

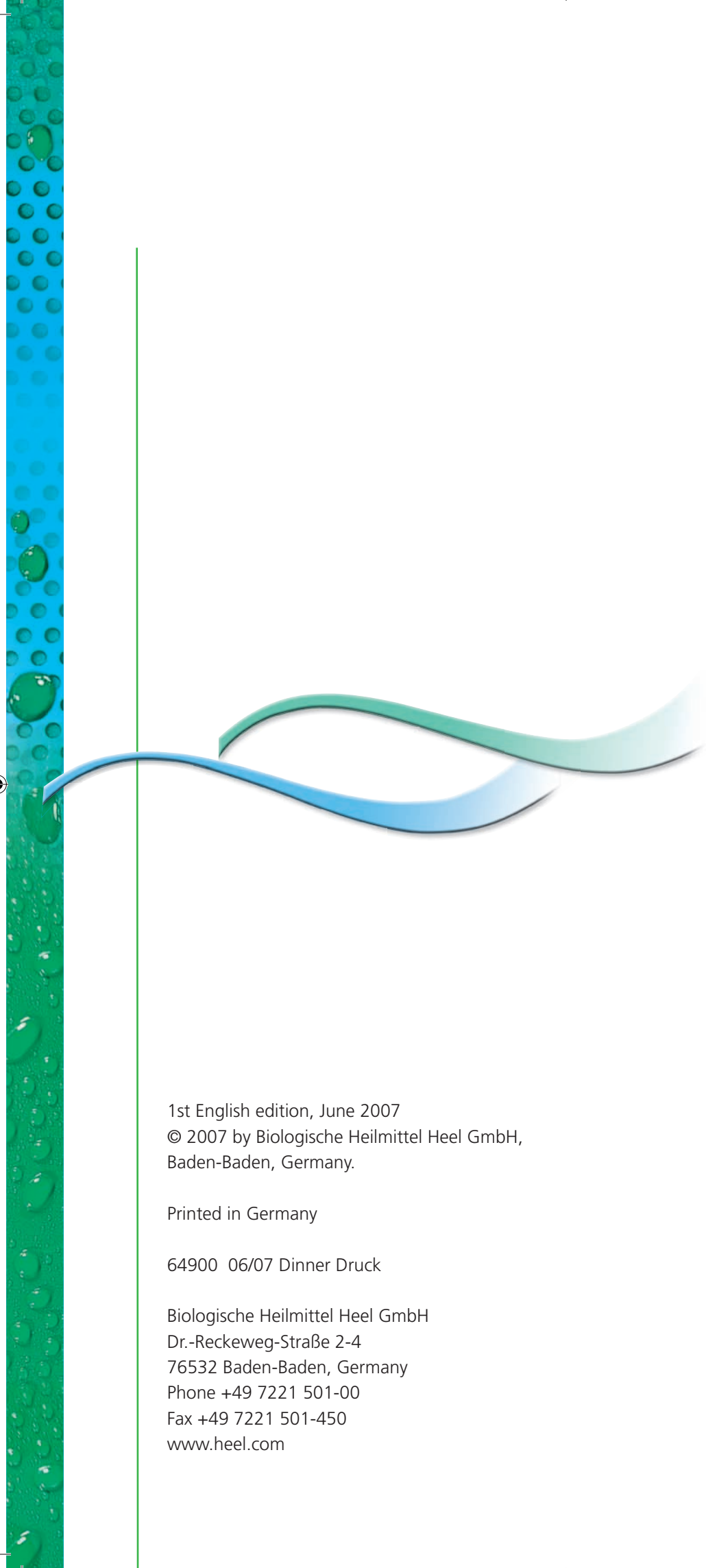
Detoxification and Drainage

A Theoretical and Practical Approach



-Heel





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Contents

Part I / Classes of Homotoxins	5	Part IV / Tools for Detoxification	30
1 Introduction	5	1 Why Does a Person Need to Detoxify and Eliminate	30
2 Effects of Toxins in General	6	2 Tools for Detoxification and Drainage	31
3 Measurement of Toxicity	6	2.1 The General Basic Detoxification	
4 Classes of Toxins	7	2.2 The General Advanced Detoxification	
4.1 Pollutants		2.3 The Catalysts	
4.2 Metals			
4.3 Agricultural Chemicals (Pesticides) Including Wood Preservatives			
4.4 Plasticizers and PBBE's			
4.5 Therapeutic Drugs and Drugs of Abuse			
4.6 Food Additives and Preservatives			
4.7 Endogenous Toxins			
Part II / The Physiology of Detoxification	13	Part V / Practical Detoxification	38
1 Absorption	14	1 Clinical Groups	38
2 Transport	14	1.1 The Detoxification Point Scale	
3 Distribution and Storage	15	1.2 The Clinical Assessment of the Patient	
4 Metabolism of Toxins	16	2 How Long Should the Patient Detox?	39
4.1 Phase I Reactions		3 Blocked Excretion	39
4.2 Phase II Reactions		4 The Decision Tree	40
5 Elimination	17		
Part III / The Organs of Detoxification and Elimination	21	Part VI / The Organ-specific Treatment	42
1 The Liver	21	1 The Liver	42
2 Excretion in Bile	22	1.1 Therapy Scheme for Detoxification in Chronic Viral Infection like Hepatitis C	
3 Entero-hepatic Circulation	22	1.2 Detoxification of the Gallbladder and the Bile	
4 The Kidneys	22	1.3 Therapy Scheme for Fatty Infiltration of the Liver in Type II Diabetics: So-called NASH (Non Alcoholic Steatotic Hepatitis Syndrome)	
5 The Matrix and Lymph	23	2 The Kidneys	46
5.1 The Matrix		2.1 Therapy Scheme for Kidney Stones	
5.2 The Lymph System		2.2 Therapy Scheme for Chronic Recurrent UTI's	
6 The Lungs	26	2.3 Interstitial Cystitis	
7 The Mucosal Membranes	26	3 The Lymphoid System	49
8 The Skin	27	3.1 Therapy Scheme for Chronic Recurrent Tonsillitis	
9 Sweat	28	4 The Skin	51
10 Hair	28	4.1 Therapy Scheme for Acne Vulgaris	
11 Other Routes of Elimination	28		
		Part VII / References	53



Note

Since this is an international publication, names and formulas of the products mentioned in this booklet may vary from one country to another.

Classes of Homotoxins

1 Introduction

To better understand the rationale and methods for “Detoxification and Drainage”, it is useful to define what are toxins, their origin and nature, how they reach the body cells and tissues, and how they eventually influence homeostasis and become eventually etiological factors for inducing disease processes.

Any agent (physical, chemical, microbial, etc.) that adversely modifies or damages a balanced biological system is considered a “toxin”. Toxins may enter the body from the external environment (exogenous – also called toxicants or xenobiotics) through the gastrointestinal system by ingestion, the respiratory system by inhalation, and the skin by passive absorption or by injection. Toxins may also originate within the body itself (endogenous toxins) as by-products of physiological metabolism (bilirubin, creatinine, lactic acid, etc.) or as metabolites under abnormal metabolic conditions (excess production/degradations of neurotransmitters and/or hormones, excess free radical formation, etc.).

Modern medicine is quite successful in diagnosing and treating acute intoxications as medical emergencies for heavy metals, drug poisoning, etc. as well as symptomatic sub-acute poisonings from a variety of toxins (chemical, drugs and/or other xenobiotics), but **only** if some laboratory evidence of intoxication is found. Unfortunately for the patient, sub-clinical or subtle states of chronic intoxications are not recognized, except for the fact that the appearance of any symptomatology is treated with suppressive medications independently of its etiology.

Biological effects of chronic subtle states of intoxications are of great importance to biological medicine. Paracelsus is often paraphrased as stating that “the dose makes the poison”. Often, if the dose is not high enough to produce immediate acute effects and/or cannot be detected with our present technological limitations, then the toxin is seen as not responsible and the question is just dismissed as not being responsible for the biological effects and influences upon the health of the individual.

Another very important consideration to bear in mind is the individual's tolerability or susceptibility to specific toxins. The tolerability of biological systems to a toxin is in part genetically determined and in part acquired on the basis of enzymatic induction an/or inhibitions, the degree of functionality of the target organ, and functional reserve capacity of specific organ-systems. The clinical manifestations of biological effects of toxins depend on the physical and chemical properties of the toxin itself, but also on the duration and route of exposure, its mechanism of action, and obviously on the individual susceptibility, as previously described.

Chemical compounds, which compromise the bulk of environmental toxins, are currently spread all over the world, even if the chemical was not used in that area. This is due to spread via the ground water, surface rain and winds.

Bioaccumulation of these compounds cause disease in living beings, and in humans, the immune system, endocrine system and neurological system is the most affected. (Crinnion, 2005)

The effects of toxins are documented in a number of diseases, ranging from asthma, allergies, autoimmunity, cancers, cognitive deficit, and obesity.

New diagnoses also include so-called sick building syndrome, and multiple chemical sensitivity. Sick building syndrome (SBS) is a combination of ailments associated with an individual's place of work (typically, but not always, an office building), though there have also been instances of SBS in residential buildings. A 1984 World Health Organisation report into the syndrome suggested up to 30% of new and remodelled buildings worldwide may be linked to symptoms of SBS. Multiple chemical sensitivity is a condition even more difficult to treat, and is recognized in some individuals who develop chemical sensitivity to a host of environmental chemicals.

2 Effects of Toxins in General

Toxins can have several effects on their environment/host namely:

- Acute lethality
- Sublethal effects on non-mammalian species
- Sublethal effects on plants
- Sublethal effects on mammals
- Teratogenicity
- Genotoxicity/mutagenicity
- Carcinogenicity

We will only consider the effect on mammals especially on man. Here the effect of the toxin on the host will be determined by several factors, namely the substance and its concentration, the rate of intoxication and the host. Toxins can cause temporary dysfunction in the body, lead to permanent damage in the case of chronic intoxication, or even to death in the case of acute intoxication. In reality all toxins can be detrimental to the body in the correct dose. In the words of Paracelsus, only the dose makes the poison.

The toxicity, or rather the effect of the toxin on the body in relationship to the dose is dependent on several factors:

1. The galenic form of the toxin. For instance, organic mercury is much more toxic in a gaseous form than as in liquid form.
2. When a toxin is mixed with other toxins, the toxicity may go up, as toxins often potentize each other. For instance, two environmental toxins may be present in a sub-toxic concentration, but together with another toxin becomes severely toxic.
3. The time in which it is taken in, thus acute, sub-acute or chronic intoxication.

If someone would drink 10 liters of water at once, it will cause hyponatraemia and death, for instance.

Often intoxication in minute amounts over time have a different effect on the organism, e.g. cause cancer, or affect the immune system, whereas an acute intoxication will have a totally different effect.

4. The patient:
 - a The ability of the patient to regulate in view of the intoxication.
 - b The gender of the patient.
 - c The body weight.
 - d A possible tolerance to the substance, especially if it is given in low doses orally over time.

The latter (a-d) has important implications for treatment strategies and will be discussed more in depth later.

3 Measurement of Toxicity

To compare the toxicity of toxins with each other, it is tested under strictly controlled laboratory conditions, mainly on animals. This is expressed as the so-called LD 50 which determines in which dose depending on the body weight, half of the test population will die. LD thus stands for lethal dose. The dose response curve of such intoxication is linear or sigmoidal. However, recently the interest has been revived in toxic exposure at doses below the so-called NOAL (no observed adverse effect level) over time.

It is now known that many environmental toxins over time will exert a stimulatory or an inhibitory effect on processes in the body in the so-called U-shaped response curves, such as seen in hormesis. This means that a toxin may only exert a certain effect in a specific low dosage range. If the concentration goes below this very low dose, it has no effect, and if the substance occurs in full strength it may also have no effect or another effect. A toxin thus may be highly toxic when given in a high dose, loose this toxicity in a lower dose, but then still have a detrimental effect over long term exposure in minute concentrations. Especially for chemical carcino-

gens acting by a genotoxic effect this is of importance. (Calabrese, 2001)

Recently, a publication in Science brought to light an even more frightening fact concerning the effect of environmental toxins. This concerns the area of epigenetics, where genetic material is damaged by toxins in one generation and the damage is transferred to the next, where the effects are seen for the first time. (Skinner et al., 2005)

The effects on reproduction correlate with altered DNA methylation patterns in the germ line. The ability of an environmental factor (for example endocrine disruptor) to reprogram the germ line and to promote a transgenerational disease state has significant implications for evolutionary biology and disease etiology.

4 Classes of Toxins

Given the large amount of toxins it is difficult to classify them chemically, either by function or by mode of action, since many of them will fall into more than one class. Toxins can enter the body through air, water, soil pollution (in terms of accumulation into food sources). Others enter the body through deliberate use, such as drugs of abuse, therapeutic drugs, cosmetics, food additives and contaminants. A number of these toxins can be classified as so-called anthropogenic toxins, as they are connected to the actions of man, for example by

- Industrial processes
- Mining and drilling
- Combustion of fossil fuel for heating and power and exhaust fumes from transportation vehicles

4.1 Pollutants

Gaseous pollutants

These substances are gases at normal temperature and pressure. Amongst the pollutants of greatest concern are:

- Carbon monoxide (CO)
- Hydrocarbons
- Hydrogen sulphide (H₂S₂)
- Nitrogen oxides (NO)
- Ozone (O₃) and other oxidants
- Sulfur oxides
- Carbon dioxide (CO₂)

Particulate pollutants

- Dust
- Fumes
- Mist
- Smoke
- Aerosols

The effects of the pollutants are numerous, but among the most important are the damaging effect on the lung and the respiratory mucosa, which contribute to allergy, asthma and cancer.

4.2 Metals

Metals are naturally occurring but accumulate due to their uses in our activities of civilization. These include arsenic, lead, mercury, cadmium and chromium. Metals have a wide range of detrimental actions on the body, and share common toxic mechanisms and sites of action.

- Enzyme inhibition/activation. Especially enzymes containing sulfhydryl (SH) groups, which bind certain metals in the body as a co-factor may be affected as the toxic metal could displace the co-factor.
- Sub-cellular organelles. Toxic metals disrupt the structure and function of a number of organelles, such as the endoplasmic reticulum, the lysosomes and the mitochondria. Metal inclusion bodies may form in the nucleus.
- Carcinogenicity: Arsenic, chromium, nickel, as well as cadmium, and cis-platin are human carcinogens. This is due to the interactions of the metallic ions with the DNA.

- **Kidney:** This is due to the fact that the main excretory organ in the body for metals is the kidney. Cadmium and mercury especially are nephrotoxic.
- **Nervous system:** Especially the lipid soluble metals, such as methylmercury and organic lead compounds are neurotoxic as they readily cross the blood brain barrier.
- **Endocrine and reproductive effects:** Because the male and female reproductive systems are under complex neuroendocrine control, any toxin interfering with any of these processes can affect the reproductive system.
- **Respiratory system:** Acute exposure to metals leads to irritation and inflammation of the respiratory tract, whereas chronic exposure may result in fibrosis (aluminium) or to carcinogenesis (arsenic, lead, nickel).
- **Metal binding proteins:** The toxicity of many of the metals, such as cadmium, lead and mercury depends on their transport and intracellular bio-availability. This is regulated by the high affinity to certain cytosolic proteins. These proteins typically are rich in thiol (SH) groups. These intracellular 'sinks' are particularly important to sequester metals away from vital organelles. The role of the extracellular matrix must also be mentioned here, as it will be an important storage place for metals before they reach the cell as it is also rich in thiol groups.

4.3 Agricultural Chemicals (Pesticides) Including Wood Preservatives

The use of chemicals to control pests goes back centuries to the ancient Chinese and the Romans. However, in the 1900's, compounds which we now identify as pesticides came into being. Ideally pesticides should be highly specific, and only harm the intended target, but subsequently many health hazards have been recognized coming from these substances. A major risk is the environmental contamination, especially where they may enter the food chain and the natural water resources. Of course a very serious

concern is the long half life of certain of these compounds, as well as their lipophilic nature, which makes bioaccumulation and especially accumulation in the human body a real threat. Many of these are classified as Persistent Organic Pesticides (POP's).

The Globally Harmonized System (GHS) for the classification and labeling of hazardous chemicals is an initiative to promote common, consistent criteria for classifying chemicals according to their health, physical and environmental hazards, and to develop compatible labeling, safety data sheets for workers, and other information based on the resulting classifications. This is an ongoing initiative of the Environmental Protection Agency (EPA) in the USA.

The primary classes of pesticides produced today are: fumigants, fungicides, herbicides, and insecticides.

In the USA alone, the total production per year is 1.2 billion pounds of such chemicals. Produced are also some 665 million pounds of wood preservatives.

Organochloride pesticides are probably the best known class of pesticides. These substances, introduced in the 1940's and 1950's include familiar pesticides such as DDT, Chlordane, and Dieldrin (developed later as an alternative to DDT).

In acute intoxication, organochlorides act as neurotoxins. The persistence of this group of pesticides for instance is a major concern, and they were banned in the USA in 1972 after the book by Rachel Carson: *The Silent Spring* in 1962. (Carson, 1962)

However, ground water in many parts of the world still remains contaminated.

Some biological effects of pesticides and wood preservatives include:

- Direct damage to DNA and thus carcinogenic
- Interference with immune function
- Induction of the P-450 enzyme detoxification system
- Endocrine disruptors

4.4 Plasticizers and PBBE's

Plasticizers, most commonly, phthalates, alkylphenols, bisphenol A are additives, which soften the materials to which they are added, e.g. those that give hard plastics like PVC its flexibility and PBBE's (flame retardants), which also include the so-called phthalates occurring in softeners of plastics, oily substances in perfumes, additives to hairsprays, lubricants, paint and wood finishers is of particular concern here. Flame retardants, such as Polybromated biphenyl ethers (PBBE's) are materials that inhibit or resist the spread of fire.

While high doses of phthalates do constitute risks in the sense of traditional toxicology, low doses also change the stakes dramatically. Research reveals that male reproductive development is acutely sensitive to some phthalates. For example, the phthalates dibutyl phthalate (DBP) and diethylhexyl phthalate (DEHP) produced dramatic changes in male sexual characteristics when exposure took place in utero, at levels far beneath those of previous toxicological concern. These changes included increases in the rates of hypospadias and other indications of demasculinization. (Clark et al., 1999)

Bisphenol also has been implicated in the development of cancer. (Welshons et al., 2003)

4.5 Therapeutic Drugs and Drugs of Abuse

This is a huge group of chemicals which will not be discussed in-depth here. Apart from the known side effects of this group, many will also disrupt the self-regulatory processes of the body and will cause deregulation and other disease. Many, who will treat one condition, will put the patient at risk for another. For instance, many immunosuppressant agents, used in auto-immune diseases are known to be carcinogenic.

4.6 Food Additives and Preservatives

Additives are added to foods as preservatives (such as methyl-p-benzoic acid, propionates) but also to change the physical characteristics, such as color (tartrazine) odor and taste (Saccharin and Aspartame, Piperonal as well as nitrates and nitrites). Certainly hundreds, and possibly thousands, of food additives are in use world wide, many with inadequate testing. Some of these were introduced when toxicity testing was not sophisticated and subsequently were showed to be toxic. The question of synergistic interactions between all of these has not been looked at adequately. Many of these are carcinogenic or mutagenic.

4.7 Endogenous Toxins

These are products of normal regulatory processes in the body, which accumulate, either through an overproduction, or due to the fact that they are not adequately metabolized or excreted. Examples of these are substances such as adrenalin and histamine.

It is important to note that these substances are also metabolized by the same processes which metabolize external toxins. When these enzyme systems are overloaded by external toxins, it can lead to the accumulation of these internal toxins. This is why for instance toxic patients will often suffer from panic attacks, as the metabolism of adrenalin will be impaired. Psycho toxins will cause an imbalance in the neurotransmitter status, and will disturb the normal homeostasis. Furthermore, the chronic stress hormone, cortisol, plays a very important role in the metabolism and the resultant detoxification of the extracellular matrix, so that chronic stress will impair the renewal of the matrix and promote an accumulation of toxins in the matrix.

CLASSIFICATION OF TOXINS

Exogenous ('Toxins')

any organ to the environment.
als, pollutants, gases, microbes,

INDOOR

nts may come from outdoor, from materials in the human activities.

Chemicals & Minerals

le
nic chemicals (VOCs)

de
de

Paints & Renovations

ls & formaldehyde from plywood, paelling, etc.)
lues, fillers, paints, stains, varnishes, etc.)
olatile fungicides, pesticides, mildew-cides)
om insulations)
flexible vinyl floors)
abrics & carpets
hyde, plasticizers, fungicides)
(contain more than 20 chemicals to kill bacteria,
rd fibers and also release acetone, benzene,
, toluene and formaldehyde ... in addition to dust,
microbes that it can harbor)

Household Products

products
ucts & fabric softeners contain
xic chemicals such as:
s (chloroform, benzyl acetate, limonene)
(camphor, ethyl acetate, benzyl alcohol,
ne)
leaning products
sed frequently)

Bacteria, Molds, Dust, Pets

ews in humid areas
mites
ses, fungi, etc.
e toxins (dander, fleas, use of
collars that have toxic chemicals, etc.)

Human activities

of microbes
ke & fireplaces
drugs etc.
e heating systems together with 'better' sealings
ors have drastically reduced natural ventilations –
exchanges have been practically eliminated (toxins
r accumulate inside)

ENDOGENOUS ('Toxins')

Produced in the Body

- 1 Physiologically
 - Bilirubin
 - Ammonia
 - Uric acid
 - Lactic acid
 - Creatinine
 - etc.

Become 'toxic' if in excess for:

 - production
 - detoxification and excretion
- 2 Under Abnormal Conditions
 - production of waste products (CO₂, H₂O₂, free radicals, etc.)
 - hormones and/or neurotransmitters
 - microbial debris
 - pH imbalances
 - etc.

Stored in the Body

- Originally from external origin but introduced into the body where they are stored and become a continuous source of 'toxic' release (Water soluble chemicals are easily excreted, but fat soluble chemicals accumulate in fat cells and cell membranes)
- 1 Dental materials
 - 2 Medical implants
 - 3 Microbes (foci)
 - etc.

DERMAL (Skin)

Active (Injections)


- 1 Prescription drugs
- 2 Recreational drugs
- 3 Animal toxins
bites or puncture by fish, arthropods, parasites, etc.

Passive

- Substances that are both water & fat soluble are more easily absorbed through the epidermis especially if not integral and through the hair follicles:
- 1 Drugs
 - 2 Cosmetics
 - 3 Chemicals
especially from the air and from waters. ...showers, bathing, etc.)
 - 4 Radiations



Conclusion

- Toxins are ubiquitous in our environment and can accumulate for years in the ground water, as well as cover vast distances due to climatic phenomena.
 - Different classes of toxins exist, such as pollutants, metals, agricultural chemicals, plasticizers, food additives, therapeutic drugs and endogenous toxins which are formed in the body and not adequately excreted.
 - Many toxins occur in the so-called NOAL (no observed adverse effect level), but still cause long-term problems such as carcinogenesis if present at minute concentrations.
 - Epigenetic effects of toxins are now recognized, where one generation is exposed to the toxin, but the effect is only seen in the offspring.
 - The toxicity of toxins range from lethality to teratogenicity to genotoxicity as well as carcinogenicity.
 - Toxins can also impair the immune system, the intracellular organelles and cause enzyme inhibition or activation, or mimic endogenous hormones, when they are called hormone disruptors.
- 

The Physiology of Detoxification

In the previous chapter we saw that the body is exposed to a wide variety of toxins present in the air, water, soil and food. The body has several inherent defense mechanisms and membrane barriers to prevent the absorption and distribution of the toxin when the intoxication has occurred. Once inside the body, the internal defense system, or Basic Bioregulatory System will be mobilized in order to eliminate the toxin or at least try to compensate for it.

In this chapter, we will look at the way the body deals with these toxins.

Before a toxin can have a detrimental effect on the body, it needs to reach the target organ or cell. In principle four steps are necessary for this:

- Absorption
- Transport
- Metabolism
- Distribution and storage
- Elimination

Toxicokinetics studies the absorption, distribution, elimination, metabolism and/or clearance that take place in the body after exposure to the toxin. Toxicodynamics on the other hand studies the biochemical and physiological effects of drugs and toxicants and determines their mechanism of action. Toxicokinetics can also be seen in the diagram below.

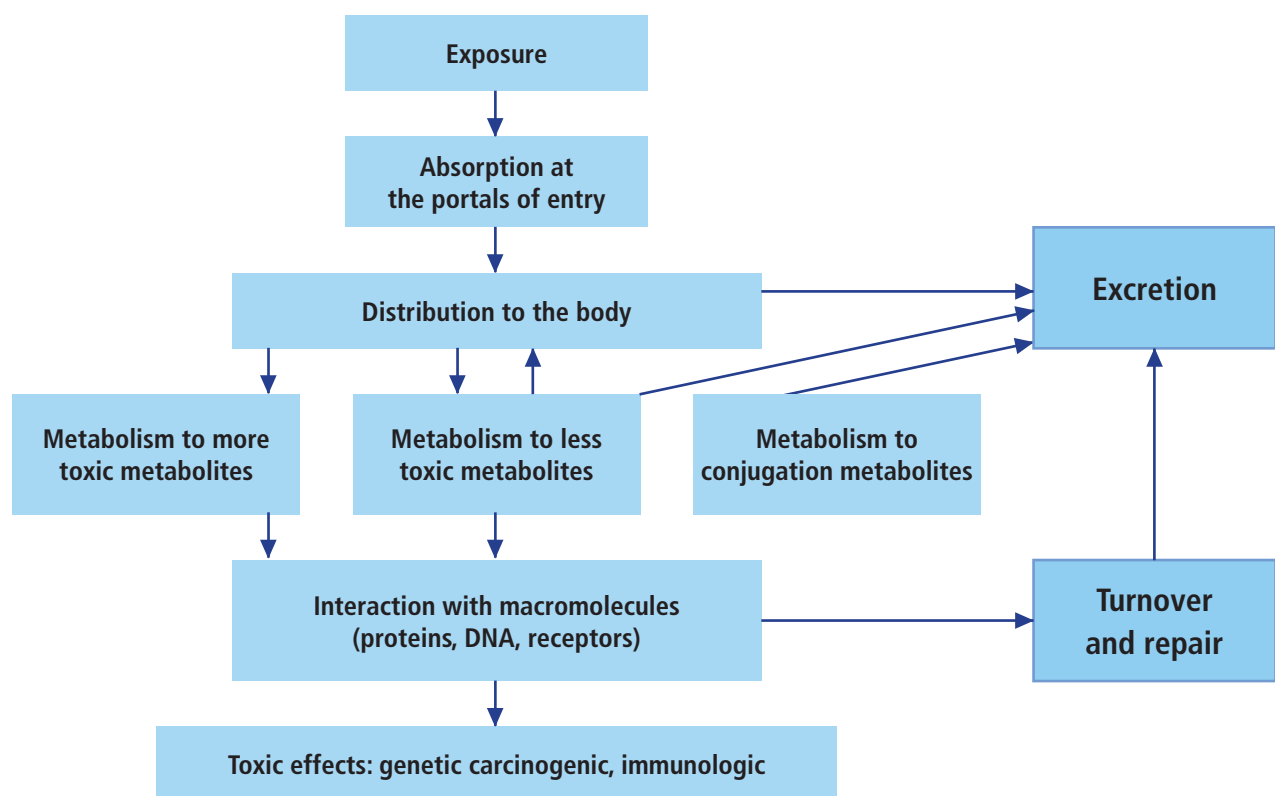


Fig. II, 1: Toxicokinetics

1 Absorption

Toxins can enter the body through all the surfaces which are in contact with the outside world. These comprise the skin, the mucous membranes and also the gastrointestinal tract. In general, the absorption over the respiratory mucosa is the quickest, whereas it is the slowest over the dermal route. The overall entry depends on the amount of toxins present, but also on the saturability of the transport process.

The mucosal surfaces have several barriers which will prevent toxins from entering the body, such as a mucosal barrier, the physical presence of symbiotic bacteria as well as the so-called tight junction. The skin also has barriers in the form of a certain level of pH, etc.

2 Transport

Once the toxicant is absorbed into the body it moves around in two ways, either by bulk transfer via the blood or lymph, but also locally through diffusional transfer over short distances. The path which a toxin takes after absorption is illustrated in Fig. II,2.

During absorption, distribution and elimination, a toxin will encounter various cell membranes before interacting with the target tissue. These membrane barriers will differ from relatively thick areas of the skin to relatively thin lung membranes, in all cases though the composition is relatively similar.

The cell membrane can be seen as a lipid matrix. It contains both phospholipids (hydrophobic) portions as well as hydrophilic heads. Intra- and extracellular proteins transverse the membrane.

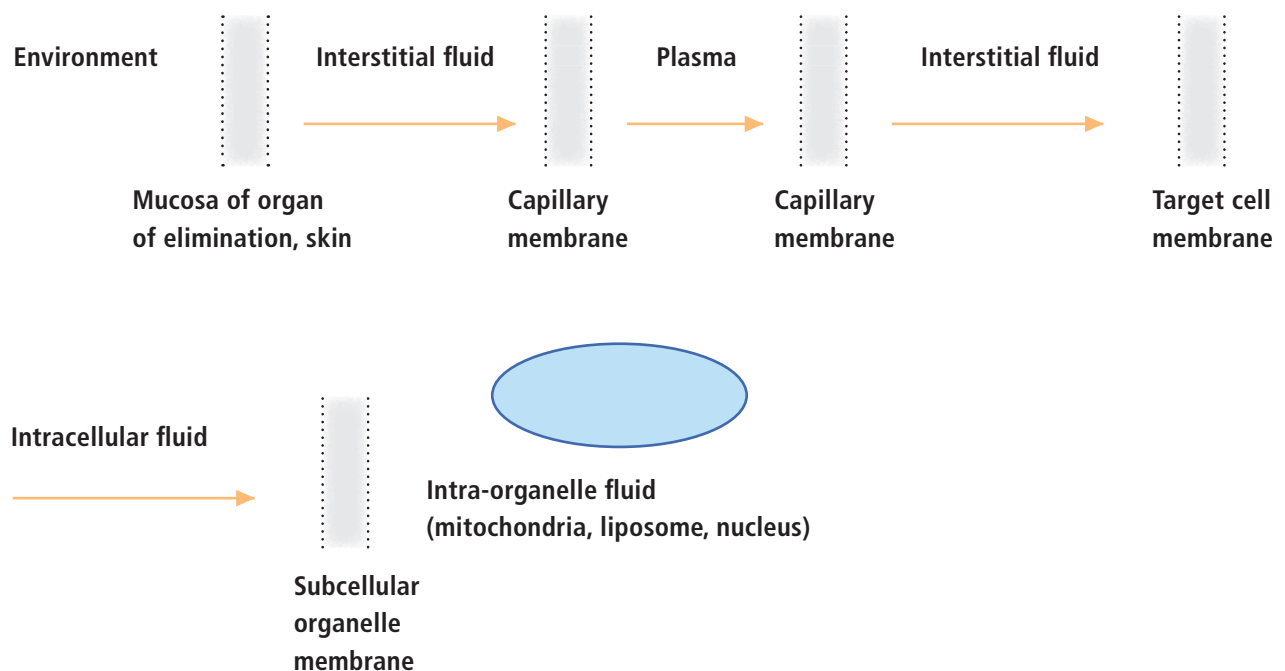


Fig. II,2: Toxin path after absorption

This will differ from organ to organ. The myelin in the brain consists of 100% lipid bilayer whereas mitochondria have only a 40% lipid bilayer. This, of course has implication for the distribution of fat soluble toxins. Depending on the fat solubility of the toxin, it will thus transverse the cell membrane. Many of the proteins which tranverse the membrane are active in transport of toxins over the cell membranes.

The distribution of the absorbed toxin will depend on various factors, such as physiological factors, but also the physiochemical properties of the drug. This process is thus a REVERSIBLE movement of the toxicant between the blood and tissues and between the extracellular and intracellular compartment. The velocity at which this movement is reversible becomes important when we address the mobilization and drainage of toxins later on.

Factors which can complicate the distribution of a toxin can be the following:

- **Perfusion of the organ**
The well perfused tissues include the liver, kidneys and brain; whereas the low perfused tissues include the bone and fat tissue where there is slow elimination from these tissues.
- **Protein Binding**
There also may be significant protein binding which could affect the delivery of the drug to the tissues and vice versa. Especially binding of toxins to the matrix structures may trap these toxins there for years and prevent elimination.

Protein binding also plays a very important role in the transport of toxins. There are many plasma proteins involved in such a transport, but mostly involved are albumin, alpha-acid-glycoprotein, the lipoproteins, and globulins.

The lipoproteins, such as HDL, LDL and VLDL are very important here, as so many toxins are lipophilic, and therefore they will carry a number of toxins. Iron and copper will again be carried by the metal binding globulins, transferrin and ceruloplasmin.

3 Distribution and Storage

Plasma protein binding is not selective and toxins can thus compete with each other and even with endogenous substances for binding.

Covalent binding to the protein forms a minor part, but the dissociation is extremely difficult and the carrier molecule is changed, and may eventually play a role in carcinogenesis.

Noncovalent binding is more common. The toxin can dissociate easier from this bond. However, in some cases the bond may be so strong that the toxin remains bound for weeks, months or years. Certain metals have high association constants and their dissociation is extremely slow.

If the affinity for an organ is large, the toxin will accumulate or form a depot for years. In general, lipid insoluble toxicants stay in the plasma and interstitial fluids, while lipid soluble contaminants reach all compartments, and may accumulate in fat.

Some toxins have specific affinity for certain tissues. Tetracyclines have a high affinity for the calcium containing tissues, which is seen in the discoloration of teeth if it is given under the age of 14 years. Similarly, the anti-malarial, chloroquine has an affinity for the melanin, and can be taken up by tissues like the retina, causing a retinitis. This drug is often used in lupus and other connective tissue diseases, which makes an ophthalmic check up every six months mandatory.

Bone will also concentrate certain toxicants such as lead where a sudden loss of bone can lead to acute release of the toxin and have dire consequences, especially after menopause when there may be a sudden bone loss.

This will be discussed later when we look at the ideal rates of detoxification.

Lipophilic pesticides, such as the organochlorines and PCB's can be expected to accumulate in fat tissues.

The affinity of metals to SH groups have also been addressed in the previous chapters.

The binding of these metals to the numerous thiol groups in the extracellular matrix is of special concern.

Certain areas will be naturally less penetrable to toxins. The brain, which is protected by the blood brain barrier, is such an example. Disease processes such as meningitis and other inflammatory or infective processes can disrupt this barrier and thus cause toxins to enter the brain tissue.

Other tissue blood barriers include the prostate/blood barrier and the testis /blood barrier.

Unfortunately, other than what is generally believed, the placenta is a poor barrier and the fetus is thus exposed to all the toxins to which the mother is exposed. This has been seen in fat tissue biopsies which were performed on newborns and found numerous toxins such as PCB's, dioxin and others in the tissues. We need thus to assume in today's environmental pollution, that our newborns are already contaminated with toxins.

4 Metabolism of Toxins

One of the most important determinants of the persistence of toxins in the body is the extent to which they can be metabolized and excreted.

Several families of metabolic enzymes are active in metabolism of endogenous and exogenous toxins.

These include one of the most important, the P450 system, but also the flavin containing monooxidases (FMO's), the alcohol and aldehyde dehydrogenases, amine oxidases cyclooxygenases, reductases, hydrolases and the conjugating enzymes such as the methyltransferases as well as the glutathione transferases to name a few.

Most of the metabolism takes place in the liver, and as most of the toxins entering the body are lipophilic, they need to become water soluble for excretion. After entrance to the liver and other organs, xenobiotics may undergo two phases of metabolism. This is demonstrated in Fig II,3.

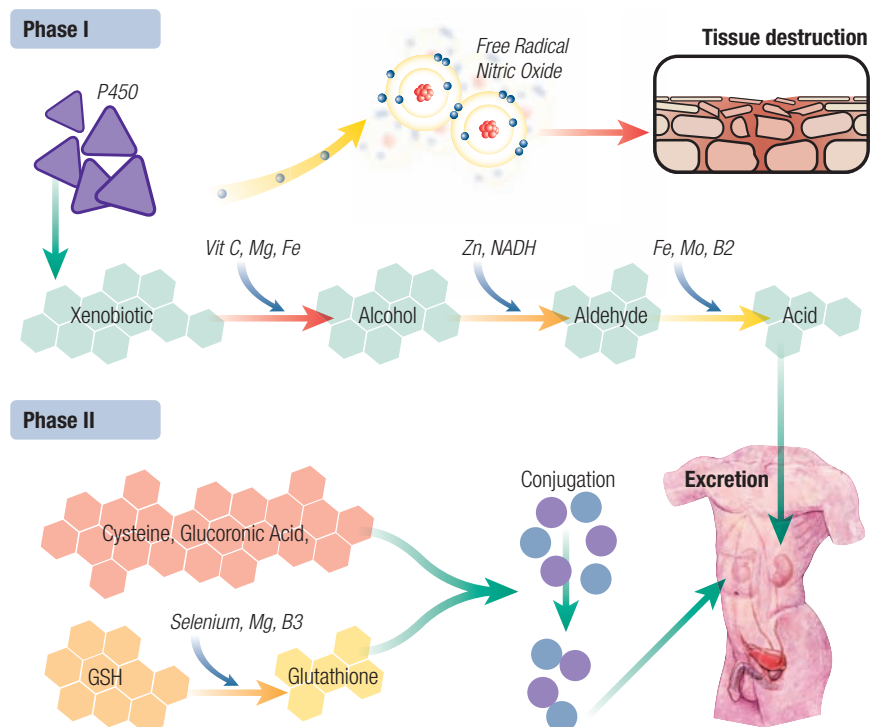


Fig II,3: Liver metabolism pathways

4.1 Phase I Reactions

Phase I metabolism involves mainly the CYP (P450) system, the FMO's and the hydrolases. Following the addition of a polar group, conjugating enzymes typically add more constituents, such as sugars, sulfate- or amino acids which make the compound more water soluble.

In this process, however sometimes more toxic intermediate metabolites are formed, these then will have to be detoxified again. These intermediate metabolites are likely to react with nuclear parts of macromolecules unless they are further detoxified. An example is the breakdown of alcohol to acetaldehyde, which is much more toxic than the alcohol.

The CYP system or P450 plays a very important role in the phase I reactions. The CYP's which constitute the carbon monoxide-binding pigment of the liver microsomes are heme proteins. A nomenclature has been developed for the different types and isoforms.

Although mammals are known to have 18 CYP families, only three are responsible for xenobiotic metabolism. The remaining are involved in steroid hormone production. They are classified according to the gene, subfamily and lastly the isoform (arabic numeral, letter, arabic numeral).

Thus CYP 3 A 4 is responsible for the metabolism of many drugs as well as endogenous toxins and exogenous toxins.

Its activity can also be influenced by a host of drugs and chemicals, and it can either be induced, which will have the result that certain drugs are broken

down too quickly, e.g., warfarin, whereas grapefruit juice in large quantities is known in fact to damage this system irrevocably and thus may lead to an accumulation of drugs.

The Phase I detoxifying pathway takes care of environmental toxins such as pesticides, pollutants and food additives as well as drugs and alcohol. The end products of our own metabolism are also processed here for excretion. Fat soluble toxins are changed by way of oxidation, reduction and hydrolysis to make them more water soluble for excretion via the bile and the kidney.

It is important to note that these enzymes need certain co-factors to fulfill their action. These are trace elements, vitamins, amino acids and substances like NADH. (see Fig II,3)

Phase I produces significant amounts of free radicals during this detoxification process, and if the antioxidant status of the patient is not adequate tissue damage may occur if the P450 is overloaded, or induced. Some substances, such as caffeine, alcohol, certain drugs, dioxin and organophosphates (used as pesticides), and paint fumes can induce this pathway. Sometimes intermediate substances like the acetaldehyde formed during the metabolism of certain toxins, like alcohol, can be more toxic to the body than the original substance. Certain people, called fast acetylators, will then be more prone to damage of the liver, as the toxin is fast metabolized to this dangerous intermediate, and then the process is slow again. These individuals are at higher risk for liver damage during ingestion of toxins which will use the alcohol dehydrogenase pathway to be detoxified, for example when paracetamol overdose occurs.

4.2 Phase II Reactions

The Phase II pathway or conjugation pathway uses substances rich in sulfhydryl groups to metabolize toxins. A number of these substances, like cysteine and taurine as well as glutathione which are formed from glycine, glutamine and cysteine under influence of a selenium dependent enzyme, also act as free radical scavengers and heavy metal chelators. During conjugation of toxins they are lost to the body forever, as they are excreted with the toxin, whereas as free radicals they can be regenerated. Some substances will only use phase I or phase II to be detoxified, others will use both. It is thus clear, that if the phase II pathway is overloaded, the free radical scavenging ability will be given up in favor of the conjugation function and further damage to the liver parenchyma may occur. Also if the patient is deficient in selenium for instance, glutathione production will be impaired, with the resultant of toxicity and free radical damage.

5 Elimination

After the toxins have gone through these two phases, they are ready to be eliminated. However, if the intermediary toxin is not broken down, or the toxin load is too high there will be bioaccumulation of the toxin.

The ability to detoxify and eliminate toxins is paramount to the maintenance of health in an organism.

For unicellular organisms a simple process of diffusion is enough to eliminate toxins, however, multicellular organisms, especially if there has been an increase in complexity, needs to find other ways to eliminate toxins.

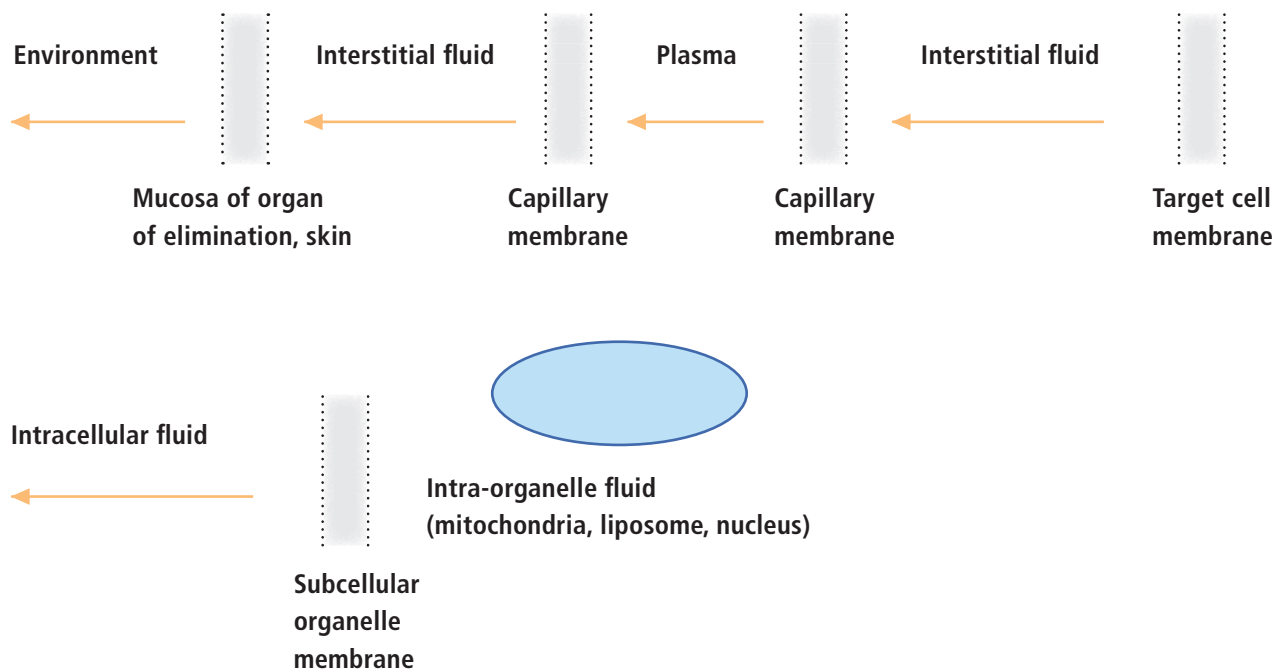


Fig II,4: Toxin path for excretion

With an increase in complexity, organisms have developed an increase in size, a decrease in surface area to body mass ratio, compartmentalization of cells and organs, as well as an increase in lipid content. Together with the fact that organisms need to protect themselves from the environment with barriers such as scales and skin, means that there is less possibility for toxins to diffuse out of the body. This was solved, by developing specialized methods of metabolism for toxins and specialized routes of elimination. We have thus major and minor elimination routes

The major routes involve the liver, the kidneys, the mucous membranes and the lungs as well as the skin, whilst the minor routes involve the saliva, sweat, milk, hair, and secretion from reproductive organs.

To eliminate the toxin, it must go through the reverse route as was described in section II from the place of storage back to the external environment (Fig II,4).

Chemicals are transported from the place of storage mainly via the blood stream. As the circulatory system leans itself toward the transport of water soluble substances, the more lipophilic substances are, the less likely they are to freely diffuse into the blood and thus the mobilization of these toxins from their place of storage is more difficult. The same process as was discussed in section II, where binding of toxins to carrier proteins and lipoproteins is the way these toxins will enter the blood stream.

The toxins are thus transported back to the organs of elimination, but if these organs are dysfunctional, overloaded or damaged, the toxins cannot be excreted. This means that such toxins will circulate further in the blood stream and through diffusion enter some compartments again, e.g. a fat soluble toxin may now be stored in the brain, with dire consequences. The stimulation of toxins out of their compartments should thus be a slow and careful process.

Here we distinguish two groups of compartments:

- 1 The *rapid-exchange system*
in these compartments, tissue concentration of toxicant is similar to that of the blood
- 2 The *slow-exchange system*
in these compartments, tissue concentration of toxicant is higher than in blood due to binding and accumulation-adipose tissue, skeleton and kidneys can temporarily retain some toxins, e.g. arsenic and zinc.

The important fact is that Detoxification and Drainage should carry on so long till the slow exchange system is given a chance to give up all the toxins. The organs involved in the Detoxification and Drainage of the toxins will be discussed in the next section.





Conclusion

- Toxins have to cross several membranes in the body to be absorbed, and to eventually be stored, or eliminated via the organs of elimination.
- Toxins follow simple kinetics, and observe the diffusion over semi-permeable membranes till a steady state is achieved on both side of the membrane.
- These basic kinetics are different for toxins who has a high association co-efficient with proteins and cellular structures, be it in the blood or in the organ of storage.
- These kinetics affect both the storage and the mobilization of toxins in and out of these compartments and needs to form the basis on which the practical Detoxification and Drainage is executed.
- Two groups of compartments can be distinguished, depending on the perfusion of the organ and the amount of toxin bound to protein.
 - The *rapid-exchange system*.
In these compartments, tissue concentration of toxin is similar to that of the blood.
 - The *slow-exchange system*
In these compartments tissue concentration of toxin is higher than in blood due to binding and accumulation.
- Many toxins are metabolized before they can get excreted. One of the main purposes of this is to render fat soluble toxins water soluble for excretion in the bile and kidneys.
- The P450 system of enzymes plays a major role here, especially in the liver, where it comprises the phase I reactions. This is augmented by the phase II reactions.
- Organs are at danger during the act of Detoxification and Drainage, due to the high concentration of toxins moving through the organ at the time, and through the generation of free radicals during the detoxification process.
- Support of these organs is thus of utmost importance during detoxification and the elimination of the toxin.

The Organs of Detoxification and Elimination

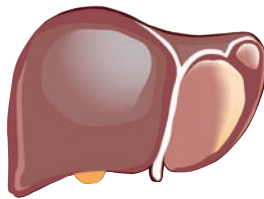
As was seen in the previous chapter, many organs and tissues are involved in the absorption, the transport, the metabolism, the storage and the elimination of toxins. These highly complex processes require special properties of the organ to fulfill this function. Often, the organ itself may be endangered by disease due to the excretion, storage and movement of toxins through it.

We shall now consider these organs in more depth.

1 The Liver

The liver is one of the most important detoxifying and elimination organs in the body, and metabolically the most complex. The liver is a major organ of chemical elimination

in that it takes up chemicals from blood, metabolizes chemicals, and ensures the biliary and renal secretion of toxins. The liver detoxifies a large array of external and internal toxins. It also plays a role in the cholesterol metabolism, glycolysis and gluconeogenesis, providing many of the plasma proteins neces-



sary for carrying hormones, fats and provides clotting factors, to name a few of its numerous functions.

The principal cell in the liver responsible for the detoxifying action is the hepatocyte which facilitates the two pathways discussed in section II in dealing with mainly fat soluble toxins in order to render them hydrophilic or water soluble.

We have seen that most toxins reach the organs of elimination via the blood stream. The liver is very well perfused, and gets its blood from two sources: the arterial oxygen rich blood which is delivered through the hepatic artery, and the venous blood through the portal vein from which the liver gets all the blood that is shunted from the capillaries of the gut and spleen.

Hepatocytes are practically bathed in blood as this blood transverses a system of sinusoids. This provides a very large surface for chemicals to easily diffuse into the liver cells or hepatocytes (see Fig III,1). Due to the high lipophilic character of many of the chemicals which are metabolized by the liver, to be able to enter the water soluble area, they will need carrier proteins. Several intracellular carrier proteins are present in hepatocytes.

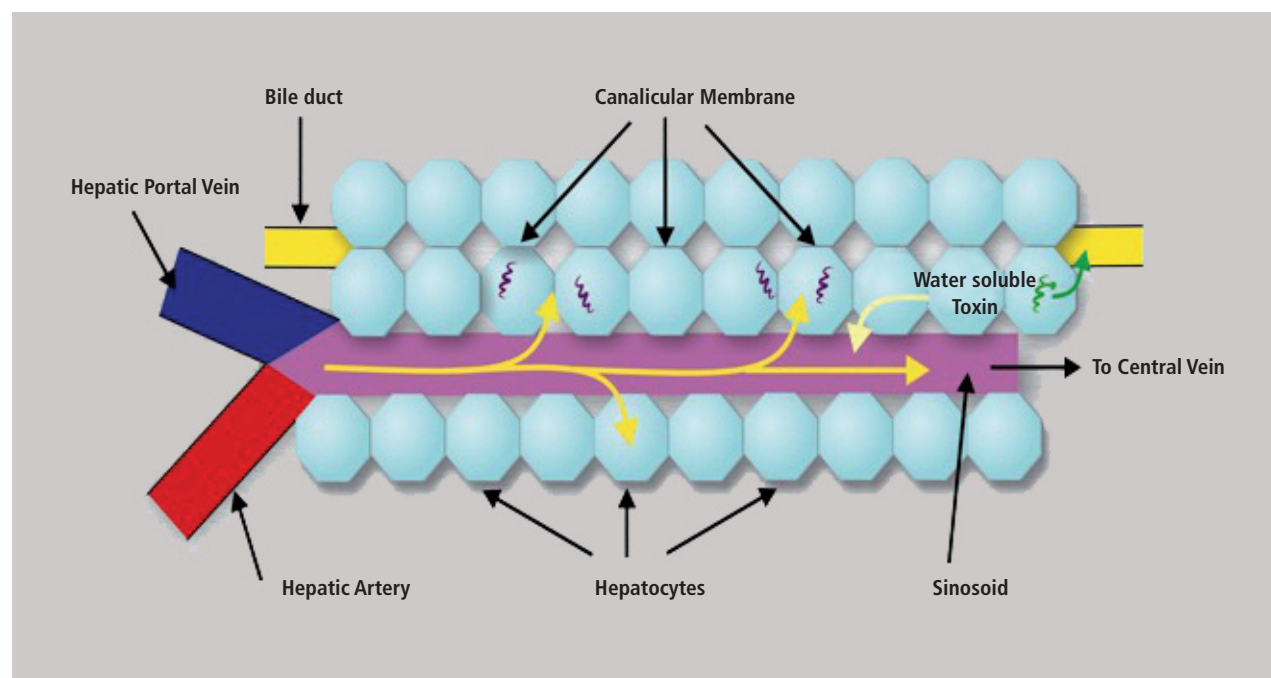


Fig. III, 1: The liver as detoxification organ

Once inside the hepatocyte the chemical can interface with the phase I and II enzymes to undergo bio-transformation and become water soluble. A number of these substances then diffuse back into the blood, where they will be transported to the kidneys for elimination.

2 Excretion in Bile

These bio-transformed molecules can also diffuse over the membranes of the bile canalliculus, and therefore flow into the bile duct. This is then further delivered with the other constituents to the gallbladder which excretes the bile into the intestine for fecal elimination. (See Fig. III,1)

In many instances we also want to facilitate the drainage of bile. The gallbladder's primary function is to secrete bile and release it through the cystic duct. This duct joins the hepatic duct from the liver to create the common bile duct, which then empties into the upper part of the small intestine, thus into the duodenum. Bile not only carries away and neutralizes toxins, but it stimulates and aids digestions by emulsifying fats, stimulating peristalsis, and acting as a natural laxative.

3 Entero-hepatic Circulation

This is a process whereby already conjugated chemicals which are water soluble is deconjugated by hydrolytic enzymes in the gut, and then rendered lipophilic again, and are once more reabsorbed by the gut. The liver is thus exposed to another round of the same toxin to reprocess it again and again. This increase the retention time for toxic chemicals in the

liver, and may increase liver toxicity. Some of these metabolites are more dangerous than their original substance and as we saw above, the P450 is also a source of free radicals which will thus further damage the liver cell.

It is thus imperative to protect the liver as well during the process of Detoxification and Drainage. This will be further discussed in the section on methods of detoxification.

4 The Kidneys

The kidneys are organs specialized in the excretion of numerous water soluble toxins and metabolites, maintaining homeostasis of the organism. The kidneys detoxify

- Drugs
- Heavy metals
- Other toxins

Each kidney possesses about one million nephrons able to perform excretion. Renal excretion represents a very complex event encompassing three different mechanisms:

- Glomerular filtration by Bowman's capsule
- Active transport in the proximal tubule
- Passive transport in the distal tubule

Blood is delivered to the kidneys via the renal artery and about 625 ml of plasma move through the kidneys per minute, and of that 125 ml is filtered through the glomerular membrane. Most of the water is then reabsorbed again in the proximal and distal tubule, so that only approximately 1-2 liters of urine is formed per day. (See figure III,2)



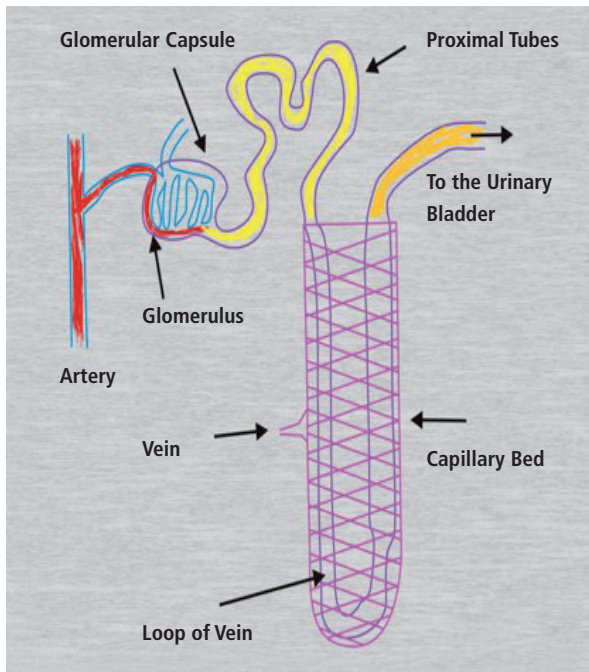


Fig. III,2: Filtration in the kidney

Some filtered substances, such as glucose will also be totally reabsorbed, so that in normal conditions there is no glucose in the urine. Other substances, many of which are harmful to the body are filtered, secreted and then minimally reabsorbed. Creatinine is such a substance, and can thus be used to test the efficiency of the kidneys in clearing harmful substances. It accumulates in the blood when the kidneys are dysfunctional. If the kidneys are damaged through disease or toxins (drugs and chemicals), their ability to excrete drugs is reduced, and in conventional medicine, the dose of drugs in needs to be adjusted accordingly.

It is important for the urine to be on the alkaline side, as it facilitates the secretion of certain drugs, like barbiturates for instance, and alkaline urine will prevent urinary tract infections.

The kidneys commonly bear the brunt of chemical toxicity since the nephron tends to concentrate the toxin and thus increase levels of toxic exposure in the tubules.

The kidneys thus also need protection and support throughout the Detoxification and Drainage stages.

5 The Matrix and Lymph

5.1 The Matrix

This forms the final biophysical layer between the cell and the regulatory organs. This system was largely forgotten since Virchow, a physician who worked in Vienna and a contemporary of Freud, saw a cell through a microscope and postulated that all diseases originated on a cellular level. Another physician working there at the time, Rokitansky, wanted to still bring in the humeral theory, but was largely ignored.

Pischinger and Heine, two modern researchers, brought this back into balance, and the newer molecular biology texts increasingly recognize the role of the matrix.

The cell on its own is actually an abstraction. The cell does not come in contact with the blood vessels, nerves, veins and lymph vessels which deliver nutrients and messengers and remove toxins. It relies for this on the biophysical layer made up of highly polymerized sugar protein complexes called Glycoaminoglycans (GAG's) like hyaluronic acid, chondroitin

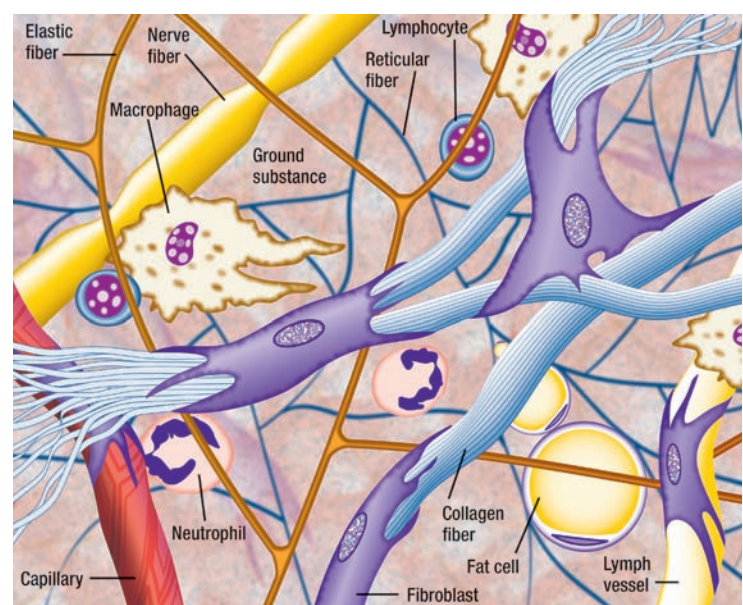


Fig. III,3: The extra-cellular matrix

sulphate and heparin or when they are linked to a protein backbone, they are called proteoglycans (PG's). This molecular sieve must be crossed by the entire array of metabolic products.

Sugar protein complexes are phylogenetically considered the best carriers of information. Heine and Pischinger could show that if the matrix is disturbed by a pin prick in one place, the disturbance is communicated to the whole matrix in seconds. This makes it an ideal system through which to give any information to the body. The acupuncture point is an anatomical structure originating in the matrix, a bell like structure, and it offers a wonderful 'window' into this system.

Unfortunately, because of the chemical and electrical charges on the GAG's and PG's, they also become the place where toxins are stored for a long time.

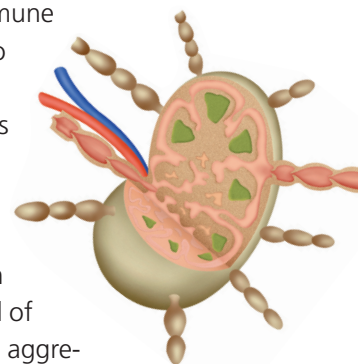
The matrix is also one of the tissues with a slow perfusion, and thus will have pattern of slow turnover. The matrix has its own biorhythm, and is dependent for instance on cortisol and thyroid hormone to be activated. During the early hours of the morning, the body goes into an ebb phase with a low cortisol, and it is during this ebb phase that the matrix will purge itself from toxic materials. Stressed patients, or patients who through a change in their sleep-wake cycle have lifted or disturbed the diurnal rhythm of cortisol, will not be able to detoxify, as there may be a 'misfiring' between the matrix and the liver. Cortisone in high doses as medication will also disturb the innate rhythm of the body, and result in matrix toxicity. We can see that in patients who has been on cortisone therapy, as they become swollen and puffy in the matrix. Patients who are hypothyroid have been described as having 'myxoedema' in the older textbooks. The same swelling will be apparent in the matrix if the matrix biorhythm is disturbed. Many toxins are hydrophilic and will draw fluid into the matrix. The result is edema, which we in clinical medicine see as cyclical edema in females or as cellulite.

It is clear from the above that if the molecular sieve of the biophysical layer fails, is polluted that there will be distortion of information to and from the cell. If the disturbance is severe enough, cellular disease will ensue.

Newer molecular biological research shows that the matrix is the site for many messengers which codes for intracellular phenomena, which, if disturbed, can contribute to many disease phenomena, including cancer. (Lukashev ME, Werb Z, 1998)

5.2 The Lymph System

Apart from its role in the immune system, the lymph system also acts as a detoxifying organ and drains most of the toxins from the matrix or connective tissue via the lymph vessels, which finally drain into the superior vena cava. The lymph system is made up of a myriad of little lymph vessels which then aggregate into larger vessels. These larger vessels are interspersed by aggregations of lymphoid tissue, which are made up of immune competent cells. These lymph nodes, as the aggregations are called, really function as super detection centers for antigens, but it is also here where sensitized immune cells will migrate in order to produce millions of similar clones of that sensitized cell. The migration is called "homing" in immunology and the multiplication, cloning. The swelling we see in these lymph nodes during an infection is due to the activation of the immune cascade by these sensitized cells. This will cause an inflammation of the lymph node.



A major portion of our immune system is located in these lymph aggregations, and in fact the largest part of our immune system is found in the gut lining's so-called Peyer's patches. This is the reason why we can manipulate the whole of the immune system by intervening on the level of the gut lining.

Physiological considerations

The lymph system is a slow drainage system, and the propulsion of lymph towards the heart is dependent on a number of factors. Firstly, the lymph vessels have no valves, but depend on a sort of negative suction action of the truncal vessels, which is similar to that of an amphibian heart. The lymph flows relatively slowly at a rate of 1-2 ml/min, against a high resistance, whereas the venous flow is rapid at 2-3 l/min against a low resistance. Two thirds of the body fluid is located in the intracellular space, whilst a third is located in the extra-cellular space. Of this, 75% is in the interstitial space or connective tissue and about 25% circulates as plasma. The lymph and venous flow is responsible for circulating most of the extra-cellular fluid, and the interstitial fluid in particular is drained mainly by the lymph system.

From the above it is clear that the factors which will control the fluid interchange will be:

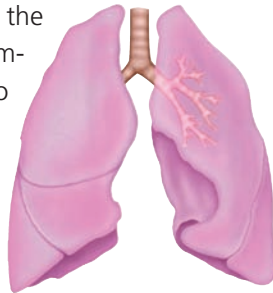
- **Oncotic pressure** of the plasma and the lymph is determined by the amount of macromolecules such as protein, and the electrolyte content such as sodium, potassium, etc. in the solution. Solutes exert a certain pressure in any fluid, as they 'draw water' so to speak and the more there is of them in a solution, the higher the pressure. When a patient is protein deficient for instance, through malnutrition or disease, we see that there are not enough macromolecules to keep the fluid in the vascular compartment, and the fluid will leak out into the interstitium, with edema as the result. Kidney failure on the other hand results in an accumulation of electrolytes and other macromolecules in the interstitium. The result is that the oncotic pressure in the interstitium will exceed that of the plasma, and again edema will ensue.
- The **hydrostatic pressure** is a mechanical pressure, which can be compared to a hose pipe connected to an open tap. The smaller the diameter of the hose pipe, the higher the pressure, the more open the tap is, the higher the pressure, and if there is an obstruction like a kink in the hose, the higher the pressure before the kink, and the lower the pressure after the kink. Fluid always tends to drain from a high-pressure area to a low-pressure area over a semi permeable membrane, which is represented by the venous capillary or the lymph capillary, until the pressure is equal on both sides. Thus if there is obstruction in the venous system, similar to a kink in the hose, there will be a high pressure in the vein, and the body will try to equalize the pressure between the vein and the interstitium, thus the fluid will also accumulate in the interstitium.
- If there is for instance cardiac failure, we see a **back pressure into the venous system**, and in our hose model above, this will represent a wide open tap, with more pressure in the venous system, and then more fluid in the interstitium.
- Lastly if there is an obstruction of the lymph flow, we will see a **back pressure in the lymph system** and edema will again be the result. We see this in diseases of the lymph vessels like Elephantiasis, where the lymph vessel is scarred by a parasite for instance.

The lymph system as a detoxifying organ

The lymph system has a special relationship with the matrix. It is so to say as the only way out for toxins which are stored in the matrix is via the lymph system. It also means that if the matrix is overloaded with toxins, the lymph system will be overloaded with toxins as well, as the lymph system has to remove the toxic debris out of the interstitium, and at a certain point will also be clogged with these. The stimulation of lymph flow is thus one of the most important steps to achieve when cleaning the matrix.

6 The Lungs

Not only does the mucosa of the respiratory tract play an important role as a barrier to toxins as was discussed earlier, the lungs are also one of the main points of excretion of gaseous and volatile drugs such as anesthetics and even alcohol.



Elimination via the lungs is typical for toxins with high volatility (e.g. organic solvents). Gases and vapours with low solubility in blood will be quickly eliminated this way, whereas toxins with high blood solubility will be eliminated by other routes.

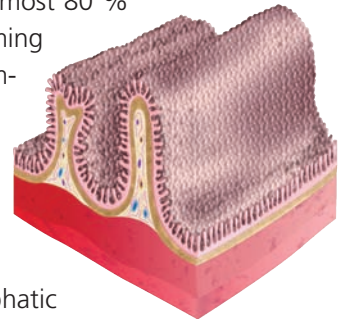
Organic solvents absorbed by the GIT or skin are excreted partially by exhaled air in each passage of blood through the lungs, if they have a sufficient vapour pressure. The breathalyser test used for suspected drunk drivers is based on this fact. The concentration of CO_2 in exhaled air is in equilibrium with the CO_2 -Hb blood content. Another example is the radioactive gas radon which appears in exhaled air due to the decay of radium accumulated in the skeleton.

A number of toxins and bacteria are also secreted in the mucous of the respiratory tract, and expectoration is thus welcomed and supported.

7 The Mucosal Membranes

Mucosal membranes form the largest part of our bodies in contact with the outside world, and they are therefore very specialized. A mucosal surface is like a micro cosmos in itself, and a good example of all the components of the auto regulatory system active in one organ. With almost 80 %

of the immune system forming the mucosal associated lymphoid tissue (MALT), some hormones having receptors on the mucosal cells, a full complement of nerves mediated by the autonomic nervous system, an active lymphatic



drainage, and the large complement of extra-cellular matrix, the mucosal membrane comprise one of the most important regulatory organs. Not only does it form a very selective barrier with the tight junction in between the epithelial cell and adhesion molecules playing an important role in deciding what will enter the body, mucosal surfaces can also let some of the immune cells, like neutrophils through the tight junction to ingest toxic material in the lumen. It further protects against toxins by secreting chloride and other solutes into the lumen which will osmotically draw water in order to wash away the offender, a fact that we see as diarrhea in the gut for instance.

The integrity of these surfaces is thus of major importance in the defense against toxins.

The symbiotic gut bacteria also need mentioning here as a barrier function. Not only do they form a passive barrier against toxins coming in contact with the epithelial surface, they also contribute to the defense against toxins by producing certain metabolites which will serve as fuel for the gut lining, and as such will then help the mucosal cell to keep the integrity of the tight junction. However, due to the hydrolytic enzymes produced by them, they can also contribute to the dangerous entero-hepatic circulation mentioned above.

Absorption via gastrointestinal tract

Toxins can be ingested in the case of accidental swallowing, intake of contaminated food and drinks, or swallowing of particles cleared from the respiratory tract.

In the case of toxins biotransformed in the liver to less toxic or non-toxic metabolites, ingestion may represent a less dangerous portal of entry. After absorption in the GIT these toxins will be transported by the portal vein to the liver, and there they can be partially detoxified by biotransformation.

The active area for absorption in the intestines is about 100 m².

Some toxic metal ions use specialized transport systems for essential elements: Thallium, cobalt and manganese use the iron system, while lead appears to use the calcium system.

Many factors influence the rate of absorption of toxins in various parts of the GIT:

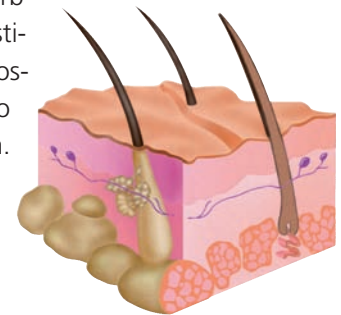
- Physico-chemical properties of toxins, for example, particle size is important, the smaller the size, the higher the solubility.
- Quantity of food present in the gut (diluting effect).
- Residence time in each part of the GIT (from a few minutes in the mouth to one hour in the stomach to many hours in the intestines).
- The absorption area and absorption capacity of the epithelium.
- Local pH, which governs absorption of dissociated toxins; in the acid pH of the stomach, non-dissociated acidic compounds will be more quickly absorbed.
- Peristalsis (movement of intestines by muscles) and local blood flow.
- Gastric and intestinal secretions transform toxins into more or less soluble products; bile is an emulsifying agent producing more soluble complexes (hydrotropy).

- Combined exposure to other toxins, which can produce synergistic or antagonistic effects in absorption processes.
- Presence of complexing/chelating agents.
- The action of micro flora of the gut comprising about 1.5 kg made up of 60 different bacterial species which can perform bio transformation of toxins.


When we thus detoxify and drain, it is also imperative to support the actions of the gut, but also to support the integrity of the barrier function in the gut.

8 The Skin

The skin forms the second largest surface of our body after the mucosa which is in constant contact with the outside world. Apart from the barrier function, it is also a major detoxifying organ, and has the same P450 system seen in the liver, as well as glutathione to take care of polycyclic aromatic hydrocarbons. The skin can absorb many substances (like pesticides and chemicals in cosmetic products), and has to be able to detoxify them. Another important function of the skin is to protect us against the harmful UV rays from the sun.



The glutathione and other free radical scavengers like catalase and super oxide dismutase are of importance, as they scavenge the free radicals formed by the UV ray exposure. Like in the liver though, induction of the detoxifying P450 pathway will also generate free radicals so that in the presence of toxins the skin is more exposed to the effects of free radicals, which leads to immunotoxicity, tissue destruction and eventually skin ageing as well as cancer. Conversely, UV rays damage the detoxifying ability of the skin (the P450), and sun damaged skin is thus less able to deal with toxins.



Due to its role in detoxification, and being one of our most important excretory organs (through sweat and evaporation), we also see the skin often bearing the brunt when other detoxifying organs like the liver are overloaded. Eczema, drug induced rashes and increased sweating are examples of this. In these cases it is thus important to support other organs like the liver for detoxification in skin disease. The liver and skin for instance break down histamine in the body through the P450. If the systems are overloaded, allergy will ensue. Histamine and other amines are also formed during the inflammatory process, and many environmental toxins, like alcoholic drinks, especially red wine can contain a large amount of histamine.

9 Sweat

Many non-electrolytes can be partially eliminated via skin by sweat: ethyl alcohol, acetone, phenols, carbon disulphide and chlorinated hydrocarbons.

10 Hair

Analysis of hair can be used as an indicator of homeostasis of some physiological substances. Also exposure to some toxins, especially heavy metals, can be evaluated by this kind of bioassay.

11 Other Routes of Elimination

Milk

Many metals, organic solvents and some organochlorine pesticides (DDT) are secreted via the mammary gland in mother's milk. This pathway can represent a danger for nursing infants.

Saliva

Some drugs and metallic ions can be excreted through the mucosa of the mouth by saliva, for example, lead ("lead line"), mercury, arsenic, copper, as well as bromides, iodides, ethyl alcohol, alkaloids, and so on. The toxins are then swallowed, reaching the GIT, where they can be reabsorbed or eliminated by feces.



Conclusion

- Many organs are involved in the storage, metabolism and elimination of toxins once the toxin is absorbed into the body.
- The liver is one of the major detoxification organs, and plays an especially important role in the processing of toxins being absorbed via the oral route.
- The liver is well perfused and also equipped with enzymes to render fat soluble toxins to water soluble toxins to be excreted in the kidney and bile.
- The kidney deals with the above mentioned water soluble toxins, but is also the major organ of elimination dealing with heavy metals and several drugs.
- The lung plays a major role in the elimination of volatile gases, e.g. organic solvents and gases and vapours with high solubility in the blood.
- The mucous membranes act as a barrier, but also contain the P450 system of enzymes and can actively metabolize and excrete toxins.
- The symbiotic micro flora plays a special important role here.
- Sweat, hair, milk and saliva are minor elimination organs, and can be used to test the elimination of toxins such as heavy metals and other toxins.
- Excretion of toxins in milk pose a risk to the infant.
- The matrix and also with it the adipose tissue form a major site of deposition of both water and fat soluble toxins, and due to the fact that this is a slow exchange compartment and in close association with the cell, is a major area of concern in chronic intoxication.
- The lymph system is the only significant way toxins can be drained from this compartment and therefore needs special attention during the drainage process.

Tools for Detoxification

In the previous sections we looked at the various toxins which can affect the organism as well as at the way the organism deals with the toxin under normal physiological conditions. In this and the next section we will explore how to support this process in well persons but mostly in patients with mild or serious disease.

We have seen in the previous sections that:

- 1 We are surrounded by toxins, and that there is no place on earth that is safe anymore.
- 2 That these toxins can enter the body, and if not metabolized and eliminated can stay in the body for years, in compartments that are relatively poorly perfused, like the fat tissue and the connective tissue.
- 3 That these toxins can have detrimental effects in the body, even if present in minute amounts over many years.
- 4 That the human body being a complex organism has developed sophisticated mechanisms to sequester, metabolize and eliminate these toxins.
- 5 That the organs of elimination can be less efficient through disease and overload or, through the lack of vital co-factors needed for the proper functioning of enzymes.
- 6 Those toxins follow simple toxicokinetics in that they diffuse over several membranes as well as bind to plasma proteins. This will determine the rate that they enter the body and certain tissue compartments, but also the rate that they are removed from these compartments.

1 Why Does a Person Need to Detoxify and Eliminate?

It should be clear from the above that toxins stored in the body or not eliminated, will be detrimental for various reasons. Toxins can have a wide range of effects, such as fatigue, brain fog, concentration loss, but also other not such apparent manifestations such as the so-called chloracne which is caused by halogenated toxins.

As we saw above, some toxins can be endocrine disruptors, cause immune dysfunction, and in the worst scenario act as carcinogenic substances.

Due to the wide distribution of toxins, and our fast lifestyle with modern malnutrition and toxic food, as well as the increase in psychological stress, the need for Detoxification and Drainage exist in every patient.

Detoxification and drainage requirements, however, will be different in different populations.

The aims of detoxification can be summarized as the so-called 4-S treatment:

STOP	external supply of toxins.
SUPPORT	the organs of Detoxification and Drainage.
STIMULATE	elimination of toxins.
SENSITIZE	the patient for further detoxification.

We saw in part II of this booklet that toxins have basic kinetics. Toxins need to diffuse over several membranes, to reach different compartments. Most toxins reach the other compartment by passive diffusion over semipermeable membranes. Toxins are carried to and from compartments in the blood, and therefore it means that we would like to reduce the concentration of toxins in the blood so that the toxins can start to diffuse back into the blood stream again.

For this reason we put the patient on a non-toxic diet, give a lot of fluids during the detoxification period, and also pro-actively stop the supply of toxins, such as inhalants, alcohol and other toxins. This is the first S: STOP.

In other cases, the toxins are bound to proteins and also to SH groups in the cell and in the matrix. We often then have to stimulate the release of the toxin from these molecules. This is an active process and needs support. To get the body to free itself of toxins we need to do two things: Support the organs which

metabolize harmful substances, support the function of the organs which store toxins, such as the matrix, and lastly we also have to stimulate elimination from these organs.

It is important to note that once stored toxins are released they often have not completed their metabolism, and therefore still need to be made water soluble in the liver before getting excreted in the kidney and other organs.

If the stored toxins are released too rapidly all at once, or the liver and other metabolizing and elimination organs are overloaded or not functioning properly, the released toxins will diffuse into the blood, but cannot be excreted. They will thus circulate in the blood stream till they found a compartment where the concentration is less than in the blood and then diffuse into this compartment. The crux is that in this way toxins are merely shifted from point A to B. This is not such a problem in well persons or patients with mild toxicity, but in patients with severe toxicity it may have repercussions, such as heavy metals now entering the brain where it is extremely difficult to remove them.

Especially in patients where the organs of elimination are not functioning properly or burdened by disease or with other toxins (such as seen in patients on chemotherapy), this needs to be considered. In these patients we need to support the organs of detoxifi-

cation and elimination first before we actually drain the tissues.

It is also important to note that the process of Detoxification and Drainage puts a severe burden on the body, and thus in the very frail and sick patients it can put another burden on the body and in these patients detoxification should be done as a later event, when the patient has received other medications to support the body. Detoxification and drainage also needs energy, and therefore the catalysts are a standard addition to more strenuous detoxification programs. Apart from the fact that they also play a role in cellular detoxification. (See below)

2 Tools for Detoxification and Drainage

For each organ there is a product which will support the tissues. These are mostly the so-called composita preparations which also contain tissue extracts and often catalysts. And there are basic preparations which are combinations of plant materials and also minerals on the other hand are mostly (but not only) used to stimulate elimination. We shall now discuss the various medications available for detoxification. Firstly the basic regimens, which can be generally applied in all diseases, and then a number of disease processes will be discussed separately.

Mild to moderate toxicity	Organs	Moderate to severe toxicity
Detox-Kit contains Nux-vomica Homaccord, Berberis-Homaccord and Lymphomyosot	Liver	Hepar compositum
	Kidney	+ Solidago compositum
	Matrix	+ Pulsatilla compositum/Thyreoida compositum
Coenzyme compositum	Cell	+ Ubichinon compositum/Glyoxal compositum
Use at least for 6 weeks		Use first for six weeks, then Detox-Kit for another 6 weeks

Fig. IV,1: General Detoxification and Drainage

2.1 The General Basic Detoxification

This regimen is often used initially in patients with mild to moderate toxicity. With this basic regimen, we want to support the liver and gut, the kidneys and drain the matrix of toxins as well as help the excretion.

These preparations come in drop form and 30 drops of each can be added to a 1.5 liter bottle of water to be taken over the day. This is thus a convenient method to deliver the medications.

Nux vomica-Homaccord supports the liver and the gut. Like with most Homaccords this medication is also functiotropic to the liver and gut, which means that it will improve the function of these organs.

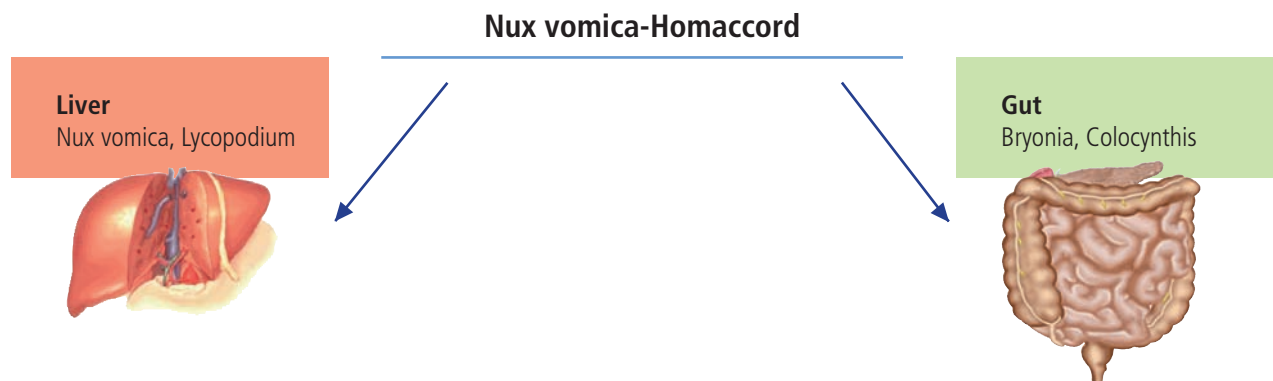


Fig. IV,2: Nux vomica-Homaccord

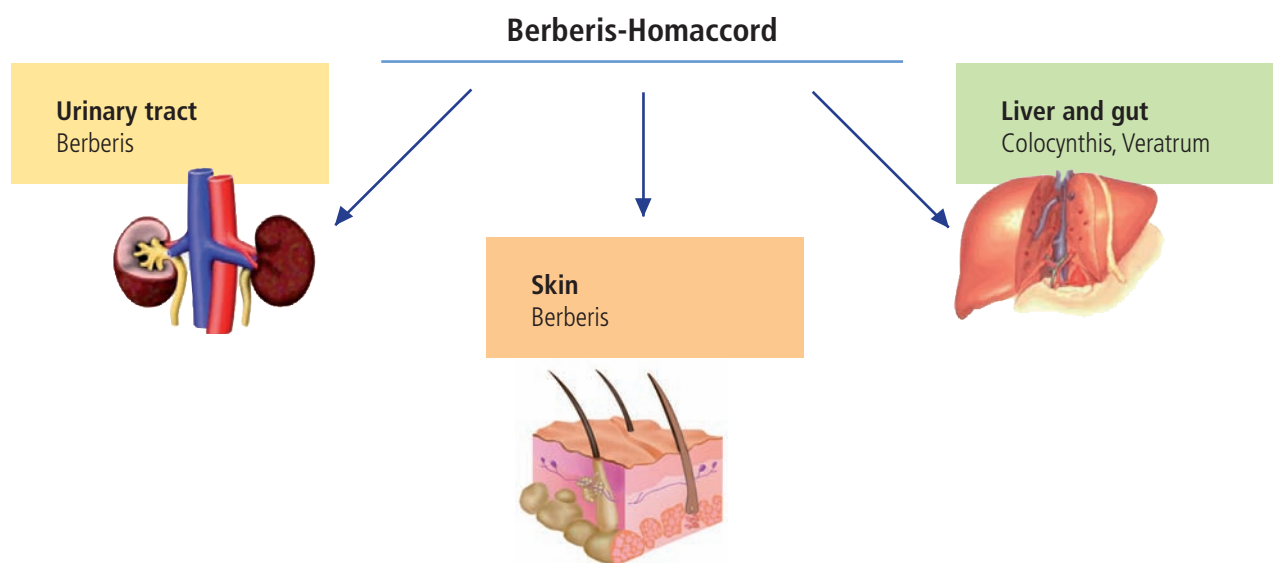


Fig. IV,3: Berberis-Homaccord

Berberis-Homaccord has the same effect as above, but is more functiotropic for the kidneys, however, it also has an action on the liver and gallbladder.

Lymphomyosot has been designed to be a drainage remedy, and should not be used initially in the case of severe toxicity, or if the liver and kidneys are overloaded.

It has several components which helps drain the tissues of the various organs. It is thus a universal drainage remedy and can also be used in the case of disease of the lymphoid organs. **Lymphomyosot** has been studied in cases of diabetic neuropathy where it was seen to be as effective as alpha lipoic acid infusions, which are currently the treatment of choice for diabetic polyneuropathy.

The postulation was that **Lymphomyosot** will drain the so-called Advanced Glycosylation End products (AGE's) in the matrix of these patients and thereby reduce the inflammatory potential around the nerves. (Dietz et al., 2004)

The actions of the various constituents of **Lymphomyosot** are depicted in the figure below.

In some countries, **Nux vomica-Homaccord**, **Berberis-Homaccord** as well as **Lymphomyosot** are combined into one pack, the so-called **Detox-Kit**.

In most patients with mild to moderate toxicity the three products can be given together as **Detox-Kit**.

Often **Coenzyme compositum** is given together with these three products. The catalysts will be discussed separately below, but this is mainly to support the Krebs cycle, and also to detoxify the cellular structures. This makes the Detoxification and Drainage quite complete.

The symptoms of Detoxification and Drainage can vary from patient to patient. Most patients start with a diuresis, or losing water, while others may drain preliminarily over the gut, with slight diarrhea and loose stools. The color of the urine and stools may also change. Some patients will use the skin and the lungs to detoxify, which manifests as an increase in sweat with odor or with a tachypnea.

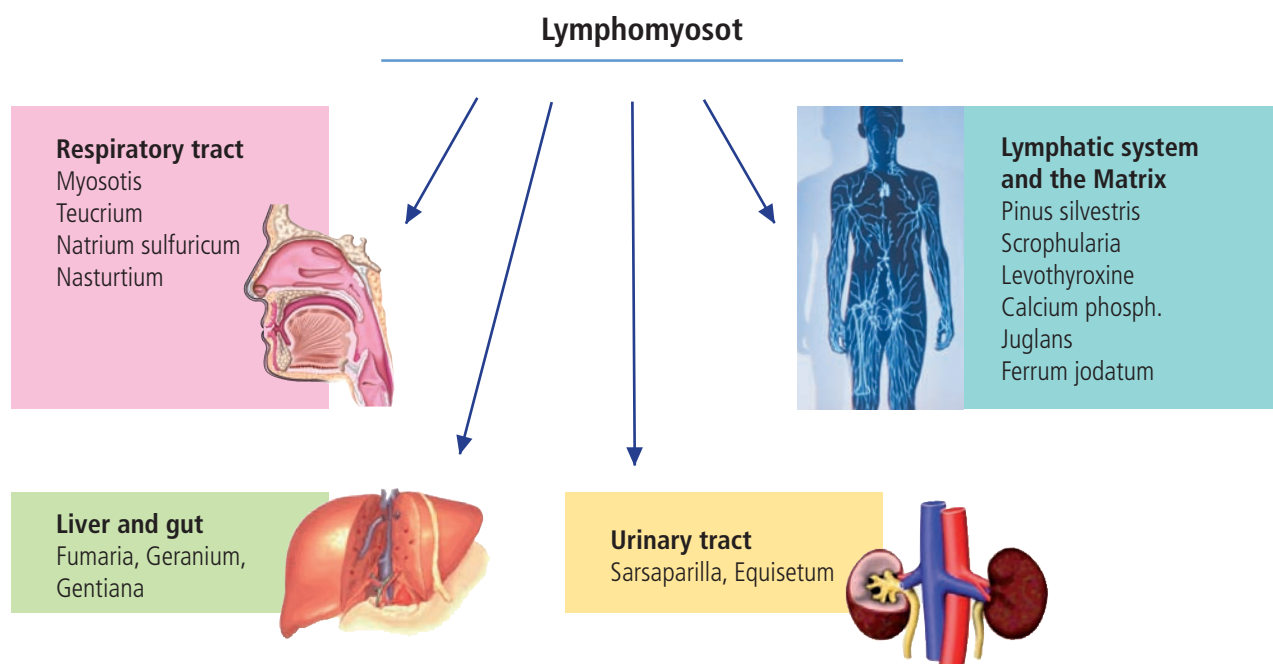


Fig. IV,4: Lymphomyosot

2.2 The General Advanced Detoxification

The purpose of this advanced detoxification is to support the organs of detoxification, especially in patients with a high toxic burden, or in patients where the organs of Detoxification and Drainage are not functioning optimally. This is also true for patients who are debilitated.

In these patients it is very important not to increase the load of toxins too early, as these patients often already have genotoxic effects of toxins or active cancer. For instance, if a patient with breast cancer is highly contaminated with DDT, which is an estrogenic like substance, it can act as a promoter for the cancer. Experiments with ovariectomized mice have shown that the mice can develop breast cancer if they are intoxicated with DDT, then ovariectomized so that there is no internal source of estrogens. The mice then developed breast cancer from the release of DDT from the tissues. (Bigsby et al., 1997)

It is thus wise to go slowly in patients with decreased detox ability, or high loads of toxins as well as in obese patients which could store a number of lipo-

philic toxins. Fasting should be avoided in most patients for this reason, as fasting causes a very quick release of toxins from the storage compartments into the blood stream due to the fact that there are no immediate toxins coming in from the food, and the elimination and detox organs will then turn their attention to older stored toxins and these may then be released in large amounts and at once.

The advanced detoxification products aim to support the major organs of Detoxification and Drainage (see Fig IV, 5). These products are mostly composita preparations, which implies that they have a special formulation with plant and mineral material, but then also contain organ extracts of the specific target organs, or tissue which will support the target organs, as well as catalysts and sometimes vitamins in dilution.

The plant material is in a low dilution and has a homeophytherapeutic effect, whilst the minerals, catalysts and organ extracts occur in concentrations which are thought to be stimulatory. These concentrations are the same as those in which many of the body's internal messengers such as neurotransmitters and cytokines are present.

	Liver	Urinary tract/ Kidney	Lymph	Skin	Gut	Gallbladder	Connective tissue	Respiratory tract
Basic detoxification/ drainage	Detox-Kit	Detox-Kit	Detox-Kit	-	Detox-Kit	Chelidonium- Homaccord	Detox-Kit	Bronchalis-Heel
Advanced detox 1	Hepar comp.	Solidago comp.	Tonsilla comp.	Cutis comp.	Mucosa comp.	Hepar comp.	Thyreoidea comp.	Mucosa comp.
Advanced detox 2	Hepeel	Reneel H	Galium-Heel/ Lymphomyosot	Schwef-Heel	Nux vomica- Homaccord	Leber-Galle Tropfen (new)	Pulsatilla comp.	
Advanced detox 3						Injeel-Chol	Galium-Heel/ Lymphomyosot	
For cellular detoxification in addition	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.

Fig. IV,5: Advanced detoxification products

The support medication for the liver is **Hepar compositum**. This product has the typical compositum configuration, and will also support other tissues such as the pancreas and the colon. It is designed to support the detoxifying ability of the liver and gallbladder.

For the kidney, the medication of choice is **Solidago compositum**. Again this typical compositum product combines organ extracts with plant materials and minerals as well as with some catalysts. This product has a strengthening and toning effect on the renal tract.

The last part of the advanced detox is the support and activation of the extra cellular matrix. It is important to realize that fat tissue, bone, and also cartilage are all part of the extra cellular matrix, albeit

with differences in density and types of fibres. However, these compartments are relatively poorly perfused and all drained by the lymph system. They all also share the high concentration of negatively charged amino acids and SH groups which will all bind toxins tightly and will keep these toxins sequestered for years. Furthermore, adipose tissue offers a large reservoir for fat soluble toxins.

The matrix is in constant renewal through a balanced process of controlled degradation and controlled repair. The degradation is mediated via the pro inflammatory cytokines which in turn will mobilize the so-called matrix metalloproteinases (MMP's) which dissolves the tissue of the matrix and through this method also get rid of toxic complexes. (See Figure IV,6)

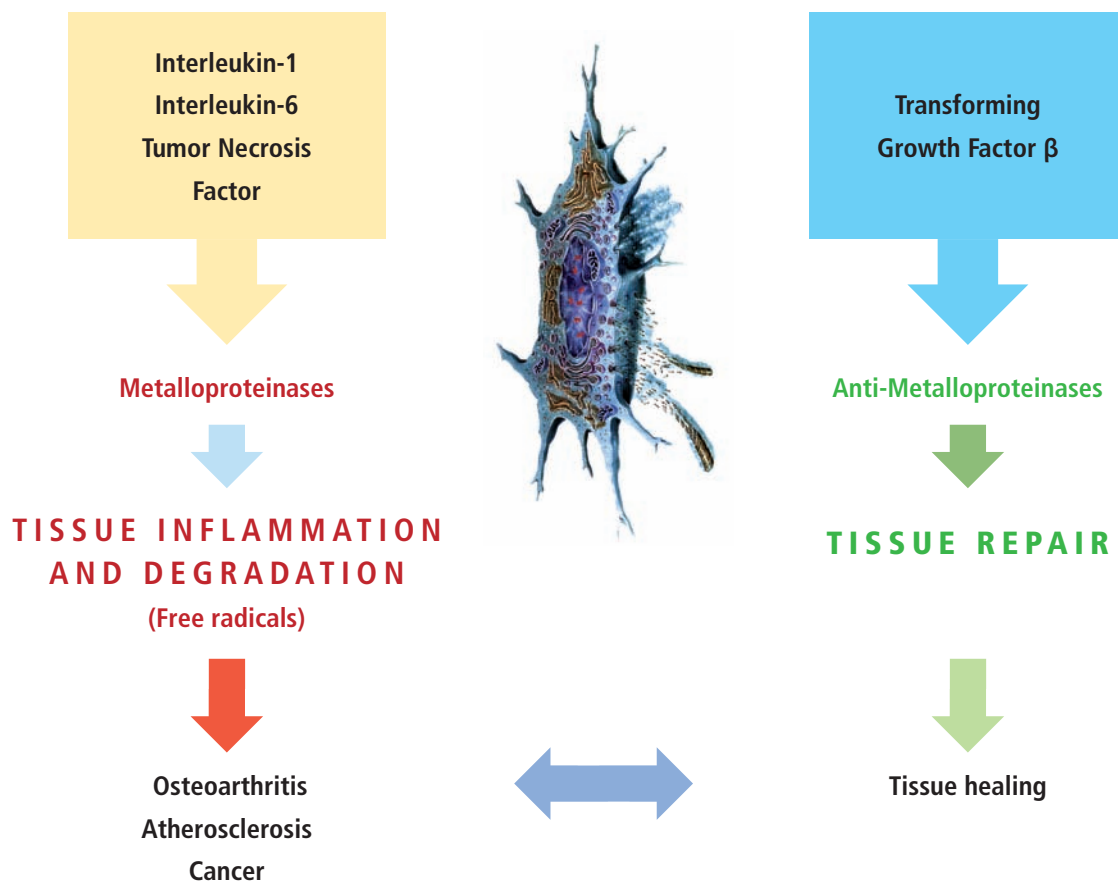


Fig. IV,6: Degradation and repair in the matrix

This process is under control of several physiological substances, like cortisol and thyroid hormone to name a few. If patients for instance lose the bio-rhythm of cortisol which we need to control this repair process in the matrix, the patient will end up with a toxic and edematous matrix, such as seen in patients on long-term cortisol therapy.

In such cases and in cases where the patient has been under severe psychological stress, we need to activate the matrix as an organ again.

This is best achieved by products containing the factors needed for the activation and strengthening of the matrix, and therefore we use products such as **Thyreoidea compositum**, as it has a number of suis embryological and stem tissues in it, such as Funiculus umbilicalis made from Wharton's jelly. These have a strengthening and activating effect on the mesenchyme, of which the matrix is part of.

One other medication used in the activation of the matrix is **Pulsatilla compositum**. This medication contains a plant, Pulsatilla, the mineral sulfur in homeopathic form and lastly also cortisone in a high dilution. This high dilution will have a homeopathically reversal effect if a patient had a high dose of cortisone over time. The sulfur is thought to activate the sulfur containing substances of the matrix.

2.3 The Catalysts

This group of substances are used in detoxification in two ways, namely as support for the Krebs cycle and secondly as cellular detoxifiers.

There are three of them, the first being **Coenzyme compositum**, the second **Ubichinon compositum**, and lastly **Glyoxal compositum**.

Coenzyme compositum has all the factors in the Krebs cycle and many of the co-factors involved in the Krebs cycle. The vitamins in dilution are thought to have a detoxifying effect on the cellular structures.

Ubichinon compositum has a number of quinones in and apart from supporting the electron transfer chain during cellular respiration, they are also empirically used in cancer patients.

Glyoxal compositum which is a mixture between Glyoxal and Methylglyoxal will have a stimulating effect on the cellular respiration. The latter is thought to have the most stimulatory effect, although this has not been studied. Current studies are being initiated to scientifically prove the action of these homeopathically prepared catalysts which has been empirically used since 1976.

The catalysts play a specifically important role in detoxification, and are added to detoxify cellular structures. The action of **Glyoxal compositum** is thought to be deeper than that of **Ubichinon compositum** and **Coenzyme compositum**. **Glyoxal compositum** is used in patients who have a severe cellular toxicity, such as cancer patients. **Glyoxal compositum** is used in longer intervals, together with **Ubichinon compositum** and **Coenzyme compositum**. For instance, **Glyoxal compositum** can be given 1x per week for 4 weeks together with the other catalysts with a break of several months in between and then used again.

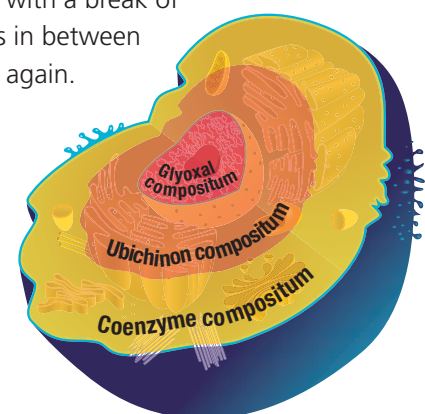


Fig. IV,7: Action of catalysts

Conclusion

- Most people need to detoxify and drain due to the environmental load of toxins.
- Toxins accumulate through a combination of increase load as well as modern malnutrition and psychological stress, which impacts on the ability of the body to detoxify and drain.
- The 4-S regimen is a practical way to approach the problem of toxin accumulation:

STOP	external supply of toxins.
SUPPORT	the organs of detoxification and drainage.
STIMULATE	elimination of toxins.
SENSITIZE	the patient for further detoxification.

- Antihomotoxic tools for Detoxification and Drainage can be used in two regimens, the basic and the advanced.
- General support of regulation is also needed in the form of vital co-factors to the detoxification systems (minerals, vitamins, trace elements, amino acids).

- The basic detoxification products **Nux vomica-Homaccord**, **Berberis-Homaccord** as well as **Lymphomyosot** form a trio to support the function of the liver, the kidneys and finally to drain the tissues via the lymph system.
- The advanced detoxification offers a comprehensive support of the organs of detoxification and elimination and is used as a preparation phase in patients where detoxification needs to be done at a slower pace, or where the organs of Detoxification and Drainage have been weakened by disease or overload.
- Special considerations need to be observed in certain clinical groups, such as obese patients, patients on chemotherapy, the elderly as well as patients with a history of drug abuse in the past. The preparation phase in the advanced detox is mandatory in these groups.



Practical Detoxification

This section will deal with the way we approach Detoxification and Drainage in the different patients.

1 Clinical Groups

The assessment on where to start with the detoxification process is made with two tools:

- **The detoxification point scale**
- **The clinical assessment of the patient**

1.1 The Detoxification Point Scale

This is built up to incorporate all the major toxicity symptoms. Patients evaluate their symptoms on a scale of 0 to 4:

Point count

0 = Never or almost never have the symptom

1 = Occasionally have it, effect is not severe

2 = Occasionally have it, effect is severe

3 = Frequently have it, effect is not severe

4 = Frequently have it, effect is severe

Points are then totaled, yielding a score that indicates the severity of the patient's toxic burden:

Total points < 100:

Patient with mild to moderate toxicity

Total points > 100:

Patient with moderate to severe toxicity

1.2 The Clinical Assessment of the Patient

Group 1

Point count < 100:

mild to moderate toxicity

Mostly the well/healthy person who wants to clean her or his body and optimize the drainage of toxins as well as the patient with mild disease such as skin conditions, fatigue, acne, irritable bowel syndrome and other signs of mild toxicity.

→ **Basic Detoxification and Drainage with Detox-Kit**

Group 2

Point count > 100:

severe toxicity

Mostly the patient with some diagnosed disease process, including autoimmunity and pre-cancerous conditions as well as the patient with severe toxicity. But also all the following patients must be regarded as special groups and will need advanced support first:

- The cancer patient on active treatment such as chemotherapy and radiation therapy
- The older patient
- The obese patient with metabolic disease
- The patient with impairment of the elimination organs, such as the liver or the kidney
- The patient who had significant drug addiction in the past, even if this was a long time ago

→ **Advanced Detoxification and Drainage**

Note: Patients in the special groups are always classified into group 2 regardless of their point count.

We also use the point scale to follow our treatments and to decide when a patient with initial severe toxicity should switch to the basic regimen. (See Fig. V,1: The Decision Tree)

2 How Long Should the Patient Detox?

From our discussion above, we see that there are in general two waves of drainage when we start to apply the 4-S regimen:

STOP	external supply of toxins.
SUPPORT	the organs of Detoxification and Drainage.
STIMULATE	elimination of toxins.
SENSITIZE	the patient for further detoxification and lifestyle changes.

First we see a fairly fast drainage of toxins through the well perfused compartments. This will result in an increase in urinary flow, loose stools, and increase in sweating and mild headache.

After a few days the patient will feel better, but one should not stop the Detoxification and Drainage, as a second wave of Detoxification and Drainage will follow from the lower perfused compartments, such as the fat tissues and the connective tissues. It is thus important to clear these compartments totally, over weeks. In patients with severe toxicity (group 2) it is even good to continue the drainage process with **Lymphomyosot** up to 12 weeks or even longer, whilst in others, the patient can go on **Lymphomyosot** for 4-6 weeks (group 1).

Note: If the patient has a point score of < 50 from the outset, only Lymphomyosot is used as treatment for 4 weeks.

3 Blocked Excretion

Most patients drain the fast exchange compartment relatively easy and this will result in a fast excretion of toxins from the interstitium into the lymph system and blood stream. The toxins will thus move to organs of excretion or they may have to be made water soluble if they were stored in the lipophilic form.

Increased urination, loose stools or mild diarrhea, mild fatigue as well as increased sweating are signs of a healthy excretory phase!

If the organs of excretion are overloaded, lack cofactors to detoxifying enzymes or are diseased, and they have not been prepared with the advanced support first, the patient may have symptoms of blocked excretion. This can manifest as severe headache, nausea, muscle pain and joint pain. As this almost never happens in the support phase, we are looking at patients on the **Detox-Kit**. A strategy change is then required and may be solved in two ways.

The first strategy is to separate the three products and give only the bottle of **Nux vomica-Homaccord** first, followed by the **Berberis-Homaccord**, and then followed by **Lymphomyosot**. Then a trial of all three together is made.

The second strategy persists, go to a support phase first for six weeks and then to the **Detox-Kit** again. The latter strategy is often used when a patient still has signs of blocked excretion after reintroduction after the second challenge with the whole kit.

If no symptoms of blocked excretion occur on rechallenge, continue with the **Detox-Kit** as described below in the decision tree.

4 The Decision Tree

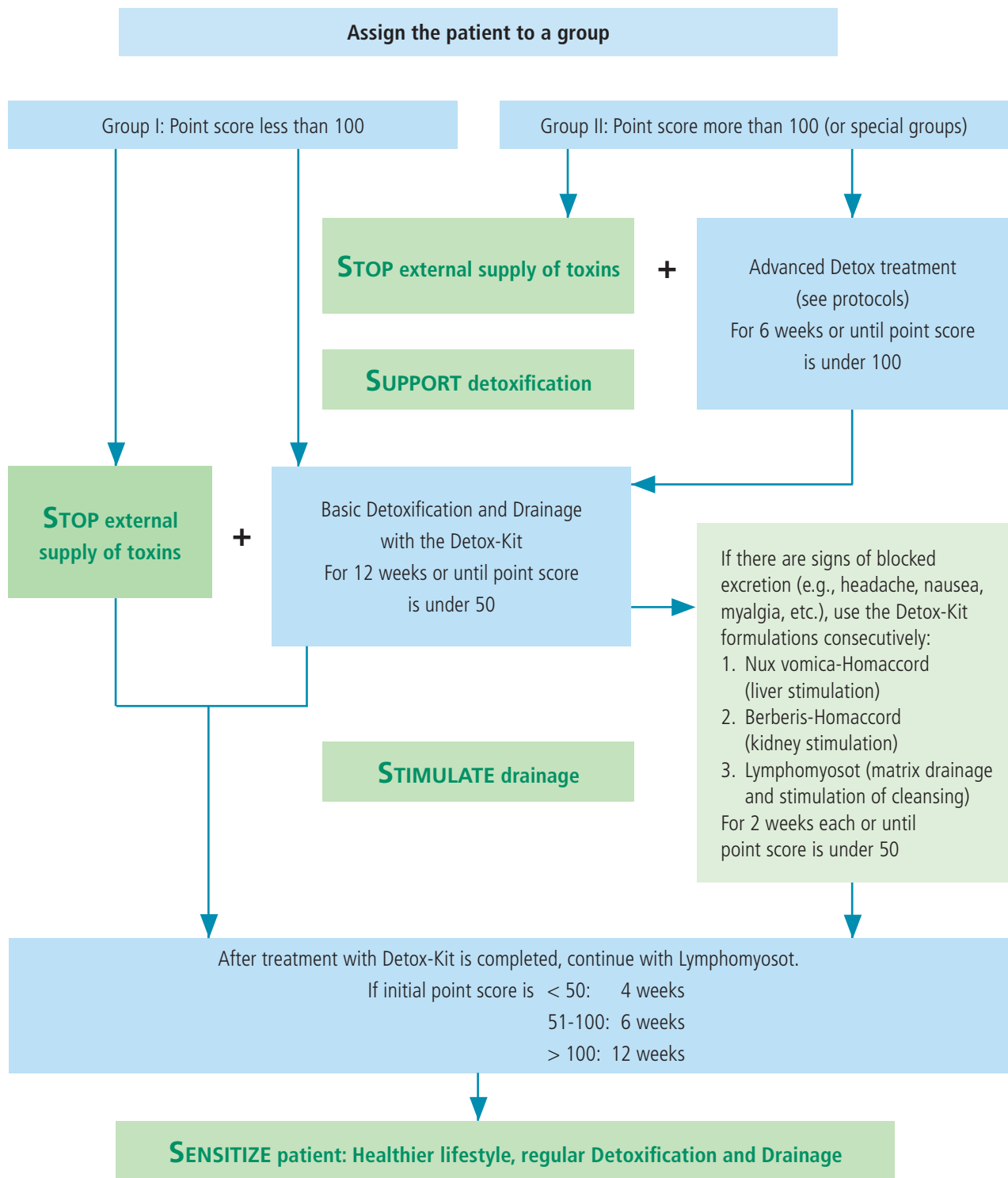


Fig. V,1: Detoxification and Drainage decision tree

Conclusion

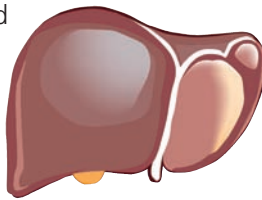
- Practical tools for planning detoxification in a patient is the practice based detoxification questionnaire, which is a semi-subjective tool, as it is based on the assessment of the patient on her or his symptoms.
- Clinical assessment of the patient concludes the picture, and especially the special groups are considered.
- The decision tree is condensed into a flow chart.
- Although special tests for Detoxification and Drainage are available, they are still largely invalidated, and whilst giving important information on the ability of the patient to detoxify remains impractical in general practice, due to the cost and the collection of samples.
- The total toxin load can be determined finally only by tissue samples which are out of the reach of most patients and practitioners.

The Organ-specific Treatment

Certain medications are also very specific for conditions which affect certain organs.

1 The Liver

In terms of basic and advanced detoxification we already looked at **Nux vomica-Homaccord** and **Hepar compositum**. A few other medications though need mentioning:



Hepeel is a combination product existing of plant material and minerals. Although this is classified as a simple combination, it has been shown to have antioxidant and antiproliferative properties. (Gebhardt et al., 2003)

Recent in vitro studies also looked at the role of **Hepeel** in view of the protection it offers in terms of exposure to heavy metals like cadmium. (Unpublished data)

The protective antioxidant and antiproliferative effect of **Hepeel** on liver cells has also been shown experimentally. (Gebhardt et al., 2003)

We mentioned already in the previous sections the fact that detoxification through the Phase I reaction will generate large amounts of free radicals. By adding a compound such as **Hepeel**, which will at the same time stimulate drainage and act as an anti-oxidant; it will support the tissues during periods of increased detoxification. This is important in diseases such as alcoholic liver disease, as well as in viral diseases such as Hepatitis C where the tendency is towards fatty infiltration and proliferation.

1.1 Therapy Scheme for Detoxification in Chronic Viral Infection like Hepatitis C

In this type disease, the detoxification should be a late event, and the main aim is to support and protect the liver tissue. In all of the chronic viral diseases there is a tendency towards fatty infiltration, fibrosis and finally cancer.

Protocol for Hepatitis C*

Disease-specific treatment Engystol N → Cellular Immunity
 Hepeel → Liver protection

The above regimen for 4 weeks before the detoxification, continue with Hepeel during the detoxification for 12 weeks.

Detoxification treatment

Advanced support for 6 weeks or until point count is under 100

	Liver	Urinary tract/ Kidney	Lymph	Skin	Gut	Gallbladder	Connective tissue	Respiratory tract
Basic detoxification and drainage	Detox-Kit	Detox-Kit	Detox-Kit	–	Detox-Kit	Chelidonium-Homaccord	Detox-Kit	Bronchalis-Heel
Advanced detox 1	Hepar comp.	Solidago comp.	Tonsilla comp.	Cutis comp.	Mucosa comp.	Hepar comp.	Thyreoidea comp.	Mucosa comp.
Advanced detox 2	Hepeel	Reneel H	Galium-Heel/ Lymphomyosot	Schwef-Heel	Nux vomica-Homaccord	Leber-Galle Tropfen (new)	Pulsatilla comp.	
Advanced detox 3						Injeel-Chol	Galium-Heel/ Lymphomyosot	
For cellular detoxification in addition	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.

Basic Detoxification and Drainage when point count is under 100

	Liver	Urinary tract/ Kidney	Lymph	Skin	Gut	Gallbladder	Connective tissue	Respiratory tract
Basic detoxification and drainage	Detox-Kit	Detox-Kit	Detox-Kit	–	Detox-Kit	Chelidonium-Homaccord	Detox-Kit	Bronchalis-Heel
Advanced detox 1	Hepar comp.	Solidago comp.	Tonsilla comp.	Cutis comp.	Mucosa comp.	Hepar comp.	Thyreoidea comp.	Mucosa comp.
Advanced detox 2	Hepeel	Reneel H	Galium-Heel/ Lymphomyosot	Schwef-Heel	Nux vomica-Homaccord	Leber-Galle Tropfen (new)	Pulsatilla comp.	
Advanced detox 3						Injeel-Chol	Galium-Heel/ Lymphomyosot	
For cellular detoxification in addition	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.

Note: Hepeel protects the liver cell from damage by the virus and endogenous immune system.

Dosage: Ampules: In general, 3-1 times weekly 1 ampule i.m., s.c., i.d.
 Drops: In general, 10 drops 3 times daily

* Products to be used for detoxification are highlighted

1.2 Detoxification of the Gallbladder and the Bile

Certain medications have a special affinity for the liver and especially the bile duct and the gallbladder. Such medications often contains the ingredients Chelidonium and Carduus marianus or Sylimarin.

Protocol for Gall Stones*

Disease-specific treatment Chelidonium-Homaccord → see note below

Detoxification treatment For 6 weeks

	Liver	Urinary tract/ Kidney	Lymph	Skin	Gut	Gallbladder	Connective tissue	Respiratory tract
Basic detoxification and drainage	Detox-Kit	Detox-Kit	Detox-Kit	–	Detox-Kit	Chelidonium- Homaccord	Detox-Kit	Bronchalis-Heel
Advanced detox 1	Hepar comp.	Solidago comp.	Tonsilla comp.	Cutis comp.	Mucosa comp.	Hepar comp.	Thyreoidea comp.	Mucosa comp.
Advanced detox 2	Hepeel	Reneel H	Galium-Heel/ Lymphomyosot	Schwef-Heel	Nux vomica- Homaccord	Leber-Galle Tropfen (new)	Pulsatilla comp.	
Advanced detox 3						Injeel-Chol	Galium-Heel/ Lymphomyosot	
For cellular detoxification in addition	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.

Note: Hepar compositum in this case will support the tissues of the liver and gallbladder. It should be used in patients who have big gallstones or obstruction of the bile duct. In obstruction of the bile duct with a stone, no drainage remedy such as Chelidonium-Homaccord should be used. Thus if a patient is jaundiced from gall stone obstruction, or in acute cholecystitis, Chelidonium-Homaccord should not be used.

Dosage: Ampules: In general, 3-1 times weekly 1 ampule i.m., s.c., i.d.
Drops: In general, 10 drops 3 times daily

Use for six weeks, then reassess with ultrasound. This regimen can be repeated after a 4 week interval of rest. Often 3-4 cycles are needed.

* Products to be used for detoxification are highlighted

1.3 Therapy Scheme for Fatty Infiltration of the Liver in Type II Diabetics: So-called NASH (Non Alcoholic Steatotic Hepatitis Syndrome)

Protocol for Fatty Infiltration of the Liver as seen in NASH and Alcoholic Liver Disease*

Disease-specific treatment Syzygium compositum
Nux vomica-Homaccord → in alcoholic liver disease

Concomitant detoxification Advanced support for 12 weeks

	Liver	Urinary tract/ Kidney	Lymph	Skin	Gut	Gallbladder	Connective tissue	Respiratory tract
Basic detoxification and drainage	Detox-Kit	Detox-Kit	Detox-Kit	–	Detox-Kit	Chelidonium-Homaccord	Detox-Kit	Bronchalis-Heel
Advanced detox 1	Hepar comp.	Solidago comp.	Tonsilla comp.	Cutis comp.	Mucosa comp.	Hepar comp.	Thyreoidea comp.	Mucosa comp.
Advanced detox 2	Hepeel	Reneel H	Galium-Heel/ Lymphomyosot	Schwef-Heel	Nux vomica-Homaccord	Leber-Galle Tropfen (new)	Pulsatilla comp.	
Advanced detox 3						Injeel-Chol	Galium-Heel/ Lymphomyosot	
For cellular detoxification in addition	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.

Note: Advanced support in this case for 12 weeks, independent of point count, as the tissue support is imperative before the drainage takes place. The fat tissue in the liver will also store many fat soluble toxins, which will put the liver further in danger when toxins are drained too quickly.

Basic Detoxification and Drainage

	Liver	Urinary tract/ Kidney	Lymph	Skin	Gut	Gallbladder	Connective tissue	Respiratory tract
Basic detoxification and drainage	Detox-Kit	Detox-Kit	Detox-Kit	–	Detox-Kit	Chelidonium-Homaccord	Detox-Kit	Bronchalis-Heel
Advanced detox 1	Hepar comp.	Solidago comp.	Tonsilla comp.	Cutis comp.	Mucosa comp.	Hepar comp.	Thyreoidea comp.	Mucosa comp.
Advanced detox 2	Hepeel	Reneel H	Galium-Heel/ Lymphomyosot	Schwef-Heel	Nux vomica-Homaccord	Leber-Galle Tropfen (new)	Pulsatilla comp.	
Advanced detox 3						Injeel-Chol	Galium-Heel/ Lymphomyosot	
For cellular detoxification in addition	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.

Note: Detox-Kit for further 6 weeks, and then Lymphomyosot only for further 8 months.

Dosage: Ampules: In general, 3-1 times weekly 1 ampule i.m., s.c., i.d.
Drops: In general, 10 drops 3 times daily

* Products to be used for detoxification are highlighted

2 The Kidneys

We have seen that the kidneys are mainly organs of elimination, and that they concentrate toxins, which may damage the kidneys themselves. The perfusion of the kidneys plays a very important role in the excretory function of the kidneys. The flow of urine also is important in the excretion.

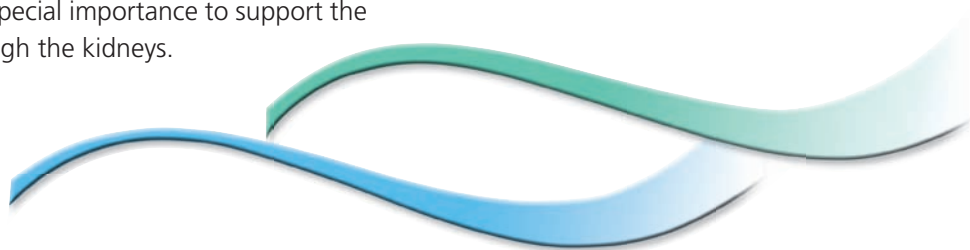


The support of the kidney function is thus of major importance in the process of draining of toxins, and it must be ensured that the kidneys are not overloaded, or impaired with disease.

Three medications have a special importance in the treatment of the kidneys. **Solidago compositum** and **Berberis-Homaccord** have already been discussed above as they are part of the advanced and basic Detoxification and Drainage regimens. It is also important to mention that **Berberis-Homaccord** has an important function in treatment of inflammatory conditions of the kidneys.

Reneel H is a further medication which is available as a drainage preparation for the kidneys.

Certain diseases affect the kidneys, where drainage of toxins through the renal tract may play a role. In these cases it is of special importance to support the detoxification through the kidneys.



* Products to be used for detoxification are highlighted

2.1 Therapy Scheme for Kidney Stones

These could be through an accumulation of internal toxins, such as uric acid, calcium or oxalates in the urine, which then precipitates into aggregations. The pH of the urine may play a crucial role here, it is thus important to do the 4-5 regimen here. The patient must in the first case STOP the supply of toxin, or the food which could lead to an accumulation of the toxin. In the case of uric acid this will be food like red meat, alcohol and shell fish. In the case of oxalates the green vegetables, such as spinach must be avoided.

Protocol for Kidney Stones*

Disease-specific treatment Berberis-Homaccord → Initially on its own, then after point count is under 100 as part of the Detox-Kit

Detoxification treatment

Advanced support for 6 weeks or until point count is under 100

	Liver	Urinary tract/ Kidney	Lymph	Skin	Gut	Gallbladder	Connective tissue	Respiratory tract
Basic detoxification and drainage	Detox-Kit	Detox-Kit	Detox-Kit	–	Detox-Kit	Chelidonium-Homaccord	Detox-Kit	Bronchalis-Heel
Advanced detox 1	Hepar comp.	Solidago comp.	Tonsilla comp.	Cutis comp.	Mucosa comp.	Hepar comp.	Thyreoidea comp.	Mucosa comp.
Advanced detox 2	Hepeel	Reneel H	Galium-Heel/ Lymphomyosot	Schwef-Heel	Nux vomica-Homaccord	Leber-Galle Tropfen (new)	Pulsatilla comp.	
Advanced detox 3						Injeel-Chol	Galium-Heel/ Lymphomyosot	
For cellular detoxification in addition	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.

Basic Detoxification and Drainage when point count is under 100

	Liver	Urinary tract/ Kidney	Lymph	Skin	Gut	Gallbladder	Connective tissue	Respiratory tract
Basic detoxification and drainage	Detox-Kit	Detox-Kit	Detox-Kit	–	Detox-Kit	Chelidonium-Homaccord	Detox-Kit	Bronchalis-Heel
Advanced detox 1	Hepar comp.	Solidago comp.	Tonsilla comp.	Cutis comp.	Mucosa comp.	Hepar comp.	Thyreoidea comp.	Mucosa comp.
Advanced detox 2	Hepeel	Reneel H	Galium-Heel/ Lymphomyosot	Schwef-Heel	Nux vomica-Homaccord	Leber-Galle Tropfen (new)	Pulsatilla comp.	
Advanced detox 3						Injeel-Chol	Galium-Heel/ Lymphomyosot	
For cellular detoxification in addition	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.

Note: This must be accompanied with a diet low in oxalates, if the stones are oxalate stones, and also with a low uric acid diet if the stones are due to hyperuricemia. In this case, Hepar compositum is also continued throughout the detoxification to support the liver.

Dosage: Ampules: In general, 3-1 times weekly 1 ampule i.m., s.c., i.d.
Drops: In general, 10 drops 3 times daily

2.2 Therapy Scheme for Chronic Recurrent UTI's

This is a problem especially in small children and in females, for different reasons. In children the problem is more of a reflux, whereas in females there is an anatomical as well as a hormonal reason. In both cases, drainage and support of the renal tract is of utmost importance.

Protocol for Chronic Recurrent Urinary Tract Infections*

Disease-specific treatment Berberis-Homaccord → Initially on its own, then after point count is under 100 as part of the Detox-Kit
Echinacea compositum → Add in the case of acute infection

Detoxification treatment

Advanced support for 6 weeks or until point count is under 100

	Liver	Urinary tract/ Kidney	Lymph	Skin	Gut	Gallbladder	Connective tissue	Respiratory tract
Basic detoxification and drainage	Detox-Kit	Detox-Kit	Detox-Kit	–	Detox-Kit	Chelidonium-Homaccord	Detox-Kit	Bronchalis-Heel
Advanced detox 1	Hepar comp.	Solidago comp.	Tonsilla comp.	Cutis comp.	Mucosa comp.	Hepar comp.	Thyreoidea comp.	Mucosa comp.
Advanced detox 2	Hepeel	Reneel H	Galium-Heel/ Lymphomyosot	Schwef-Heel	Nux vomica-Homaccord	Leber-Galle Tropfen (new)	Pulsatilla comp.	
Advanced detox 3						Injeel-Chol	Galium-Heel/ Lymphomyosot	
For cellular detoxification in addition	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.

Basic Detoxification and Drainage when point count is under 100

	Liver	Urinary tract/ Kidney	Lymph	Skin	Gut	Gallbladder	Connective tissue	Respiratory tract
Basic detoxification and drainage	Detox-Kit	Detox-Kit	Detox-Kit	–	Detox-Kit	Chelidonium-Homaccord	Detox-Kit	Bronchalis-Heel
Advanced detox 1	Hepar comp.	Solidago comp.	Tonsilla comp.	Cutis comp.	Mucosa comp.	Hepar comp.	Thyreoidea comp.	Mucosa comp.
Advanced detox 2	Hepeel	Reneel H	Galium-Heel/ Lymphomyosot	Schwef-Heel	Nux vomica-Homaccord	Leber-Galle Tropfen (new)	Pulsatilla comp.	
Advanced detox 3						Injeel-Chol	Galium-Heel/ Lymphomyosot	
For cellular detoxification in addition	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.

Note: Mucosa compositum supports the renal epithelium and Solidago compositum supports the whole renal tract. On this treatment, the patient may still suffer with acute UTI's.

Dosage: Ampules: In general, 3-1 times weekly 1 ampule i.m., s.c., i.d.
Drops: In general, 10 drops 3 times daily

* Products to be used for detoxification are highlighted

2.3 Interstitial Cystitis

This is a very difficult condition to treat. In this case the patient will first need the advanced support and then the basic detoxification with a continuation of **Lymphomyosot** after that.

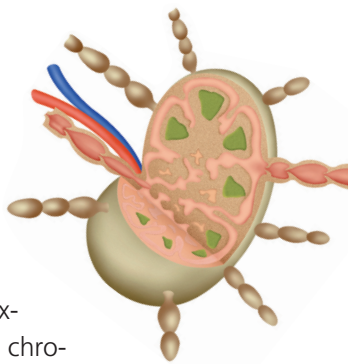
Especially the addition of the tissue medications for the mesenchyme, such as **Thyreoidea compositum** and **Mucosa compositum** plays a vital role in this instance. The catalysts are added as a routine and only over months the relapses will get less and less as well as the severity diminish. In the end it is vital to drain the Interstitium over several months with **Lymphomyosot**.



3 The Lymphoid System

The lymphoid system has two functions. That of a detoxifying and drainage organ and that of an immune function. Apart from edema which is mildly present in toxic people, we also see a higher rate of benign lymphadenopathy and of course also more tissue infections when the lymph system does not function sufficiently.

A number of products will support the lymphoid system especially, but the two most important are **Lymphomyosot** and **Tonsilla compositum**. Tonsilla compositum is a complex combination of plant, mineral, catalyst and organ extracts. It is especially effective in the chronic recurrent infections, whether it is in childhood or that of the elite sportsman. Together with Lymphomyosot, which add the drainage, many of these syndromes can be eliminated.



3.1 Therapy Scheme for Chronic Recurrent Tonsillitis

Protocol for Chronic Recurrent Tonsillitis*

Disease-specific treatment Calcoheel

Detoxification treatment

Advanced support if the point count is above 100 or in specialized groups

	Liver	Urinary tract/ Kidney	Lymph	Skin	Gut	Gallbladder	Connective tissue	Respiratory tract
Basic detoxification and drainage	Detox-Kit	Detox-Kit	Detox-Kit	–	Detox-Kit	Chelidonium-Homaccord	Detox-Kit	Bronchalis-Heel
Advanced detox 1	Hepar comp.	Solidago comp.	Tonsilla comp.	Cutis comp.	Mucosa comp.	Hepar comp.	Thyreoidea comp.	Mucosa comp.
Advanced detox 2	Hepeel	Reneel H	Galium-Heel/ Lymphomyosot	Schwef-Heel	Nux vomica-Homaccord	Leber-Galle Tropfen (new)	Pulsatilla comp.	
Advanced detox 3						Injeel-Chol	Galium-Heel/ Lymphomyosot	
For cellular detoxification in addition	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.

Basic Detoxification and Drainage when point count is under 100

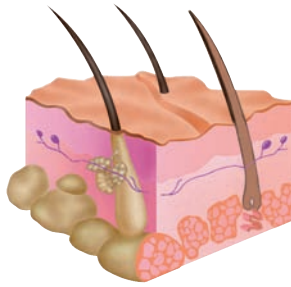
	Liver	Urinary tract/ Kidney	Lymph	Skin	Gut	Gallbladder	Connective tissue	Respiratory tract
Basic detoxification and drainage	Detox-Kit	Detox-Kit	Detox-Kit	–	Detox-Kit	Chelidonium-Homaccord	Detox-Kit	Bronchalis-Heel
Advanced detox 1	Hepar comp.	Solidago comp.	Tonsilla comp.	Cutis comp.	Mucosa comp.	Hepar comp.	Thyreoidea comp.	Mucosa comp.
Advanced detox 2	Hepeel	Reneel H	Galium-Heel/ Lymphomyosot	Schwef-Heel	Nux vomica-Homaccord	Leber-Galle Tropfen (new)	Pulsatilla comp.	
Advanced detox 3						Injeel-Chol	Galium-Heel/ Lymphomyosot	
For cellular detoxification in addition	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.

Note: In chronic tonsillitis or tonsillar hypertrophy this is an excellent adjuvant treatment to diminish acute infections. This is not a regimen for the acute infection in these patients. The presence of beta-hemolytic Streptococci is a reason for conventional treatment.

Dosage: Ampules: In general, 3-1 times weekly 1 ampule i.m., s.c., i.d.
Drops: In general, 10 drops 3 times daily

* Products to be used for detoxification are highlighted

4 The Skin



4.1 Therapy Scheme for Acne Vulgaris

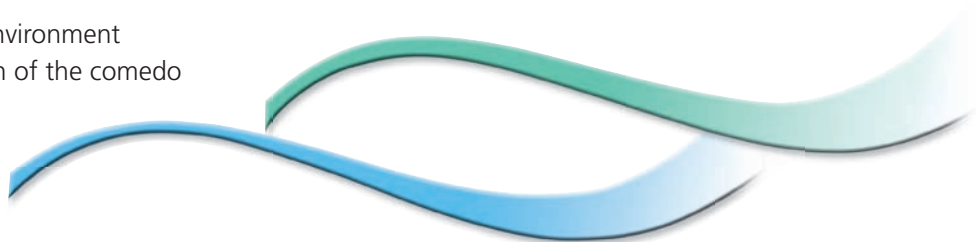
In patients with acne vulgaris, the detoxification should run parallel to the treatment scheme. It is better to do the advanced detox in patients with severe acne, but in patients with milder symptoms the basic support often is enough.

The pilosebaceous unit (the sebaceous follicle, sebaceous glands, and sebaceous ducts) is where acne occurs. Pilosebaceous units are concentrated in body sites that are prone to acne – the face, back, and chest. The pathogenesis of acne is complex and multifactorial. Although the etiology of acne is not clear, or why acne remits or resolves in most individuals but not in others the central pathogenic factors have been delineated. These are:

- Excessive sebum production secondary to androgen stimulation
- Altered follicular keratinization and desquamation, resulting in follicular plugging
- Proliferation of *Propionibacterium acnes*, an anaerobic organism normally resident in the follicle
- Inflammation following chemotaxis and the release of proinflammatory mediators, such as IL-1

Aims of the treatment:

- Reduce sebum formation
- Reduce inflammation
- Normalize hormonal environment
- Combat super infection of the comedo



Protocol for Acne*

Disease-specific treatment Hormeel
 Traumeel
 Echinacea compositum → in super infections of the comedo

Detoxification treatment

Advanced support if the point count is above 100 or in specialized groups

	Liver	Urinary tract/ Kidney	Lymph	Skin	Gut	Gallbladder	Connective tissue	Respiratory tract
Basic detoxification and drainage	Detox-Kit	Detox-Kit	Detox-Kit	–	Detox-Kit	Chelidonium-Homaccord	Detox-Kit	Bronchalis-Heel
Advanced detox 1	Hepar comp.	Solidago comp.	Tonsilla comp.	Cutis comp.	Mucosa comp.	Hepar comp.	Thyreoidea comp.	Mucosa comp.
Advanced detox 2	Hepeel	Reneel H	Galium-Heel/ Lymphomyosot	Schwef-Heel	Nux vomica-Homaccord	Leber-Galle Tropfen (new)	Pulsatilla comp.	
Advanced detox 3						Injeel-Chol	Galium-Heel/ Lymphomyosot	
For cellular detoxification in addition	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.

Basic Detoxification and Drainage when point count is under 100

	Liver	Urinary tract/ Kidney	Lymph	Skin	Gut	Gallbladder	Connective tissue	Respiratory tract
Basic detoxification and drainage	Detox-Kit	Detox-Kit	Detox-Kit	–	Detox-Kit	Chelidonium-Homaccord	Detox-Kit	Bronchalis-Heel
Advanced detox 1	Hepar comp.	Solidago comp.	Tonsilla comp.	Cutis comp.	Mucosa comp.	Hepar comp.	Thyreoidea comp.	Mucosa comp.
Advanced detox 2	Hepeel	Reneel H	Galium-Heel/ Lymphomyosot	Schwef-Heel	Nux vomica-Homaccord	Leber-Galle Tropfen (new)	Pulsatilla comp.	
Advanced detox 3						Injeel-Chol	Galium-Heel/ Lymphomyosot	
For cellular detoxification in addition	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.

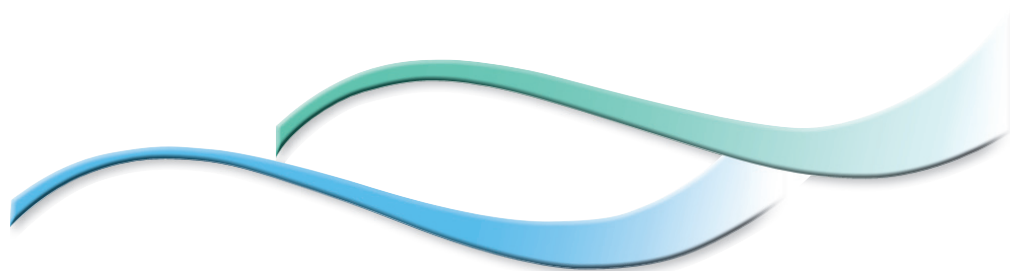
Note: Hormeel can also be used in males for the treatment of acne.

Dosage: Ampules: In general, 3-1 times weekly 1 ampule i.m., s.c., i.d.
 Drops: In general, 10 drops 3 times daily

* Products to be used for detoxification are highlighted

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