%) are deaf. The remaining animals are either hearing impaired to a different degree (but not deaf) or have normal hearing. A small proportion (~1%) of unilaterally-deaf animals can also be identified. The

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cats often have a blue eye ipsilateral to the deaf ear and a non-blue eye ipsilateral to the hearing ear. To eliminate this inherent variability, hearing screening must be performed early in life. If diagnosed as deaf in this screening, the resulting animals are called 'congenitally deaf cats'. Even non-white cats can theoretically be deaf, but the proportion of such animals is very low.

Do deaf white cats have any other functional deficits? Theoretically, genes causing deafness may affect other bodily functions. However, white cats, even congenitally deaf cats, behave otherwise normally. Several studies directly compared parts of the brain and its functions to hearing animals. Neither in the somatosensory, motor nor the visual system are congenitally deaf cats impaired compared to hearing animals. In fact, it has been demonstrated that the visual functions of congenitally deaf cats are supranormal, presumably to compensate for the loss of hearing, and they have enhanced integrative visual functions like visual motion detection and localization. For these supranormal functions, portions of the acoustically-deprived auditory cortex are recruited. Similar supranormal visual functions have been observed in perinatally deaf humans.

Are deaf white cats different from deafened animals? In addition to hereditary deafness, hearing loss can also be induced by local or systemic application of drugs that destroy hair cells. The histology of the inner ear differs between deafened animals and deaf white cats. Ototoxic drugs as a rule destroy not only hair cells but also other cells in the organ of Corti and neurons that give rise to fibers of the auditory nerve. In combination, this leads to pronounced loss of auditory nerve fibers that provides an additional complication when comparing hearing and deafened animals. However, the advantage of pharmacological deafening is that it can be induced at any age. Consequently, to understand the complex effects of deafness, it needs to be investigated in both congenital and acquired deafness models.

Can hearing be restored in deaf white cats? Yes, it can. In fact, deaf cats have been an exceptionally useful model for studying effects of such restoration in the brain. The feline auditory system is similar to humans; cats can perform similar acoustic functions as humans. Their brain is gyrencephalic (unlike rodents), containing many cortical auditory areas (over a dozen), and cats have a similar low-frequency hearing ability to humans (which is not the case, for example, in mice or rats). Furthermore, cats are an excellent model for investigating multimodal interactions, as cats are highly visual and auditory, unlike rodents that mainly use their hearing and their somatosensory system (whiskers) for orientation. As the cochlea of these animals is large enough, a neuroprosthetic device, called a cochlear implant, can be used to restore hearing at nearly any age. Such studies have revealed that early hearing is important for normal development and maturation of the auditory system. Furthermore, limits of such plasticity ('sensitive periods') and their possible mechanisms have been explored using this animal model.

Where can I learn more?

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Primer

Polyploidy

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Polyploidy is defined as an increase in genome DNA content. Throughout the plant and animal kingdoms specific cell types become polyploid as part of their differentiation programs. When this occurs in subsets of tissues within an organism it is termed somatic polyploidy, because it is distinct from the increase in ploidy that is inherited through the germline and present in every cell type of the organism. Germline polyploidy is common in plants and occurs in some animals, such as amphibians, but will not be discussed further here. Somatic polyploid cells can be mononucleate or multinucleate, and the replicated sister chromatids can remain attached and aligned, producing polytene chromosomes, or they can be dispersed (Figure 1). In this Primer, we focus on why somatic polyploidy occurs and how cells become polyploid — the first of these issues being more speculative, given the status of the field.

Why cells become polyploid

The clearest general use of somatic polyploidy appears to be as a mechanism to produce large cells. This is exploited in some developmental contexts in which fewer, larger cells have functional advantages over a similar total mass of an increased number of smaller cells. Polyploidy additionally may augment gene expression or metabolism.

Polyploidy as a means to increase cell size

One use of polyploidy is to generate large cells, such as mammalian megakaryocytes or the giant cells that contribute to the structure of organs such as *Arabidopsis* leaves. It has been appreciated since late in the 19th century that cell size is proportional to nuclear size, and this was subsequently shown to reflect DNA content. Thus, both polyploid and polytene cells are of increased size, some attaining sizes orders of magnitude larger than diploid cells, with corresponding