

Commentary

Allergy is rare where butterflies flourish in a biodiverse environment



Figure 1. Painted Lady (*Vanessa cardui*) is a cosmopolitan and one of the most widespread butterflies in the world. Population explosion happened in 2009.

Butterflies, the showy 'flying flowers' are used a lot as environmental indicators. In Europe, out of 576 butterfly species, at least 71 (12%) are severely threatened (1). Many other are rapidly declining. The major threat is habitat loss; intensive urban and industrial development and effective land use isolate butterfly populations. They form large metapopulations in spatial landscapes, where a balance of extinction and colonization of new popula-

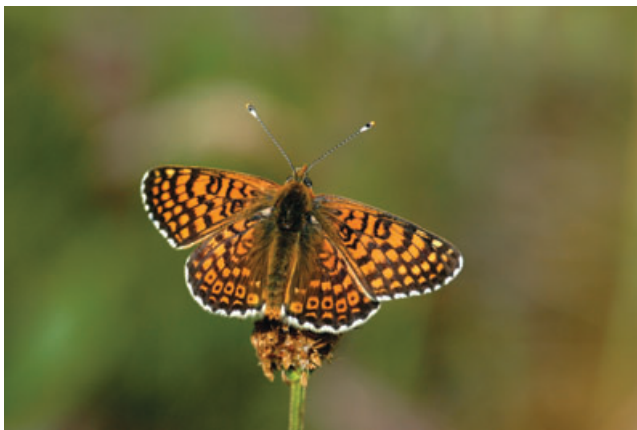


Figure 2. Glanville Fritillary (*Melitae cinxia*) is the legendary butterfly chosen for field experiments by ecologist Ilkka Hanski from Helsinki University. The real-life experiments in the Åland archipelago, Finland, formed the basis for the mathematical models of the metapopulation theory (22).

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tions exists (2). The vitality of a metapopulation decreases if the local populations become extinct more often than new colonies emerge. The fragmentation becomes crucial when distances between the colonies increase. The metapopulation starts to suffer with the poor gene flow between isolated colonies. The disequilibrium is a death spiral and sooner or later the species is lost. This 'island effect' and extinction can even be mathematically predicted (3).

Only a few species have undergone an increase. In summer 2009, all over Europe we have enjoyed millions of Painted Ladies (Fig. 1), which migrated everywhere



Figure 3. Small Apollo (*Parnassius phoebus*) is a very local butterfly in the Central European Alps. It is threatened by overgrazing of alpine and subalpine grasslands, tourist industry, and smelting of the glaciers.



Figure 4. Corsican Swallowtail (*Papilio hospiton*) is endemic to Sardinia and Corsica. It is strictly protected and threatened by human activities.



Figure 5. Balkan Copper (*Lycaena candens*) is a stunning but rare sight in the southern Balkans. The habitats, the wet hillside bogs, are endangered by land drainage.



Figure 6. Nogel's Hairstreak (*Tomaes nogelii*), the tiny jewel, has almost disappeared from Europe. It lives in small isolated colonies in southeastern Romania. Agricultural changes and tourist activities are destroying the populations.



Figure 7. Chequered Blue (*Scolitantides orion*) has a large but discontinuous distribution in Europe. It is declining in North and Central Europe and considered threatened, but the reasons are unknown.

from northern Africa to Greenland. This population explosion was caused by last winter's unusual rains. We saw a lot of butterflies, but they were of the same species, while in pristine natural environment, we come across only a few butterflies, but every individual seems to be of different species. Painted Ladies thrive in city gardens and waste land, at the top of mountains and seaside. They conquer the earth when the more vulnerable and demanding species disappear. This is globalization in the butterfly world; everything becomes the same. Climate change affects the habitats and larvae food plants. While some species seem to gain new territories, this does not change the net effect; butterflies are in trouble in all over the industrialized world. This also indicates alarming shrinkage of biodiversity, the crucial condition for all life.

Diseases date back to the dawn of humankind and come and go. Rare diseases have become common and once common ailments have disappeared. Diseases succeed and fail in response to human development. About 10 000 years ago, the hunter and nomad invented agriculture and started to domesticate animals. That was an ecological jump to a different world—especially in terms of microorganisms—to a world which formed basis of modern civilization and gave impetus to massive increase of human population. Humans became susceptible to cholera, tuberculosis, measles, smallpox, and zoonoses of many kinds. In the 19th century, improved hygiene and sanitation started to reduce many of the infections and old plagues. Industrialization and scientific revolution gave us antibiotics and vaccines, polio is near extinction and smallpox is history.



Figure 8. Polar Fritillary (*Clossiana polaris*) is one of the rarest butterflies, living only in the arctic regions of Europe. Global climate change may push it over the cliff. The very northern species may be the most vulnerable and do not have a place to escape.

Now diseases previously of secondary importance are on a rapid increase in the developed but are also appearing in the developing world; chronic immunological disorders, allergy among them, cardiovascular diseases, cancer, and depression. Etiology of these diseases is not known and is multifactorial and genetically complicated. We can call them 'civilization diseases'.

In allergic individuals, exposure to allergens/bioparticles does not lead to the development of tolerance as in healthy individuals, but instead, results in prolonged inflammatory responses. The crucial players are regulatory T cells. The question in broken tolerance appears to be of imbalance between different T cell types. In atopic individuals, the proportion of regulatory T cells is markedly diminished or their function is impaired (4, 5). Generational analyses showed that



Figure 10. Elban Heath (*Coenonympha elbana*) is small and goes easily without notice. It is endemic to Elba and the nearby mainland. The butterfly lives in a very restricted area, some of which is now protected.



Figure 9. The two-tailed Pasha (*Charaxes jasius*) is big and strong and flies around the Mediterranean coast. It is the one and only butterfly of the Charaxes family in Europe. It is threatened by construction and business development of the coastal areas.

asthma incidence increased progressively by birth cohort among subjects born between 1946 and 1971, and changes in environmental exposure seem the major reason (6). Sensitization rates against inhalant allergens by birth cohorts born in 1923–1990 have shown similar trends (7). Environment rich in microbes in childhood reduces the risk of developing atopic disease later in life (8). Along with urbanization, the perpetual coexistence of environmental microorganisms with man has been severely disturbed. Continuous stimulation of the innate immunity by commensals and saprophytes is necessary for mucosal homeostasis (9). Such continuous stimulation of the immune system through the skin, respiratory tract, and gut activates the regulatory network, which is decisive in the development of tolerance (10, 11).



Figure 11. De Lesse's Brassy Ringlet (*Erebia nivalis*) reflects metallic brass amongst limestone outcrops above 2000 m in eastern Central Alps, in the evolutionary centre of the Erebia Family. Its early developmental stages are threatened if snow and ice disappear.

Table 1. Practical recommendations to obtain and maintain tolerance (23, modified)

Primary prevention	Secondary and tertiary prevention
Support breastfeeding, solid foods from the age of 4–6 months.	Promote regular physical exercise in children and adults, and especially in asthmatics.
Do not avoid environmental exposure unnecessarily (e.g., food, pets).	Promote healthy diet (e.g., Mediterranean type of diet improves asthma control).
Strengthen immunity by increasing connection to natural environment.	Consider use of fermented food or other preparations including probiotic bacteria.
Strengthen immunity by regular and moderate physical exercise.	Consider allergen-specific immunotherapy:
Strengthen immunity by healthy diet (e.g., traditional Mediterranean or Baltic type).	– allergens as is (food)
Use antibiotics with thought. Vast majority of microbes are useful and support health.	– sublingual tablets or drops (e.g., timothy, birch), SLIT
Probiotic bacteria in fermented food or other preparations may strengthen immunity.	– subcutaneous injections, SIT.
Do not smoke.	Hit early and hit hard respiratory or skin inflammation.
	Find treatment for long-term control.
	Do not smoke.

We used to think allergy as hyper-responsiveness, i.e., too active immune response, but it may be the other way around. It might be caused by epithelial hyporesponsiveness to bioparticles, as a consequence of ‘poor training’ by microbial exposure, especially in early childhood. During the birch pollen season, more transcripts show modified expression levels in nasal epithelium in healthy compared to allergic subjects (12). The hyporesponsive immune system has not had the practice to make the difference between danger and nondanger, self and nonself.

An urban environment appears to lack elements that are necessary for the proper development of tolerance against foreign proteins (13). The key issue in tolerance development might well be the diversity of microorganisms in our environment. The microbial quantity and diversity in the drinking water and house dust were strikingly different in Finnish and Russian Karelia—with highly contrasting allergy prevalence—and had allergy protective effect (14–16).

IgE system seems to act complementary to other immune responses, and it is one of the guardian angels monitoring the borders between man and environment. If poorly educated, it gets activated of innocuous proteins and attaches to the short fragments of polypeptide chain located in the beta strands of the epitopes. These strands cover a flat area on the allergen surface and may mimic similar structures in pathogens like parasites (17).

The diversity of butterflies was comparable in Russian and Finnish Karelia (18), but in Finland, they escaped to small areas compared to Russia, where the more natural

conditions allowed wider distribution of both species and individuals. Isolation and ‘island effect’ are threatening the Finnish fauna (19). More generally, in areas with high butterfly diversity, allergies are rare. In those areas, humans are more closely connected with soil, and the immune system is still adapted to the agricultural era. In Karelia, this was demonstrated for CD14 and CC16 polymorphism; both CD14 C-159T and CC16 A38G, the risk allele for atopic phenotypes in Finland, were the protective allele in Russia (20). No doubt, epigenetic mechanisms will gradually adapt humans to live with concrete and glass, in the urban jungles (21). The natural environment with all the microorganisms, some of them potentially dangerous, may, in future, be a real surprise to the highly sophisticated urban T cells.

In the wake of immunologically new humankind, I add one recommendation to the means in the Finnish Allergy Programme (Table 1) to obtain and maintain tolerance; let us take care of the butterflies! Their disappearance indicates loss of life. When the last tiger is killed in India, it may hit the headlines, however, shrinkage of biodiversity also takes place in the micro-world close to us, but without notice. Preserving biodiverse life might have a preventive effect on allergy and other diseases of modern civilization.

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