Summary: Why Zebras Don't Get Ulcer

Robert M. Sapolsky – The Acclaimed Guide to Stress, Stress-Related Diseases, and Coping. (Chapter 1,2,8)

Chapter 1: Why Zebras Don't Get Ulcer

This book is about stress related diseases and the mechanisms of coping with stress.

Some initial concepts

Reasons to stress:

- Acute physical crises
- Chronic physical challenges
- Psychological and social disruptions

Homeostasis: state in which all sorts of physiological measures are being kept at the optimal level (finding a balance).

Stressor: anything in the outside world that knocks you out of homeostatic balance.

Stress-response: what your body does to reestablish homeostasis.

Unlike less cognitively sophisticated species, we can turn on the stress-response by thinking about potential stressors that may throw us out of homeostatic balance far in the future → stress-response can be mobilized not only in response to physical or psychological insults, but also in expectation of them

Selye (1930):

- The body had a surprisingly similar set of responses (which he calles the general adaption syndrome, but which we now call the stress-response) to broad array of stressors.
- If stressors go on for too long, the can make you sick.

Homeostatis plus: The more stress-appropriate concept of allostasis

Original conception of homeostatis:

- There's a single optimal level for any given measure in the body.
- You can reach the ideal set point through some local regulatory mechanism, whereas allostasis recognizes that any given set point can be regulated in a zillion different ways, each with its own consequence.

Allostatic thinking → the body doesn't pull off all the regulatory complexity only to correct some set point that has gone awry, but it can also make allostatic changes in anticipation of a set that is likely to go awry.

What your body does to adapt to an acute stressor

A stressor is anything that throws your body out of allostatic balance and the stress-response is your body's attempt to restore allostasis.

One of the hallmarks of the tress-response is the rapid mobilization of energy from storage sites and the inhibition of further storage. Another thing, is that, during stress, digestion is inhibited, there isn't enough time to derive the energetic benefits of the slow process of digestion, so why waste energy on it? Your body halts long-term, expensive building projects. Immunity is also inhibited. Another feature of the stress-response becomes apparent during times of extreme physical pain. With sufficiently sustained stress, our perception of pain can become blunted. Finally, during stress, shifts occur in cognitive and sensory skills.

Three-part view of how stress-response system works (Selye):

1. In the initial alarm stage a stressor is noted → metaphorical alarms go off in your head.
2. Adaption/resistance → Successful mobilization of the stress-response system and re-attainment of allostatic balance.
3. Exhaustion → stress-related diseases emerge. On becomes sick because of the hormones secreted during the stress-response are depleted (no defenses left).

But it is not so much that the stress-response runs out, but rather, with sufficient activation, that the stress-response can become more damaging than the stressor itself.

If you constantly mobilize energy at the cost of energy storage, you will ever store any surplus energy. If you constantly turn off long-term building projects, nothing is ever repaired. If you are constantly under stress, a variety of reproductive disorders may ensue. If you suppress immune function too long and too much, you are now more likely to fall victim to a number of infectious diseases, and be less capable of combating them once you have them. Also brain systems can be damaged during stress.

Comparing two kids and two elephants which are trying to keep their balance on a seesaw:

- Enormous potential energies of the two elephants are consumed balancing the seesaw, instead of doing something more useful → diverting energy from various long-term building projects in order to solve short-term stressful emergencies.
- Stress-related diseases will run through many of the subsequent chapters. It is hard to fix one major problem in the body without knocking something else out of balance. Great quantities of hormones can make a mess of something else in the process → tear throughout the body: allostatic load.
- Sometimes stress-related disease can arise from turning off the stress-response too slowly, or turning off the different components of the stress-response at different speeds.

Two punch lines in the book:

1. Two critical classes of hormones are secreted during stress. If you plan to get stressed, you should appropriately turn on the stress-response, otherwise you are in big trouble.
2. If you repeatedly turn on the stress-response, or if you cannot turn off the stress-response at the end of a stressful event, the stress-response can eventually become damaging. Chronic or repeated stressors can potentially increase your risk of getting diseases.

Chapter 2: Glands, Gooseflesh and Hormones

The purpose of this chapter is to learn a bit about the lines of communication between the brain and elsewhere.

Stress and the autonomic nervous system

Peripheral way:

- Voluntary nervous system (your decide to move something and it happens)
- Automatic nervous system (less control, heart rate etc.) → has everything to do with your response to stress.
    - Sympathetic nervous system (action, because of (nor)adrenaline/(nor)epinephrine).
        - Epinephrine is secreted in your adrenal glands (above the kidneys), norepinephrine is secreted by all the other sympathetic nerve endings through the body.
    - Parasympathetic nervous system (everything but the four F's: flight, fight, fright and sex)
        - It promotes growth, energy storage and other optimistic processes
    - The sympathetic and parasympathetic nervous systems work in opposition!

Your brain: the real master gland

Difference between hormones and neurotransmitters:

- Neurotransmitter: if a neuron secretes a chemical messenger that travels a thousandth of an inch and causes the next cell in line to do something different.
- Hormone: If a neuron secretes a messenger that, instead, percolated into the bloodstream and affects events far and wide. All sorts of glands secrete hormones.

Peripheral gland: pancreas, adrenal, ovaries, testes etc. People used to think that the peripheral glands 'decides' when to secrete their messengers, without directions from any other organ.

If aging testes are secreting less testosterone, it is not because the testes are failing, but because another organ is no longer telling them to do so → peripheral hormone-secreting glands are not autonomous, but are under control of something else, the pituitary gland. Later in time, it was quite obvious that the pituitary glands need brain control to release hormones. After many years of research (Guillemin and Schally) it is recognized that the base of the brain, the hypothalamus, contains a huge array of releasing and inhibiting hormones, which instruct the pituitary, which in turn regulates the secretions of the peripheral glands.

Hormones of the stress-response

Glucocorticoids are steroids hormones which also response to stress, secreted by the adrenal glands. Epinephrine acts within seconds, glucocorticoids back this activity up over the course of minutes or hours.

When something stressful happens or you think a s stressful thought, the hypothalamus secretes an array of releasing hormones into the hypothalamic-pituitary circulatory system. The hormones, called CRH (corticotropin release hormone), trigger the pituitary to release the hormone ACTH (cortocotropin). After ACTH is released into the bloodstream, it reached the adrenal gland and triggers glucocorticoid release.

Together, glucocorticoids and the secretions of the sympathetic nervous system (epinephrine and norepinephrine) account got a large percentage of what happens in your body during stress.

In the meantime your pancreas is stimulated to release glucagon. Glucocorticoids, glucagon and the sympathetic nervous system raise circulating levels of the sugar glucose, these hormones are essential for mobilizing energy during stress.

The pituitary secretes prolactin (suppressing reproduction during stress). Both the pituitary and the brain also secrete a class of endogenous morphine-like substances called endorphins and enkephalins, which help blunt pain perception among other things. The pituitary also secretes vasopressin, aka antidiuretic hormone, which plays a role in the cardiovascular stress-response.

The secretion of various reproductive hormones such as estrogen, progesterone, and testosterone is inhibited. Also growth hormones and secretion of insulin are inhibited.

A few complications

Shelley Taylor of UCLA suggests that the fight-or-flight response has been overemphasized as a phenomenon, because of the long-standing bias among mostly male scientists to study males rather than females. Taylor argues that the physiology of the stress-response can be quite different in females. Taylor suggests that rather than the female stress-response being about fight-or-flight, it's about 'tend and befriend'. Taylor also emphasizes a hormonal mechanism that helps contribute to the 'tend and befriend' stress-response. Oxytocin is secreted during stress in females.

A few critics of Taylor's influential work have pointed out that sometimes the stress-response in females can be about fight-or-flight rather than affiliation and vice versa with men. Nevertheless, there is a widespread acceptance of the idea that the body does not respond to stress merely by preparing for aggression or escape and that there are important gender differences in the physiology and psychology of stress.

Not all of the features of stress-response built around fight-or-flight are the same in different species.

Another complication concerns the time course in actions of epinephrine (in seconds) and glucocorticoid (after minutes our hours). Some glucocorticoid actions do help mediate the stress-response, but others help mediate the recovery from the stress-response. And some glucocorticoid actions prepare you for the next stressor.

Another complication concerns consistency of the stress-response when it is activated. Not all stressors produce the exact same stress-response (speed and magnitudes).

Finally, two identical stressors can cause very different stress signatures, depending on the psychological context of the stressors. Every stressor does not generate exactly the same stress-response.

Chapter 8: Immunity, Stress, and Disease

There is a strong link between the nervous system and the immune system. This chapter discusses what stress does to immunity and how this might be useful during stressful emergency. Also it examines whether sustained stress, by twat of chronic suppression of immunity, can impair the ability of a body to fight off infectious disease.

Immune system basics

Immune system: to defend the body against infectious agents. The immune system must tell the difference between body cells and invaders, and must remember how the infectious agent looks like.

Immune defenses by white blood cells:

- Monocytes
- Lymphocytes:
    - T-cells (matures in thymus) (see illustration on page 147!):
        - T cells bring about cell-mediated immunity. A monocyte called macrophage recognizes an infectious agent in the body (alarm). T cells begin to proliferate in response to the invasion. Cytotoxic killer cells attack and destroy the infectious agent.
        - Different types of T cells:
            - T helper cells
            - T suppressor cells
            - Cytotoxic killer cells etc.
    - B-cells (matures in bone marrow) (see illustration on page 148!):
        - T helper cells stimulate the proliferation of B cells. The main task of B cells is to differentiate en generate antibodies, large proteins that will recognize and bind to some specific feature of the invading infectious agent. In binding to the specific feature, antibodies immobilize the infectious agent and target it for destruction.

Cytokines: blood-borne chemical messengers that communicate between different cell types.

Macrophages release interleukin-1. This messenger triggers the T helper cell to release interleukin-2. Interleukin-2 stimulates T-cell growth. On the antibody front, T cells also secrete B cells growth factor.

Errors:

- The immune system misses an infectious invader.
- The immune system is overreacting: part of your own body is seen as an invader.

There are two kinds of immunity: acquired immunity and innate immunity.

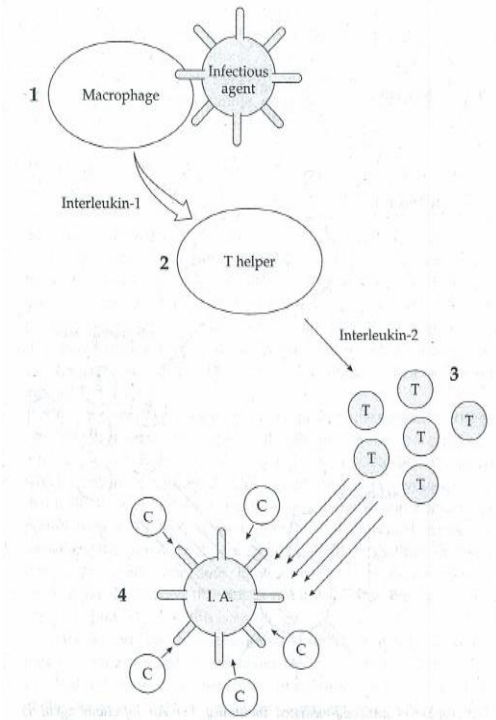
(Biologie, de twee pagina's in de binas!)

Acquired immunity:

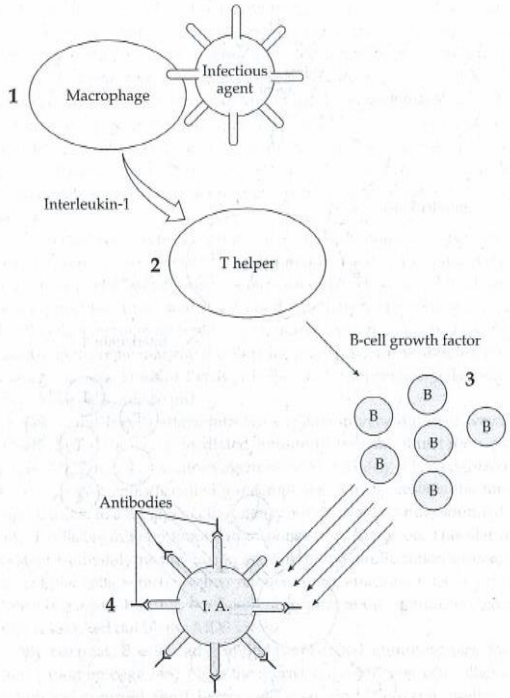
1. Able to target X with antibodies and cell-mediated immunity that recognize X.
2. It takes some time to build up immunity when you are first exposed to X
3. Repeated exposure to X will boost targeted defenses even more.

Innate immunity (skin/mucosal tissue):

1. Your salvia contains a class of antibodies that attack any sort of microbe that it encounters.
2. Capillaries loosen up, allowing cells (macrophages, neutrophils and natural killer cells) to response to slip out of the circulation to infiltrate the immediate area of infection.



The cascade of cell-mediated immunity. (1) An infectious agent is encountered by a type of monocyte called a macrophage. (2) This stimulates the macrophage to present the infectious agent to a T helper cell (a type of white blood cell) and to release interleukin-1 (IL-1), which stimulates T helper cell activity. (3) The T helper cell, as a result, releases interleukin-2 (IL-2), which triggers T-cell proliferation. (4) This eventually causes another type of white blood cell, cytotoxic killer cells, to proliferate and destroy the infectious agent.



The cascade of antibody-mediated immunity. (1) An infectious agent is encountered by a macrophage. (2) This encounter stimulates it to present the infectious agent to a T helper cell and to release interleukin-1 (IL-1), which stimulates T helper cell activity. (3) The T helper cell then secretes B-cell growth factor, triggering differentiation and proliferation of another white blood cell, B cells. (4) The B cells make and release specific antibodies that bind to surface proteins on the infectious agent, targeting it for destruction by a large group of circulating proteins known as complement.

How does stress inhibit immune function?

Niet samen te vatten, gewoon alles opnieuw lezen! Vanaf hier niet meer echt goed samengevat.

Why is immunity suppressed during stress?

Stress causes the active expenditure of energy in order to disassemble the preexisting immune system.

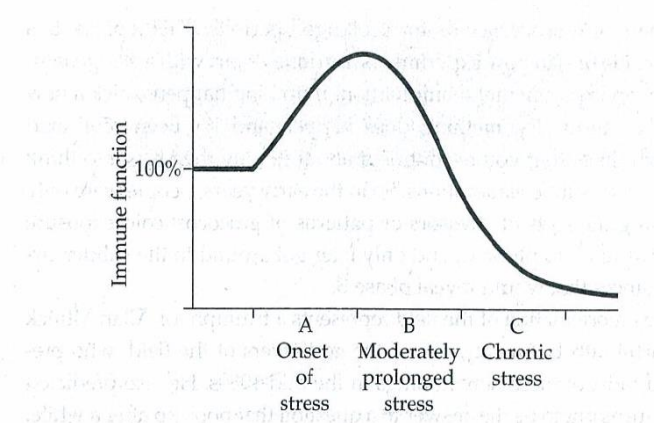
Under some circumstances, the immune system will ask the body to secrete hormones that will ultimately suppress the immune system → during infections the immune system releases the chemical messenger interleukin-1, which among other activities stimulates the hypothalamus to release CRH. CHR stimulates the pituitary to release ACTH, which then causes adrenal release of glucocorticoids. These in turn suppress the immune system.

Surprise

A. Onset of stress: your immune defenses are enhanced.

B. Moderately prolonged stress:

C. Chronic stress



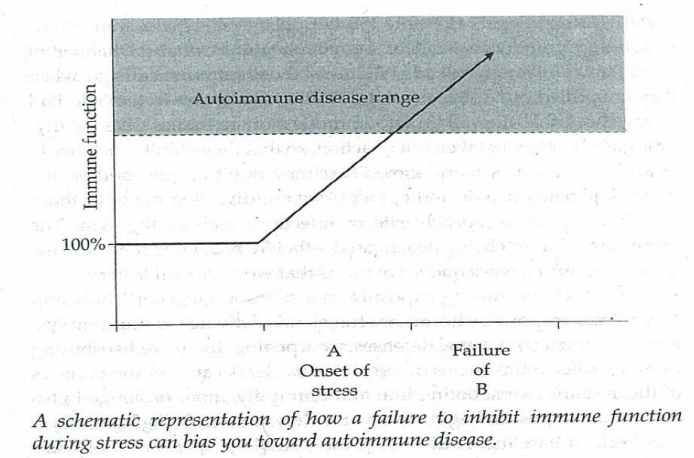
Stress turns out to transiently stimulate the immune system.

Reasons why people took so long to figure this out:

- They were actually studying the recovery of the immune response to stress, instead of the immune response to stress.
- Experiment manipulation. (only stressors that get into phase C)

A system which is always at its max costs too much, it's also with your immune system. If the defense is always at max, they begin to mistake part of you for being something invasive.

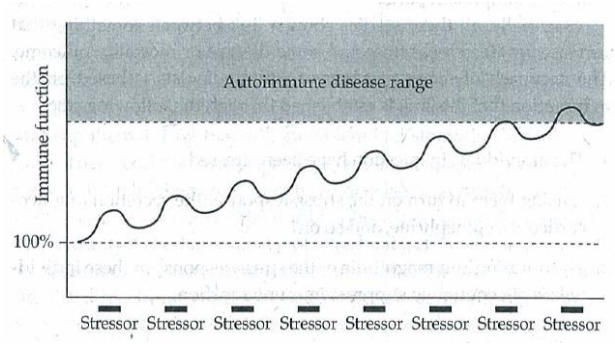
If you fail to have phase B, if you don't coast that activated immune system back down the baseline, you're more at risk for an autoimmune disease. Early on in the stress-response, the immune system is being activated, rather than inhibited, and the stress-response makes sure that immune activation doesn't spiral into autoimmunity.



A schematic representation of how a failure to inhibit immune function during stress can bias you toward autoimmune disease.

Two facts about autoimmunity:

1. Autoimmune diseases involve over activation of the immune system.
2. Stress can worsen autoimmune diseases.



Graph:

- Numerous transient stressors increase the risk of autoimmunity.
- Phase A not followed by phase B also increases the risk of autoimmunity.

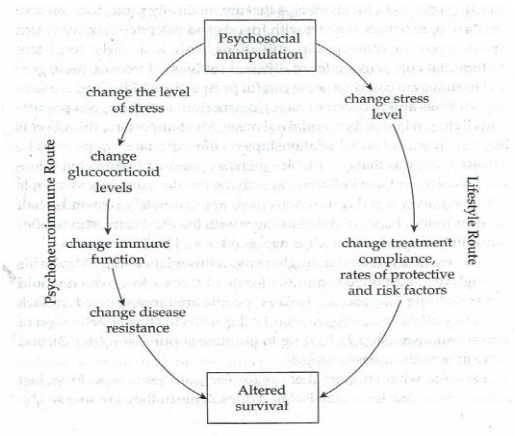
Chronic stress and disease risk

Stress may impair our immune systems and increase the risk of illness, but chronic stress makes you more vulnerable to diseases that would normally be fought off by the immune system.

The Psychoneuroimmune route; approach of 4 steps:

1. The individuals in question have been stressed
2. Causing them to turn the stress-response
3. The duration and magnitude of the stress-response in these individuals is big enough to suppress immune function
4. Which increases the odds of these individuals getting some infectious disease, and impairs their ability to defend themselves against that disease once they have it.

The next step is: is there some alternative route that explains staring with stress and getting to the disease?



Testing the tress-disease link

Social support and social isolation

It's about social isolation and the four steps.

Bereavement

Bereavement is an extreme version of social isolation.

The common cold

Being stressed increases your chances of getting a cold.

Aids

Psychoneuroimmune aspects could well contribute to a link between stress and worsening of aspects of Aids.

Latent viruses

Latency → one a virus is burrowing into some cells of yours, it goes into hibernation for a while, just lurking near your own cellular DNA. At a later point, something triggers the dormant virus out of latency and it reactivates.

Samenvatten lukt niet meer.

Cancer and miracles

Niet interessant.