Most interactions in the human body go over autoregulating systems. As autoregulating systems use input from other systems and use feedback loops to correct themselves around a setpoint we talk about regulation therapy when we intervene in such autoregulating systems. The defense system also is an autoregulating system. It tries to create a purposeful defense against homotoxins of all kind. To do so the mobilized output defense will be used as an input in the proper system to get control over the level of action of the system against the stressor. Regulation takes place over the release of stimulating and inhibiting mediators.

We can state that for each activating or stimulating mediator there is an antagonist that will inhibit the stimulated cell or process. It is almost as if the subtle regulation looks like driving a car with both feet on accelerator and breaks at the same time. Only a slight difference in emphasis of one of both will make the car accelerate or loose speed.

The defense system is an example of subtle autoregulation in which we can intervene with medications. The therapeutical use of this intervention is called ‘immunomodulation’, when we use medications affecting the immune system.
The definition of immunomodulation refers to the action undertaken by the medication on autoregulating processes that steer the immunological defense system. A lot of antihomotoxic medication intervene here and are more than useful as beside a proven therapeutic action they are extremely safe. The microdoses or nanodoses used in antihomotoxic medications exclude intoxication by the therapeutic components which are used in the formula, a phenomenon we often see in conventional medication. Macrodoses have, beside the blocking effect they often induce, often side effects or interactions with other medications or substances (like alcohol) as consequence.

In the subtle regulations induced by a microdoses or nanodoses of cytokines and other mediators, only microdoses or nanodoses therapy is at his place.
We will now discuss the three pillars or fundaments of homotoxical treatment of chronic diseases more in detail.

As time is not in favour of the cell as it comes under the influence of dysregulation and intoxication, the sooner detoxification and drainage of homotoxines take place, the better it is for the cell. That is why the first pillar of homotoxicological treatment, drainage and detoxification, is there.

The second pillar is immunomodulation. As the fastest cleansing of the extra cellular matrix is an active defense system, immunomodulation is very important in a homotoxicological treatment protocol, especially if we have to deal with a chronic disease. To activate or regulate immune reactions not only put the defense system on the right purposeful level of action, it also keeps the clinical symptoms of inflammation within for the patient acceptable levels, or stimulate a non-reactive immune system.
APC’s: antigen presenting cells will use phagocytosis to process and present antigens. Characteristic proteins of the antigen will be presented at the external wall of the APC in a changed MHC class, to chemotactically attracted T-lymphocytes (naïve prolymphocytes/TH0). The antigen characteristic (antigen peptide) will be taken from the MHC of the APC and bind to the TCR (T-Cell Receptor). From that moment on the T-cell becomes a fully in charge helper cell (T-helper cell) that will focus on the antigen defense and stimulate other actors of the defense system to eliminate it. As the motif or pattern on the TCR of the TH1 or TH2-cell is specific in function of the antigen, the tasks of the TH1/TH2 are purely to be seen as specific defense.

dendritic cell: dendritic cells play a central role in stimulating and modulating cell mediated responses. Infections have a profound effect on dendritic cells, which in turn interact with T cells and determine whether Th1 or Th2 type responses develop.

TH0-cell is a naïve prolymphocyte, not yet with a specific function. TH0-cells can differentiate to pro-inflammatory TH1 or TH2-cells or to inflammation down regulating TH3-cells, also called regulator cells or Treg-cells.

TH-1 and TH-2 cells are pro-inflammatory lymphocytes. Their main task is to trigger and stimulate the defense against a specific antigen.

TH-3 cells are inflammation regulating cells. They inhibit the function of TH-1 and TH-2 cells and are therefore down regulating their activity.
Cytotoxic T Lymphocyte Antigen 4 (CTLA-4) and CD28 are also important regulators of T lymphocyte activation. Once activated CTLA4 avoids that another than the initial antigen triggers the T-cell again which keeps the task specific.

CTLA-4 seems to play an important role in self tolerance. When the APC presents own protein to the immune system the binding of CTLA-4 will cause the T-cell to die (apoptosis), and not to react.
T Helper cells are special subpopulations of CD4+ T cells that provide help to other immune competent cells in mounting immune responses by causing cell activation or the secretion of cytokines. We divide the TH-cells into 3 classes: TH-1, TH-2 and TH-3 cells.

**TH-1 cells** are responsible for the cellular immunity. They trigger natural killer cells (NK-cells) and macrophages micro organisms or even deviating cells from proper origin (e.g. viral infected organ cells).

**TH-2 cells** direct humoral immunity. Once triggered by a motif on their TCR their activity results in a stimulation of antibody production (B-cells, plasma cells) so that antigens outside the cells (‘humoral’ = body liquids) are eliminated.

An inflammatory process can go into a mainly TH-1 mediated pathway or in a mainly TH-2 mediated one. TH-1 activity will inhibit TH-2 activity and vice versa. It is known that few contacts with micro-organisms in childhood (TH-1 reaction) will increase the risk on TH-2 mediated pathologies like bronchial asthma and other allergic reactions. In healthy persons there is a harmonious balance between TH-1 and TH-2 activity.

**TH-3 cells** are regulator cells. Their main inflammation regulating mediator is TGF-β, Transforming Growth Factor beta. Treg cells will inhibit both the TH-1 and TH-2 pathway and are therefore down regulating inflammation. In antihomotoxic medicine the stimulation of Treg cells is a common technique to intervene in inflammation processes.
Major histocompatibility complex class-I (or human leukocyte class 1) is found on the external wall of nucleated cells. It expresses the specificity of the cell and will change under influence of intruding antigens. A changed MHC class-I on the cell will trigger natural killer cells (NK cells) and cytotoxic cells (cT cells) to correct or eliminate the affected cell.

Major histocompatibility complex class-II is found on the cell wall of defense cells (APCs, dendritic cells or DCs) mostly macrophages (more precisely antigen presenting cells/APC’s). Once the defense cell has a changed MHC class-II naive T-lymphocytes are attracted chemotactically to take over the characteristic motif of the phagocytosed antigen. In thus the specific defense against the antigen is triggered and set on.

Human Leukocyte Antigen (HLA) is another name for MHC on human cells.
Pregnenolone and subsequently DHEA are called the mother of hormones by researchers because it is used by the body to manufacture many other hormones, including our sex hormones that are necessary for many body functions (e.g. estrogen, testosterone, progesterone, cortisol,...) They are responsible for the maintenance of many body functions such as fat and mineral metabolism, controlling stress, maintaining male and female characteristics and others. The body produces DHEA and then converts it on demand to these other hormones.

DHEA stimulates cellular immunity or skewing of TH-1 mediated reaction in the balance where as cortisol inhibits TH-1 reactions but will stimulate on long term TH-2 mediated reactions. We can state that a long term secretion of cortisol (e.g. stress) will induce a skewing at the TH-2 side of the balance inducing allergies, some auto-immune diseases and even cancer. Some auto-immune diseases are TH-1 driven (e.g. morbus Crohn)

As TH-3 regulator cells, over the release of TGF-β, inhibit both sides of the balance (down regulation) it does not directly intervene in the dysbalance but in the intensity of both the TH-1 or TH-2 expression.

We know from research⁴ that Traumeel S inhibits the secretion of IL-1β and TNF-α. These two mediators inhibit cortisol production. That is why Traumeel S has such an inflammation down regulating effect, amongst others.

An autoregulating system has by definition two opposite streams or states that inhibit one another. In both these states a rigidity can appear. It is as if the wave pattern process gets blocked on a certain moment of the curve and continues as a horizontal linear process.

A blocking in the TH-1 state will cause TH-1 rigidity. Typical diseases here are all the diseases where the immune system directs itself against proper tissues (cellular autoimmunity). Other examples are the great variety in chronic inflammations. Also cardiomyopathy and Crohn’s disease are a TH-1 stage rigidity.

A blocking in the TH-2 stage will cause allergic diseases at different locations. Also cellular immune dysfunctions, CFS, late AIDS stage, cancer, are all TH-2 rigidity caused.
Lymphoid tissue at the level of the mucosa (MALT: mucosa associated lymphoid tissue) will take up antigens and present them over a cascade of activated cells to the defense system. Two manners of uptake are seen: phagocytoses (big particles) and pinocytosis (small particles or liquids).
As the mucosa is extended at every location in the body where the organism gets in contact with the environment (internal skin) we divide the MALT into NALT (nasal associated lymphoid tissue: tonsils and adenoids), BALT (bronchial associated lymphoid tissue), GALT (gut associated lymphoid tissue).

Exception but similar is the SALT (skin associated lymphoid tissue) as this is not mucosa related.
Competent cells out of the different MALT levels will migrate (homing) to certain glands and encapsuled lymph tissue (lymph glands).

Above that, as the picture shows, there are possible cross reactions of certain antigens and tissues, e.g. GALT and mammary glands or GALT and synovial tissues.

The MALT also plays an important role in systemic diseases.
Mediators can be divided into pro-inflammatory and anti-inflammatory mediators. We can state that for every agonist there is an antagonist. In this way we see that both opposing pathways gives an end result that should express a balance between TH-1 and TH-2 mediated defense reactions. Of course this is the case in a normal functioning organism. Often we see a superiority in TH-1 or TH-2 mediation with the over expression of the corresponding mediators.

Degradation of tissues and inflammation inducing are IL-1, 6 and 8 and also TNF. Source for these mediators are the macrophages, TH-1 cells, chondrocytes and fibroblasts.

Tissue repair and inflammation inhibiting is induced by released IL-10 and TGF-β. Source cells are above all the regulating TH-3 lymphocytes and some other body cells.
A large number of mediators regulate an immune response. Although both sides of the TH1/TH2 balance induce different actions they both are able to 'control' and inhibit reciprocally their own actions. A TH1 mediated pathway will inhibit over the release of interferon gamma the TH2 pathway and the other way around the TH2 cell can over the release of interleukin 10 inhibit the TH1 pathway. Above TH1 and TH2 stands the regulator cell (TH3 or Treg cell) that over the release of transforming growth factor beta can inhibit both the TH1 and TH2 pathway.

In function of the cellular or humoral defense different immunocytes are activated. In both pathways the activity of the ending cell in the cascade influences the input of the pathway. Macrophages stimulate TH1 activity over the release of IL-12 but are activated themselves by the release of IFN-γ and TNF-β, both released by the TH1 cell. In this way a loop is created.

A similar loop is seen in the TH2 pathway. Mast cells induce TH2 activity that over the release of Interleukin 3, 4 and 10 will activate the mast cell.

To conclude we can state that both the TH1 and TH2 pathways, over positive feedback, stimulate their own loop which is only inhibited by the reciprocal inhibition between TH1 and TH2 and the supervising regulating effect of the Treg cells.
The number of antigen induced MHC-class II change will be decisive for the creation of TH1 or TH2 cells on the one hand or TH3 cells on the other hand. Large presentation of antigen characteristic proteins in the MHC class II of APCs and dendritic cells will lead to the creation of TH1 and TH2 cells, both pro-inflammatory T lymphocytes. A presentation of a microdoses of an antigen will induce the creation of TH3 cells who will down regulate the inflammatory pathways created by TH1 and TH2 cells.

The phenomenon in which a different doses of the same organic antigen creates opposite acting T helper lymphocytes is known as oral tolerance in modern immunology. The induction of TH3 creation instead of TH1 or TH2 creation is one of the possible action mechanisms known in modern immunology.
By the reciprocal inhibition we see in autoregulating systems, more precisely in the body’s defense activity, we must conclude that regulation patterns have a wave pattern, like the oscillations of the two arms of a balance, around a set point. Any charge in the one or other direction will immediately enlarge the oscillations that in time will get less until the set point in balance is reached again.

Oscillating around set points is one of the main characteristics of homeostasis.
In an inflammation we see TH-1 and TH-2 pathways alternating around a set point of balance. Desoxicortisol will stimulate a TH-1 state there as cortisol will induce a TH-2 state. An overweight of one of the two will cause a prolonged characteristic status of cellular or humoral defense with all the consequences mentioned already before. Keeping the wave pattern moving until a harmonious set point is reached or getting as close as possible to that is one of the targets of immunomodulation.

The picture always explains the danger of the prolonged TH-1 blocking use of corticoids in conventional therapy as this medication will push and keep the patient into a TH-2 mediated defense with all his consequences.
The immunological bystander reaction, a principle in modern immunology, was used by prof. Hartmut Heine to postulate the working mechanism of some low concentrated organic components in antihomotoxic medications.

Prof. Hartmut Heine was a histologist and has worked for many years in the anatomy division of the university of Written-Herdecke in Germany. From 1997 until 2002 he was associated with the Institute for “Antihomotoxische Medizin und Grundregulationsforschung”, an institute that did research on antihomotoxic medicine and regulation patterns in the ground system. He was also a member (until 2003) of the Scientific Advisory Board of the International Society of Homotoxicology. He performed pioneering research on the extracellular space, the anatomic-histological research of acupuncture points and the immunological stimulation by antihomotoxic medication. At the end of 1997 he published his hypothesis of the “Immunological Bystander Reaction pathway”, a pharmacodynamic model (proven in vitro) for organic substances in the range of D1 to D14.

Heine’s model is very important. Minute molecular concentrations of organic components, like in the formula of Traumeel S, stimulate a TH-3 mediated immunological reaction. The figure above explains Heine’s model.

Where an antihomotoxic agent with low potentised proteins is introduced into the GRS (Ground Regulation System) antigen presenting cells and dendritic cells will eliminate it over phagocytosis. Characteristic proteins are transported back to the macrophage’s surface in the form of short amino acid chains. These presentation is antigen characteristic and specific. It is presented as a ‘motive’ in the MHC on the cell surface (MHC – Major Histocompatibility Complex).
These motifs or patterns are recognized by passing naïve T-lymphocytes, which over their receptors will interact with them. So, over the TCRs (T cell receptors) of their own and the motif presented by the APC there is an interaction. This interaction is the signal for them to become TH-3 cells (regulating lymphocytes). The new TH-3 cells will be transported to the closest lymph ganglion (homing) where they will be identically multiplied (cloning). The activated TH-3 cells search for inflammation promoting lymphocytes (TH-1, TH-2) in the inflammation area, which motives are dependent on the foreign substances that triggered the inflammation. The TH3-cell will look for lymphocytes with a similar motive. As soon as the similarity is confirmed, the TH-3 cells immediately start with the synthesis of highly active TGF-β (Transforming Growth Factor β), which will decrease the activity of the TH-1 and TH-2 lymphocytes. The inhibition of the TH-1 and TH-2 accuracy will result in an inhibition of the inflammation stimulation by these lymphocytes, which will result in less inflammation symptoms and activity.

In one sentence we could state that Traumeel S stimulates the creation of specific TH-3 cells that by the release of TGF-β will inhibit the TH-1 and TH-2 activity.
We will often see that during lifetime the patient will evolve from a more expressed TH-1 state to a more expressed TH-2 state. In time the mentioned diseases in the picture above are characteristic for the main evolution of the status of the TH-1/TH-2 balance but also correspond to the disease evolution table (see lecture IAH AC Introduction to homotoxicology)
The scientist Hans Selye, father of the current accepted theory on stress, found out that when an organism is confronted with a stressor, 3 stages will follow one another. Mainly we can state that the organism will try to find a way out, a ‘modus vivendi’ to survive the stressor.

From an alarm phase the organism will show resistance and if ineffective and long term present, will end up in a stage of exhaustion.

The whole stress reaction, mainly driven over the increases secretion of cortisol, is only possible over the steering cascade of the hypothalamus-hypophysis-surrenal axis. In normal conditions this steering axis is autoregulating over feedback systems. The number of glucocorticoids secreted will inhibit in over secretion the inducing ACTH. In chronic stress we see an inappropriate set point level.
In the alarm stage the whole organism is set in a state of being alert to stimuli that might contain danger. Three possible ways of reacting to danger are evaluated. It is called the 3 Fs.

1. **Flee**: the organism will try to flee from the danger (in nature a rabbit, horse, most birds, …)
2. **Fight**: the body prepares itself to fight the intruder or external danger (in nature a lion, dog, crocodile, …)
3. **Freeze**: the rule behind this protection is that doing nothing seems to be better than doing something wrong. By freezing, the organism hopes it will not be seen and attacked (in nature a donkey, pheasant, …)

In the alarm phase, by the alert state of mind, people seem to function more accurate, sharp. The whole organism is investigating incoming signals for danger (great involvement of the limbic system). Reactions are quick, accurate and protective.
During the resistance state against a stressor we see a higher glucocorticoid secretion. This is biologically normal. Glucocorticoids suppress any feeling of disease (it is not opportune to feel inflammation symptoms if you need to fight the attacking lion). On long term that the negative effects of continuous glucocorticoid secretions will be seen in the organism.

The higher secretions of glucocorticoids may induce all kind of deregulation diseases like hypertension, hyperinsulinism, TH-2 rigidity, etc…
If the ineffective resistance state takes too long the body will get exhausted. Beside a general fatigue we might see dysfunctions on physical and psychological level. By the long term exposure to higher levels of proper glucocorticoids all kind of TH-2 mediated diseases might appear. Allergies and in a later stage auto immune diseases are very common in the exhaustion stage of stress.
Prolonged stress has very negative effects on health in general. Not only psychologically the mind status can become more depressed, more anxiety, sleep disorders, poor appetite might be the consequences, but also physically. Stress can inhibit reproduction, cause gastrointestinal problems like leaky gut syndrome, decrease immunity, metabolic syndrome and increase weight…

Although stress can be very positive to make us move, act, decide, create… a prolonged status of hyper excretion of stress hormones will induce an unpleasant status of psychosomatic related diseases that will be translated after a while in real somatic dysfunctions and chronic degenerative states.
To conclude we can state that stress is needed to live but in a prolonged stressful situation the organism can get exhausted and dysbalanced which will lead to certain types of condition and even diseases. It is all in the balance and the capability to maintain the set points.

Stress doesn’t have an effect on one parameter in the autoregulating systems of the body. Over mainly the secretion of cortisol during stress it comes between autoregulating systems all over the body and therefore has a great impact on human’s health.