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8th ESCP Conf., Strasbourg 1986, pp. 1-14 (Karger, Basel 1987)**Exposure to Stressful Environments**

Strategy of Adaptive Responses

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Abstract. Any new natural environment may generate a number of stresses (such as hypoxia, water lack, and heat exposure), each of which can produce strains in more than a single organ system. Every strain may in turn stimulate the body to adapt in multiple ways. Nevertheless, a general strategy of the various adaptive responses emerges when the challenges are divided into three groups. The first category includes conditions that affect the supply of essential molecules, while the second is made up by those stresses that prevent the body from regulating properly the output of waste products, such as CO₂ and heat. In both classes, there is a small number of responses, similar in principle, regardless of the specific situation. The third unit is created by environments that disrupt body transport systems. Problems may arise when there is a conflict between two stresses requiring conflicting adaptive changes. An alternative to adaptation, creation of micro-environment, is often favored by the animal.

Survival of a population often hinges on its ability to occupy new ground. Relocation may be forced upon a species by a variety of causes, chief among which are natural disasters, gradual changes in the climate, displacement from the ecological niche by a dominant competitor, or the disappearance of some other animals or of plants upon which the group under consideration depends in one respect or another, usually as a food source. Spill-over into an adjacent territory also occurs when successful colonization creates an unacceptable increase in population density. Unfortunately for the migrators, contiguous areas frequently have different climatic features and therefore provide new living conditions, making existence syno-

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Table I. Stresses produced by some environments

Environmental challenge	Stress				
	O ₂ balance	heat balance	water balance	food supply	etc.
Altitude	+++	++	++	?	
Diving	+++	+++			
Desert life		+++	+++	+++	
Jungle life		+++			
Confinement	++	++	++	?	
Acceleration	+++				
Etc.					

A number of environments are listed in the leftmost column. The *major* stresses created by each are shown in the subsequent columns, with a gradation indicated by the number of + signs. 'Etc.' indicates that the table should be extended in both directions by adding environments and stresses.

nymous with the talent to adjust to altered, and often unfriendly, environments. The gamut of possible adaptive responses is extensive, covering subtle modifications in behavioral patterns at one end of the spectrum and major remodeling of anatomical or biochemical structures at the other extreme, with functional modifications making up the mid-range. Some of the adaptive changes may occur during the lifetime of a single individual, others require several generations.

In discussing the fundamentals of adaptation, Dejours [1] defined this process as 'a change minimizing the physiological strain which results from a stressful environment'. The chain of events can therefore be summarized by the following progression:

New environment → stress → strain → adaptation.

The scientist who works at the bench is usually interested in a single cause-consequence pair, studying an isolated variable under carefully controlled and reproducible conditions, and therefore has no problem with this scheme. His colleague in the field who attempts to provide real-life synthesis of laboratory findings is in a far less favorable position because this deceptively simple sequence is complicated by the fact that each of the steps is multiplicative: an environment often creates more than one stress, each of

Table II. Strains caused by environmental stresses

Stress	Strain				
	circulatory system	respiratory system	urinary system	digestive system	etc.
O ₂ balance	+++	+++		+	
Heat balance	+++	+++			
Water balance	+++	+	+++	++	
Etc.					

Major strains produced by each stress are shown, with the gradation indicated by the number of + signs. 'Etc.' extends the table in both directions.

which – if severe enough – may generate several strains, and any one of these usually triggers numerous adaptive mechanisms. Table I describes the stresses that are caused by selected environments while table II lists the strains that correspond to some of these stresses.

Because the plethora of relationships shown in tables I and II would make a list of environments and adaptive steps both lengthy and unrewarding, it is necessary to resort to a simpler approach, and to attempt to sketch adaptation in broader lines, focusing on salient points only. For a more comprehensive, up-to-date review, see Senay [2].

The 'milieu exterieur' acts both as a source and as a sink, supplying the organism with its basic requirements such as metabolites, water and oxygen, and accepting in return carbon dioxide and other wastes, including heat. Thus, animals have to face two major types of environmental problems: on the 'input' side there can be a mismatch of supply to demand, while on the 'output' side, the surrounding medium may not be able to handle break-down products, forcing the body to store them. Let us examine both sets of challenges in more detail.

Environments Causing 'Input' Problems

The common adaptive strategies that one can detect are those with which we are familiar in the field of economics; when availability fails to meet demand one can reduce consumption, switch to alternate sources or

develop new routes of supply, rely on substitutes, improve internal transportation, and prioritize distribution so as to ensure that vital operations are maintained. If the problem is recurrent and can therefore be anticipated, one should stockpile essential materials before the emergency occurs. The way in which living organisms adopt these measures when they are subjected to stressful environments can be illustrated by what is intended to be a selection of appropriate examples rather than an exhaustive list.

Lack of Metabolites: Complete or Partial Starvation

Adaptation to a limited caloric intake triggers a number of the responses we have just reviewed. There is a decrease in metabolism, which has the obvious consequence of stretching the insufficient supplies. This drop in demand, reviewed by Grande [3] for man and animals can be attributed to two causes: (1) body mass shrinks, reducing the size of the body to be fed, and (2) the metabolic rate of active tissue slows down gradually, stabilizing after a few weeks. The first of these two changes cannot be considered to be adaptive; the second certainly is. In parallel, the organism develops alternate sources of essential materials, an example being provided by generation of glucose from other entities, in particular lipids. Storage of fat before an extended period of fasting has been well documented in hibernators and in birds preparing to migrate, and is discussed in terms of the incubating penguin by Le Maho [4] elsewhere in this volume.

Water Balance

Whereas some natural stresses (such as problems of O₂ supply and of insufficient food intake) can occur on their own, i.e. in the absence of other perturbing factors, this is seldom the case for water balance. Lack of water is usually associated with thermoregulatory problems, and occurs not only in very hot environments but also in extremely cold ones, where the energy needed to melt ice makes water in liquid form a scarce commodity. Furthermore, these two conditions may boost water loss, the first through sweating and/or increased insensible water loss, the second mainly by decreasing the water vapor content of the inspired air.

Water economy can be achieved only by reducing outgo. Desert rodents produce feces which are practically devoid of water, urine becomes more concentrated, sweating is reduced. A number of steps can also be taken to diminish pulmonary water vapor loss, either by having it deposit in the upper airway during expiration and entraining it during inspiration, or simply by reducing minute volume. Clearly, a sizeable drop in ventilation is

tolerable only if it is coupled with a shift of the hemoglobin dissociation curve to the left, so as to maintain adequate oxygenation of the arterial blood.

Much has been made of the ability of the kangaroo rat to obtain water from metabolic sources, allowing the animal to live without intake of preformed water. It has been pointed out [5] that H₂O extraction from food is more complex than would appear and can be successful only under certain conditions: one can calculate that as the camel uses its fat reserves, it also obtains water but the increased O₂ requirement implies the need for extra ventilation and hence a rise in respiratory water loss. The latter may exceed the gain, leaving the animal with a water deficit!

It is well known that animals can carry water reserves. In addition, the behavior of some desert rodents generates an extracorporeal water store: by hoarding grain in their burrows, where it absorbs some of the moisture [5], they recycle part of the water they lose.

Oxygen Balance

Adaptation to an inadequate supply of oxygen deserves special mention for several reasons, the most important of which is probably that the body's O₂ stores are woefully small in comparison to its needs. While life without water or metabolites is possible for variable but extended periods of time, the total amount of oxygen stored in the body and available for emergency use can last only a few minutes at rest, much less at exercise.

Another unusual feature of this stress is that there is usually no shortage (or excess) in the *amount* of O₂ available, as is the case for water or food. Even at the top of Mount Everest, a climber would have an infinite number of oxygen molecules at his disposal; his problem is that this gas is presented at a low partial pressure, which hinders its transport.

Hypoxia

Decrease in partial pressure of inspired O₂ can be caused by one of two conditions: there may be either a drop in the fractional concentration of the gas in the environment, as occurs in burrows, or a reduction in total barometric pressure, as is found at altitude. The usual adaptive response is multifaceted, and some of its features depend on whether one is looking at a single acute episode, repetitive encounters with the stress, or chronic exposure. Just as is the case with starvation, a severe deficit in oxygenation leads to a reduction in consumption [6], but the strategy relies mainly on lowering the ventilatory and the circulatory resistances to oxygen transport so as to

decrease the O_2 pressure drop at each step of the oxygen cascade. As a result of these changes, the total P_{O_2} difference between inspired and mean end-capillary blood – to the extent to which this is reflected by mixed venous blood – is reduced from more than 100 Torr at sea level to one-third of that value or less at high altitude. Note that whereas the ventilatory conductance can only be improved by increasing alveolar gas flow, the rise in circulatory conductance is due to both a quantitative factor, i.e. a boost in cardiac output, and a qualitative one, resulting from higher hemoglobin concentration and often a favorable displacement of the hemoglobin dissociation curve, this shift being particularly well illustrated in fish that breathe O_2 -poor water. When hypoxia is extreme or is combined with exercise, which increases the O_2 demand, another mechanism listed earlier, i.e. switch to a different metabolic pathway, is often invoked as the subject or animal satisfies part of the metabolic demand through anaerobic glycolysis. Clearly, this can take place for only a limited time, after which oxygen must be used to recycle lactate. For a more extensive discussion of the combined effects of hypoxia and exercise, see Cerretelli [7].

Some of the other general strategies which we have listed earlier are also implemented in specific cases of adaptation to low oxygen. As examples (1) a number of species have undergone evolutionary changes to survive in the presence of hypoxia: certain fish living in oxygen-poor water have developed lungs of various degrees of complexity, often using them as an auxiliary system, i.e. only when the water cannot supply the O_2 demand [8]; (2) diving mammals illustrate the benefits to be gained by prioritizing blood flow distribution and hence oxygen delivery: severe vasoconstriction of all the beds that subserve areas whose continuous unimpeded function is not imperative allows the animals to allocate the scarce oxygen reserves practically entirely to their heart and their brain; and (3) the blood volume of these diving mammals and their hemoglobin concentration are both high, increasing the amount of O_2 that can be stored prior to the dive [9].

Hyperoxia

At the cellular level, there are chemical reactions that scavenge superoxide and associated products, as reviewed by Crapo [10]. In contrast to the rich, assorted spectrum of systemic reactions to low oxygen, adaptive responses to hyperoxia appear to be limited to vasoconstriction and a moderate decrease in cardiac output, which reduces O_2 transport to the tissues, moderating the rise in cellular P_{O_2} . The input that triggers that

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Table III. Adaptive responses to 'input' environmental stresses

Response	Stress				
	lack of food	lack of water	hypoxia	hyperoxia	etc.
Decreased consumption	+++	+++	++		
Development of alternate sources/supply routes		++	++		
Substitution	++		+		
Transport optimization			++++	+	
Allocation of priorities	+	++	+++		
Stockpiling	++	+	++		

Only the most frequently used responses are shown. For details, see text.

response is not clear, although some experiments [11] indicate that the phenomenon is dependent, at least in part, on the P_{O_2} beyond the arterial tree.

One should note that, as opposed to hypoxia, which occurs in a variety of natural environments, hyperoxia is almost invariably an artificial challenge. It does occur in fish living in ponds or seawater pools where the photosynthesis of a rich aquatic flora creates diurnal P_{O_2} cycles with a peak that can reach 600 Torr [12], but not in air breathers. The existence of adaptive mechanisms, limited as they may be, is either fortuitous or the consequence of the fact that, as life's environment went from a reducing atmosphere to an oxidizing one, some responses against the increasing O_2 level may have emerged. Obviously, this explanation is tenable only for the cellular reactions, since complex organisms having a well-defined circulatory system developed long after oxygen had become part of our environment.

Overview of Responses

The parallelism of the various steps is emphasized in table III, which lists the most common features encountered in the environmental stresses we have just sketched. Because of space limitations, several challenges have been grouped under one heading. As an example, 'Hypoxia' covers such diverse conditions as the drop in P_{O_2} encountered at altitude or by fish living

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in waters with little oxygen, the decrease in oxygen fraction faced by the fossorial species, or the temporary lack of oxygen of an animal during a breathhold dive. Obviously, only some of the responses listed in one column will be elicited by one specific environment.

Environments Causing 'Output' Problems

With rare exceptions, problems on the 'input' side are caused by deficiency rather than by excess, since in the vast majority of cases an animal cannot be forced to avail itself of an oversupply but remains free to limit its intake to a desirable, safe amount. On the 'output' side, the stress may be either surfeit or scarcity: complete elimination of some of the important products of metabolism is often undesirable, and since many of these (such as heat and carbon dioxide output) have to be adjusted to maintain body levels within a narrow range, an abnormally high loss can be as close to catastrophic as reduced elimination.

Responses to environmental conditions that affect output are perhaps best understood in terms of a simple electrical model. In this analog, the material to be eliminated is compared to electrons moving from a high potential at the point where they are generated, to a low potential in the surrounding medium, through a series of resistors, each of which represents a step in the transport chain. The desirable level at each location – equivalent to voltage – is set by adjusting properly the different resistances. Environmental stresses may act on the system either by altering the potential of the sink or by affecting the resistance of the outermost transport link(s). It is easy to recognize immediately the possibility of three adaptive responses, namely (1) readjustment of the resistances in the transport chain; (2) change of the intensity of the current generated at the source; and (3) creation or enhancement of capacitances to better handle retention, in particular when this occurs in surges. We shall use stresses on the thermoregulatory system and on CO₂ elimination to illustrate these mechanisms.

Thermoregulation

Exposure to Heat

It is obvious that an increase in ambient temperature causes an immediate drop in the temperature gradient across the skin, which means that less heat can be dissipated if skin conductance remains fixed. The obvious

compensation, i.e., a decrease in the resistance to heat transfer across the outer insulation layers, is brought about mainly by vasodilation of the skin and the underlying tissues. At the same time, an attempt is made to cool the contact surface by evaporative heat loss, the efficiency of sweating depending of course on the ambient humidity. The problem is that these responses require an increase in peripheral perfusion, easily accomplished at rest, but not so at exercise, because (1) the skin competes with muscle for available blood flow, and (2) sweating decreases plasma volume and may therefore interfere with development of maximal cardiac output. Thus, core temperature rises during exercise, restoring (at least partly) the outward heat gradient. Interestingly, the acclimatized subject is presented with an additional problem: as he sweats more, he becomes dehydrated (and should compromise his maximum cardiac output) faster; some desert animals have risen to the challenge by developing mechanisms that allow them to maintain plasma volume while subjected to heat dehydration. For details, see the chapter by Horowitz and Samueloff [13].

Exposure to Cold

Cold stresses are generated not only when the body is exposed to a lower ambient temperature, but also when body heat is drained at too fast a rate because of an increase in thermal capacity or conductance of the surrounding medium. Not surprisingly, adaptation to cold invokes the same regulatory mechanisms as heat exposure, but in the opposite direction. When the stress is essentially continuous, as in the case of diving mammals, physical insulation is provided by a thick layer of subcutaneous fat. When the exposure is transient, but repeated, resistance to heat flow is increased by peripheral vasoconstriction, in particular in acclimatized individuals, whose maximum tissue insulation exceeds that of nonacclimatized subjects having the same cutaneous thickness [14]. Metabolism rises, generating more heat, and can of course be boosted dramatically by shivering [15].

Carbon Dioxide Retention

The first and foremost defense mechanism, increase of the CO₂ conductance, that is, hyperventilation, is brought into play whenever possible. Storage of the retained CO₂ is also attempted, and in this respect one must distinguish between animals that are faced continuously with high levels of CO₂, such as rodents living in burrows, and those that are exposed only intermittently. In either case the problem is to maintain pH, but this is accomplished by different means. The animals that live in a high CO₂

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Table IV. Adaptive responses to 'output' environmental stresses

Response	Stress			
	heat	cold	CO ₂ retention	etc.
Resistances adjustment	+++	+++	+++	
Flux adjustment	+++	+++		
Increased capacitance			+	

For details, see text.

environment retain bicarbonate in their plasma and extracellular fluid; on the other hand, diving mammals rely on better buffering power of their blood.

Overview

Table IV shows the similarity between the various mechanisms just listed. The reservations expressed in relation to table III apply here also.

Environment and Transport Problems

The preceding two sections have made it clear that optimization of the internal transport system is often the critical feature of adaptation. It is therefore appropriate to indicate here that certain environments leave the input and output sides unaltered but disrupt the ability of the body to either supply the cell or detoxify it. One such condition is exposure to high pressure, where the rise in respired gas density makes it difficult to maintain adequate alveolar ventilation. Another is increased acceleration, especially along the long axis of the body, that is foot-to-head. This stress, which is equivalent to an increase in gravitational pull, is always manmade, but is nonetheless interesting from both the scientific and the practical points of view. It acts primarily by magnifying the normal tendency of the blood to pool in the dependent parts of both the systemic and pulmonary circulations, thus reducing venous return and hence cardiac output. This sequence often lowers brain perfusion to dangerous levels or even reduces it to zero,

causing the dreaded 'black-out' of military pilots, who may be subjected to accelerations of more than 10 G.

Duration of exposure to high G is usually much too short to evoke adaptive mechanisms, but one must remember that the strain depends on the pressure exerted within the vessels in the dependent parts of the body, a pressure that is a function not only of gravity, but also of the height of the blood column. Therefore, very tall animals have to defend themselves against edema formation in the lower part of their limbs even at normal G. The complete picture of the adaptive mechanisms is not yet clear, but it is known that the skin of the giraffe's extremities is very tight and can therefore act as a natural anti-G suit.

The topic of acceleration fits perhaps best within the scope of this review when one considers the opposite end of the scale. i.e. microgravity, a situation in which the effects of gravity are counterbalanced to a greater or lesser extent. The best known example is that of astronauts in orbit, in whom centrifugal and gravitational accelerations are equal and opposite. Alternatively, during immersion, buoyancy compensates for gravity in the systemic circulation, while recumbency minimizes the length of the body axis on which gravity operates; these two types of challenge are often used as a 'poor man's zero G simulation', and have demonstrated that if the exposure is long enough, some of the adaptive mechanisms that have been developed in response to our normal 1G environment may be blunted or even disappear, a phenomenon known as deconditioning. The reasons and time course of this process are reviewed by Pendergast et al. [16] in this volume.

Adaptation: Problems and Alternatives

From what has been said so far, it is fairly clear that most environmental stresses can be minimized by the numerous adaptive responses that they trigger; we must balance the picture by indicating that the reactions themselves may not be free of problems. A conflict will arise when two different stresses, caused by the same environment, call for opposite responses. This divergence is sometimes obvious: a subject exposed to altitude must often respond to both hypoxia and water intake limitations, but whereas the former calls for hyperventilation, water conservation demands a decrease in respiratory water loss. At other times, a beneficial reaction fails to take place, and we are left with the speculation that it may be opposed by a stress and a counterstimulus that we do not see. Such is the case in the response to

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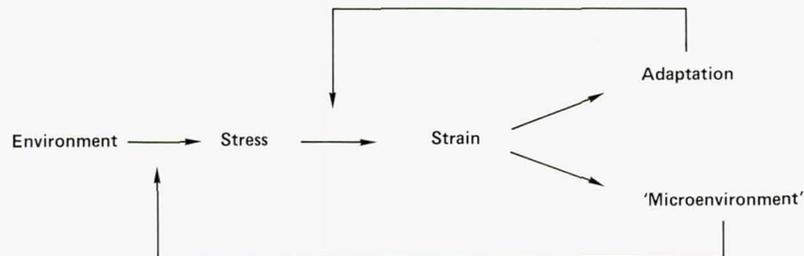


Fig. 1. Possible responses to new environments. As defined by Dejours [1], adaptive mechanisms minimize the strains caused by a stressful environment. The alternative, creation of a 'micro-environment', allows the animal to avoid or minimize some of these stresses. Such a strategy relies more on behavior than on physiological changes.

exposure to altitude, where, in spite of the increased pulmonary arterial pressure, distribution of ventilation/perfusion ratios is not improved. This has led Kreuzer et al. [17] to conclude: 'It is of great interest why such a potentially effective defense against hypoxia as a reduction in oxygen gradient should be excluded from the acclimatization process. There is no direct evidence to explain this, but in all probability the exclusion is obligatory as a result of other adaptive mechanisms.' Finally, at times, it is the adaptive response itself which creates an additional stress, as exemplified by dehydration occurring as a result of response to a heat load. Another important consideration is that long-range adaptive processes triggered by one environment may make it more difficult to respond to another stressful situation.

If adaptation to environmental stresses presents serious problems, is there an adequate substitute? Let us examine briefly two alternatives. The first is simply an increased tolerance to changes in physiological status. Along these lines, one can think of the Australian aborigine whose temperature drops during the night and of the camel who stores heat during the day and loses it during the cool desert night.

Many species have attacked the problem in a different fashion: by creating a micro-environment in which to live, one reduces or abolishes the stress and thus the need to minimize the strain (fig. 1). This micro-environment may be communal like the beaver's log house and man's climate-controlled housing, or individual like the eskimo's suit that provides its owner with semitropical conditions. Where at all possible, this strategy seems superior because it does not require changes in structure or in

physiological function and therefore ensures species survival without sacrificing flexibility. One should note, however, that in making their own 'milieu-demi-exterieur', animals often trade one stress for another. That they choose to do so raises the tantalizing question of hierarchy of stresses, a fruitful field for further investigation.

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