

## Basic research on homeopathic principles

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The homeopathic basic principles (Similia and dilution/dynamization) can be examined also using experimental animals and cell laboratory models. The cornerstone of homeopathy – that the whole clinical picture of the individual patient be taken into consideration – is not in dispute, but basic research also allow the action of drugs to be investigated in rigorous and reproducible settings. The effects of homeopathic remedies in cellular models are well documented for a wide range of dilutions/dynamizations, albeit not all homeopathic effects can be reduced to the cellular level. Many of these effects have also been explained mechanistically as modifications of receptors, transduction mechanisms and gene expression changes. Recent evidence documents the ability of highly diluted compounds to modulate gene expression in human/animal cells and unicellular organisms. There are many possible mechanisms explaining the inverse effects of drugs, according to the different doses/dilutions and the changes in sensitivity and responsiveness of target systems. Hahnemann was the first to consider a primary and a secondary action of medicines, the latter being the opposite of the former. On the basis of these scientific facts, the logic of homeopathic reasoning is evident: if the body regulates itself in the opposite direction to the stimulus, we can use this property, giving low, sub-toxic, doses of pathogenic substances that trigger a counter-regulation. At a molecular level, pharmacology recognizes the classic distinction between allosteric drugs and orthosteric drugs. Orthosteric drugs bind to the active site of a target enzyme or a receptor and block it; allosteric drugs bind elsewhere on the protein and indirectly alter the conformations at the active site. In this perspective, homeopathic drugs may work by exploiting the characteristic features of allosteric regulation. The increasing credibility and plausibility of homeopathic ideas and experiences allows us to include this pharmacological approach in the mainstream of modern science.

**Keywords:** Basic research, Laboratory models, Inverse effects

## Three Malaria studies in Kenya: a retrospective and prospective open label study and a comparison between homeopathy and coartem

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**Background:** Malaria still has in Kenya a high mortality and morbidity rate; this is coupled with rising resistance levels to the new standard drug coartem in several South Asian countries according to WHO reports. Homeopathy can be considered a form of individualized immune therapy and as such it deserves a place next to treatments focused at the microorganisms themselves. These factors require scientific evidence that may support its application in endemic diseases. We have developed a research line that comprises both qualitative and quantitative aspects of homeopathic management of malaria patients. The first two studies have been conducted in 2014, the third in 2015.

**Aims:** The first aim is the assessment of the management of homeopathically treated patients in several rural health care settings. This involved the treatment of malaria in the daily context of homeopathic clinics that also treat patients with other illnesses. We want to document how individualized homeopathy works within homeopathic clinics, not just conduct an isolated study in a context where homeopathy usually not is applied.

**Material and methods:** In a retrospective design in one clinic, the 2013–2014 rain season group of 54 malaria patients was assessed for classical malaria symptoms, homeopathic case taking, lab tests and prescription strategies. The prospective study in three clinics assessed the 2014 March–June rain season patients for the effect of homeopathic individual treatment. 86 patients were assessed and 69 completed follow up. All but one who returned for follow-up were negative for parasites. A drop-out analysis was made, indicating logistics as the main cause. In 2015 a comparative study is being made between the results of homeopathy and the standard treatment of co-artem. Both homeopathic and government clinic patients are participating.

**Results:** Results will be published in 2015 in peer-reviewed journals, indexed in Pub Med.

## Feasibility and clinical results of a pilot trial of individualized homeopathic treatment of fatigue in children receiving chemotherapy

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**Background:** We conducted this study from April 2012 to April 2014 examining the feasibility of a randomized trial of the homeopathic treatment for fatigue in children and youth receiving chemotherapy. Fatigue in this population is an area of interest due to the lack of effective interventions.

**Methods:** This was an open label pilot study of homeopathic treatment for fatigue in pediatric cancer patients treated at The Hospital for Sick Children (SickKids) in Toronto, Canada. Children (ages 2–18), diagnosed with any type of cancer who were receiving chemotherapy administered discontinuously in courses or cycles, were considered. Participants were given individualized homeopathic treatment for 14 consecutive days following a course of chemotherapy. Recruitment rates, adverse events and remedy selection were monitored and changes in fatigue was measured using the Symptom Distress Scale (SDS), the PedsQL Multidimensional Fatigue Scale and the PedsQL Generic Core Scales and Acute Cancer Module.

**Results:** 155 potential participants were assessed between April 2012 and April 2014. 45 patients were eligible to be approached, 9 consented to participate and eight participants received homeopathic treatment (one withdrawal prior to treatment). Eight participants completed 14 days of assessment. SDS scores, and proxy-report fatigue scores in general fatigue and sleep/rest fatigue had significant improvement. In spite of individualized case taking Cadmium Sulfuricum was the chosen remedy at the start of each case. One participant had a clinically observed homeopathic aggravation following a dry dose administration of a constitutional remedy.

**Conclusions:** In this setting, a future randomized trial of individualized homeopathy is not feasible for children with cancer for the purpose of fatigue reduction. There was a significant improvement of fatigue over the study period. Future study may consider an adult population, settings more familiar with homeopathy, or other study designs such as comparative effectiveness. The routine use of Cadmium Sulfuricum may be investigated.

**Keywords:** Homeopathy, Chemotherapy related fatigue, Cancer related fatigue, Fatigue, Complementary medicine

## Microimmunotherapeutic administration of cytokines improve the clinical symptoms in EAE an animal model of multiple sclerosis

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Experimental Autoimmune Encephalomyelitis (EAE) is one of the most used animal models in the study of Multiple Sclerosis (MS). EAE is induced by the injection of myelin proteins and specific adjuvants and leads to an important inflammatory process with activation of resident glial cells, principally microglia, which interact with infiltrated peripheral immune cells, mostly T-cells. In this context, and as described in MS, cytokines, play a crucial role in the cross-talk between these cell populations and in the modulation of the associated neuroinflammatory response. The main objective of our research is to interact in this process by modulating the immune response. Our work hypothesis is that the microimmunotherapeutic administration of specific combinations of cytokines closely related with the neuroinflammatory response may improve the clinical symptoms in EAE. To accomplish that, EAE was induced in C57BL/6 mice by injecting MOG<sub>35–55</sub> and Complete Freund's Adjuvant supplemented with *Mycobacterium tuberculosis* and *Pertussis Toxin*. As control some animals were injected with saline. Both, MOG-injected and saline animals, were distributed in three groups: 1) without treatment, 2) treated with placebo and 3) treated with a stimulatory/inhibitory/modulatory combination of cytokines. The specific combination of cytokines and signalling molecules used in this study were: a) the pro-inflammatory cytokines IL-1<sub>beta</sub>, IL-1<sub>r</sub>, TNF-<sub>alpha</sub>, IL-12 and IFN-<sub>gamma</sub> at inhibitory dilution (30CH), b) the anti-inflammatory molecules IL-1Ra, IL-10, IL-4, PGE2, TGF-<sub>beta</sub> and IL-13 at stimulatory dilution (4CH) and c) the IL-6 cytokine at modulatory dilution (15CH). The clinical score of the animals were recorded daily and both the glial response and the infiltration of peripheral immune cells were evaluated using flow cytometry and immunohistochemistry. Our results clearly demonstrated that the group administered with the cytokine combination presented a delay in the onset of clinical symptoms and a significant reduction of the clinical score during the chronic phase of the disease. These clinical changes correlated with a reduction in the microglial activation pattern and a low number of lymphocytes (around 50%). In conclusion, our results suggest that the microimmunotherapeutic administration of specific combinations of cytokines, exert a beneficial effect in EAE progress and could be a very good strategy for modulating the neuroinflammatory response associated with certain CNS-diseases such as MS.

**Keywords:** Immune System, Neuroinflammation, Microglia, Cytokines, Microimmunotherapy, Central nervous system, Very low doses

## Carbo animalis and immune response to Ehrlich ascites tumor in mice: an experimental model

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