Homotoxicology

Claire Haresnape

Research Student, Registered Homotoxicologist
• A little about me
• What is homotoxicology?
• What evidence exists?
• A different kind of remedy.
• The importance of the ECM.
• New scientific techniques that cast light on possible mechanisms of action
• Issues of trial design
Claire Haresnape

- Biology Graduate
- Science and Art background
- Homeopathy/Homotoxicology Training
- Practicing 10 years
- Research Project at Barts and The London
PhD

- PhD project centres around the use of homotoxicology to treat female infertility (WHO Class II)
- Hypothesis that using homotoxicology will allow lower doses of ovulation induction agents to be given
- Improve fertility outcomes
HOMEOPATHY BIRTH

From homeopathic empiricism to homotoxico logic scientific nature

H.H. RECKEWEG ENUNCIATES THE HOMOTOXICOLOGIC PRINCIPLES

New interpretation of the homeopathic principles from an immunologic and biochemical point of view

Overcoming of the mostly organicistic and mechanistic (homotoxin-homotoxicosis) vision of Homotoxicology

IN ITALY ORIGINATES THE PHYSIOLOGICAL REGULATING MEDICINE (GUNA Method)

New acquisitions about Psycho-Neuro-Endocrino-Immunology outline innovative scenarios in Homeopathy

1796

1952

1994
What from HOMOTOXICOLOGICAL PHARMACOLOGY for the P.R.M. THERAPEUTIC STRATEGY?

- Catalysts
- Nosodes
- Suis organ preparations

Metabolic Stimuli
Immune Stimuli
Function Regulation
What from:

P.N.E.I.

A) REGULATION OF THE NEURO-ENDOCRINE HOMEOSTASIS

B) RESTORATION OF THE IMMUNOLOGIC EFFICIENCY

ESSENTIAL POINTS OF THE THERAPY

• HOMEOPATHIC HORMONES
• NEUROPETIDES
  • “Suis” organ preparations

• Nosodes
• CYTOKINES
  • New immunostimulating substances
Homotoxicology

• A review of RCT was carried out by Ernst in 2003
• Published in the Eur J Clin Pharmacol 2004
• He concluded that the trials failed to demonstrate the efficacy of this therapeutic approach
Werner Frase

- VP of Int Soc Homotoxicology
- Responded in Eur J Clin Pharmacology 2005
- Questioned the exclusion of 5 RCT trials
- Homotoxicology is in the process of being updated and modernised
- Questions the conclusion of the review
Since then...

- A group of Italian and European doctors exploring the use of homeopathic doses of biological molecules such as Neuropeptides, Hormones, Cytokines and Growth Factors
  - With the support of GUNA S.p.a. -
- A new common ground is emerging -
- Recent achievements in the field of Psycho-Neuro-Endocrine-Immunology (P.N.E.I.)
- Created a climate for innovation
Clinical trial on **Eubioflor 1** and **Mycox** effectiveness in the treatment of dysbiosis.

Treatment of wrinkles and skin slackening using the intradermal injection of a complex homeopathic remedy (**Made Omeo Wrinkle**). Results of a cohort clinical study on 681 patients.

**Transfactor 11** in HPV viral pathologies (160 cases)

**Melatonin.** Clinical trial of homeopathised melatonin in 40 cases.

**Guna Flu** prevention of upper respiratory infections in paediatrics. A controlled, multicentre clinical trial.

Clinical report on the effectiveness of **Guna Throat**
Research Topics

- The experimental use of G-CSF in immunobiotherapy (Study of 33 clinical cases on the use of Granulocyte Colony-Stimulating Factor (G-CSF) in homeopathic dilution)
- Homeomesotherapy for Pain Management in primary chronic coxarthrosis with a Homeopathic Injectable Formulation (Result of a cohort, randomized, controlled clinical trial)
- Functional and iatrogenic secondary corticohypothalamic amenorrhea in P.N.E.I. Dynamics
- Polyglucosamine - action on oxidised lipids and dyslipidemias.
- Treatment of allergic manifestations with Transfer Factor (TF).
- The matrix tetrametric code: hormones, cytokines, neuropeptides, melatonin.
- Preliminary reports on complex homeopathic therapy in patients suffering from post-menopausal osteoporosis.
- The use of cytokines in Homeopathy. The fractal dynamics at the root of our bodies functioning.
- Homotoxicology and basic regulation: Bystander reaction therapy.
- The importance of oxidative stress as a risk factor for morbidity.
- Homeopathic immunomodulators: principles and clinical cases. The informative role of cytokines in fractal dynamics.
- The role of food intolerance in the pathogenesis of atopic dermatitis.
Publications since 2004

• Homotoxicological remedies vrs desmopressin vrs placebo in the treatment of enuresis: a randomised, double-blind, controlled trial
  - Pietro Ferrara, Giuseppina Marrone, Valentina Emmanuele, Alessandro Nicoletti, Antonio Mastrangelo, Eloisa Tiberi, Antonio Ruggiero, Alfonso Fasano, Fabrizia Paolini Paoletti

Conclusion

- 151 children randomised
- Homotoxicology shown to be superior to placebo ($P<0.0001$) with regard to the number of children attaining 14 consecutive dry nights during treatment
- Homotox shown to be safe and effective even if it is significantly less effective than desmopressin in this clinical condition
Mercurius Heel

• Nickel Gluconate-Mercurius Heel-Potentised Swine Organ Preparations: a new therapeutical approach for the primary treatment of pediatric ranula and intraoral mucocele

  • Salvatore Garofalo, Vito Briganti, Sebastiano Cavallaro, Ernesto Pepe, Marina Prete, Liana Suteu, Paolo Tavormina

Conclusions

• This preliminary study evaluates the effectiveness of Nickel Gluconate-Mercurius Heel-Potentised Swine Organ preparations as the primary treatment of Pediatric ranula and intraoral mucocele

• 18 children treated
• 89% ranulas and 67% labial mucoceles completely responded to the therapy
• Therapy was shown to be an effective primary treatment.
Belladonna/Echinacea

- Effects of Atropa belladonna and Echinacea angustifolia in homoeopathic dilution on experimental peritonitis
Conclusion

• Belladonna and Echinacea are used in homotoxicology as modulator of inflammatory processes
• Evaluates their effects on leukocyte migration and macrophage activity induced by experimental peritonitis in vivo (mice)
• Found to modulate peritoneal inflammatory reactions and have a cytoprotective effect on leukocytes
Molecules of emotion

• Candace B Pert PhD
• Journal of Immunology 1985
• 'A major conceptual shift in neuroscience has been wrought by the realisation that brain function in modulated by numerous chemicals in addition to classical neurotransmitters. Many of these informational substances are neuropeptides, originally studied in other contexts as hormones, gut peptides or growth factors.'
The birth of PNEI

- 'Neuropeptide receptors occur on mobile cells of the immune system....Neuropeptides and their receptors thus join the brain, glands, and immune system in a network of communication between brain and body, probably representing the biochemical substrate of emotion.'
PRM

• Restoring physiology through communicating molecules such as hormones, interleukines, neuropeptides and growth factors

• Prepared in homeopathic dilutions, which are the same physiological concentration as the body.
<table>
<thead>
<tr>
<th>Concentration</th>
<th>Effect Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$10^{-3}$</td>
<td>Toxic Concentration</td>
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<tr>
<td></td>
<td>Toxic Effect</td>
</tr>
<tr>
<td></td>
<td>Pharmacological Effects</td>
</tr>
<tr>
<td>$10^{-6}$</td>
<td>Minimal Effective Pharmacological Dose</td>
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<tr>
<td></td>
<td>Without Dynamization: No Biological Effects</td>
</tr>
<tr>
<td>$10^{-15}$</td>
<td>Minimal Effective Physiological Dose</td>
</tr>
<tr>
<td></td>
<td>No Biological Effects with or without Dynamization</td>
</tr>
<tr>
<td>$10^{-30}$</td>
<td>Ultra Low Dose Concentration</td>
</tr>
</tbody>
</table>

**Effects of Different Doses of Cytokines**

- **TM**
- **Pharmacological concentrations** (mg/ml)
- **Physiological concentrations** (mcg/ml)
- **Physiological/Pharmacological concentrations** (ng-pcg/ml)
- **Ultra Low Dose Concentration**
Aconitin experimentation


Different effects of Aconitin concentrations on isolated and perfused eel heart:

• Aconitin $10^{-5}$ M \(\times 5\) ➔ Fibrillation

• Aconitin $10^{-7}$ M \(\times 7\) ➔ Bradycardia

• Aconitin $10^{-18}$ M \(\times 18\) ➔ No effect on healthy heart

➔ Rythm normalization on preintoxicated heart
HOMEOPATHICALLY DILUTED HORMONE

Sensitization of receptors (Backup receptors)

ADENYL CYCLASE ACTIVATION

CAMP ACTIVATION
Low Doses

- The response of a cell to a messenger depends on the number of receptors occupied.
- A typical cell may have about 1000 receptors.
- Only a small fraction (10%) of the receptors need to be occupied to get a large (50%) response.
Mechanism of Action

• Sensitization or activation of some units of cellular or plasmatic receptors
• $10^{-6}$ (microgramm) or $10^{-9}$ (nanogramm) for the cytokines and $10^{-12}$ (picogram) for the hormones
• Restoration of auto-regulatory homoeostatic mechanism.
• Source: Guna Scientific Department
Malzac and Melatonin

• Malzac J. La melatonina – Sperimentazione clinica su 40 casi della melatonina omeopatizzata
• La Med Bio Suppl al No 3/1995 23-25 Investigates the use of melatonin 4CH in 140 patients presenting with various pathologies
• Pathologies including depression
• Reports clinically ‘encouraging’ results
Micro Autoradiography

- W.E Stumpf (2005)
- *J of Pharmacol and Toxicological methods 51 (2005) 25-40*
- Drug localization and targeting with receptor microscopic autoradiography
- Low dose substances interact with the cell nucleus
- Higher concentrations trigger a cellular response at cytoplasmic level
Hormesis

- Low dose stimulatory effects of toxic compounds
- Studies require attention to detail, patience and high resolution-high sensitivity approaches
- Valuable information can be gained with micro autoradiography
- With radiolabeled compounds of high specific activity target sites of low dose deposition and action can be identified
Nuclear receptor binding

• With near physiological doses nuclear receptor binding could be well recognised
• With elevated doses, nuclear uptake became saturated and extra nuclear deposition increased
• Due to initial binding and saturation of primary sites
James L. Oschman

- PhD, biophysics and biology
- Research at different universities
- In depth research on the peculiarities of the matrix, more precisely the energetic aspects
- Modern research on living matrix and his scientific base for complementary holistic medicine
• Extra-cellular matrix
• Intra-cellular matrix (cytoskeleton and other structures)
• Nuclear matrix
Hartmut Heine
born 1941

- Histologist
- Histological preparation of an acupuncture point (1987)
- Further research on ECM, especially on proteoglycans and glucosaminoglycans
- Basic research on autoregulatory processes in ECM
- Immunological Bystander Reaction as a possible working mechanism behind antihomotoxic medications (IBR)
Synonyms of the ECM

- The terrain: Claude Bernard
- The mesenchyme: old regular terminology
- Connective tissue: old regular terminology (histological) without any physiological value
- The Ground Regulating System (GRS): Pischinger
- The Basic Bio Regulating System (BBRS): Lamers, Van Wijk and Linnemans
- The Extra-Cellular Matrix (ECM): current terminology
- The Living Matrix: new terminology in complementary medicine thanks to the work of James Oschman
Histology of the ECM

• The ECM is built up like a 3-dimensional network
• Apart from the proteoglycans and glucosaminoglycans, the collagen, elastin and other basic fibers, it contains capillaries, lymphatic and nerve ends, defense cells and basal membranes
• It is present all over the organism and is the main pathway for vicariation
ECM

• The ECM is the transmitter area and main area of action of mediators in the human body
• It is part of the living matrix and not to be seen as a separate communication system
• It is the terrain where the organism deals with homotoxins in inflammatory or storage pathways
• The ECM guarantees the quality of life of the cell and is therefore crucial for the organ function
Chronic disease

Homotoxins

ECM intoxication

Cell hypoxia

Cell intoxication

Cell dysfunction

Physiological disruption
Morpho-functional unity: vessel-matrix-membrane receptor
Cytokines

- Biological response is achieved with the occupation of a minimal quantity of receptors
- 1%-2% for IL-1
- With characteristically low-dose and low titred physiological dilutions below Avogadro’s Number
  - Source: L Milani Inflammation and Physiological Regulating Medicine (2007)
The concept of BALANCE and the use of the cytokines.

Talking about cytokines it’s useful to talk about BALANCE, in particular of balance Th1-Th2.

In case of pathologies there is an imbalance; for example, in the acute inflammatory pathologies the Th1 scale pan is heavier: in these cases the therapy should make heavier the Th2 (IL4, IL10, TGF-beta) scale pan in order to redress the balance.

On the contrary, in the allergic pathologies the Th2 scale pan is heavier: in these cases the therapy should make heavier the Th1 (IL12, INF-gamma) scale pan in order to redress the balance.

The appropriate “rebalancing” cytokines will play their role working on the cell receptors.
Th17 cells in Inflammatory Conditions

- Anne Cook has produced a short review
- CD4+ T cells have been subdivided into different subsets largely on the basis of the cytokines they produce.
- Th17 cells produce IL-17
- New studies have recognised the role of Th17 cells in inflammatory conditions such as arthritis and inflammatory bowel disease
• Elevated levels of IL-17 have been detected in rheumatoid synovium and associated with MS, psoriasis and systemic lupus erythematosis.
• The role of Th17 in mediating autoimmune disease is being researched.
• Previously it was thought that these were Th1 mediated diseases.
New Therapy??

- IL-12 regulates Th1
- IL-4 regulates Th2
- TGF-Beta and IL-6 are required for Naive CD4+ cells to differentiate into Th17 cells
- This differentiation is facilitated by the absence of INF-Gamma and IL-4
The central role of Th17 and IL23 and IL17 in autoimmune diseases

AUTOIMMUNE PATOLOGIES
In autoimmune pathologies it is generally possible to detect low levels of INF-γ e IL4; since these interleukines don’t stimulate the Th0 to differentiate into Th1 or Th2, enable the IL6 to stimulate the Th17 to produce IL17, the real trigger interleukine in autoimmune diseases. According with PRM it’s important tu use opposite citokines; therefore, to slow down the IL6 it is important to use IFN-γ 4CH e IL4 4CH
**THE CONCEPT OF BALANCE**

The cytokines in a cell population stimulate the secretion of the same cytokines and the differentiation of other T helper lymphocytes in the same way. At the same time, Th1 cytokines inhibit the function and the reproduction of Th2 lymphocytes and vice versa.
THE BALANCE TH1-TH2

TYPICAL SITUATION IN CASE OF ALLERGY

TYPICAL SITUATION IN CASE OF ACUTE INFLAMMATION
The concept of BALANCE and the use of the cytokines.

**Th1**
- PRO INFLAMMATORY
  - GCSF
  - IL1
  - IL2
  - INF-gamma
  - IL6
  - IL8
  - TNF-alfa
  - IL12

**Th3**
- TOLERANCE
  - TGF-β
  - IL10

**Th2**
- ANTI INFLAMMATORY
  - IL10
  - TGF beta
  - IL4
  - IL5
  - IL6
  - IL7
  - 47
  - IL9
  - IL13
<table>
<thead>
<tr>
<th>CYTOKINE</th>
<th>THE USE OF CYTOKINES according to PRM</th>
<th>SLOW-DOWNING</th>
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<tbody>
<tr>
<td></td>
<td>STRENGTHENING</td>
<td></td>
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<tr>
<td>GCSF</td>
<td>GCSF 4CH</td>
<td>IL 10 4CH/IL 4 4CH</td>
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<tr>
<td>INF alpha/gamma</td>
<td>INF alfa/gamma 4CH</td>
<td>IL 4 4CH</td>
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<tr>
<td>IL 1</td>
<td>IL 1 4CH</td>
<td>Anti IL 1 4CH/IL 10 4CH</td>
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<tr>
<td>IL 2</td>
<td>IL 2 4CH</td>
<td>IL 11 4CH</td>
</tr>
<tr>
<td>IL 3</td>
<td>IL 3 4CH</td>
<td>IL 10 4CH</td>
</tr>
<tr>
<td>IL 4</td>
<td>IL 4 4CH</td>
<td>INF alfa and gamma 4CH/IL 12 4CH</td>
</tr>
<tr>
<td>IL 5</td>
<td>IL 5 4CH</td>
<td>TGF-beta 4CH</td>
</tr>
</tbody>
</table>
| IL 6           | IL 6 4CH                             | Acute inflammation: IL4 4CH/INF-γ 4CH 
Chronic inflammation: IL 6 4CH |
| IL 7           | IL 7 4CH                             | IL 10 4CH/ TGF-β 4CH  |
| IL 8           | IL 8 4CH                             | IL 10 4CH/FGF 4CH     |
| IL 9           | IL 9 4CH                             | IL 10 4CH             |
| IL 10          | IL 10 4CH                            | IL 1 4CH/TNF-alfa 4CH/IL 6 4CH |
| IL 11          | IL 11 4CH                            | IL 2 4CH              |
| IL 12          | IL 12 4CH                            | IL 4 4CH/IL10 4CH     |
| TGF-beta       | TGF-beta 4CH                         | IL 5 4CH/IL 7 4CH     |
| TNF-alpha      | Tnf-alfa 4CH                         | IL 6 4CH/IL12 4CH/IL 4 4CH |
The concept of BALANCE and the use of the cytokines.

Th1 Hyperactivation Diseases

- Rheumatoid Arthritis (IL1, IL6, IL2, TNF-α, IL17)
- Multiple Sclerosis (IL12, INF, TNF-α)
- Diabetys type I (IL1, TNF-α, INF-γ, IL17)
- Tuberculosis (IL12, IL18)
- Autoimmune endocrine pathologies
- IBD (IL1, IL6, TNF-α, IL23, IL17)

Th2 Hyperactivation diseases

- Allergy (IL4-IL5-IL13)
- Asthma (IL4-IL10)
- Atopic dermatitis (IL4-IL10)
- LES (IL10-IL6, IL17)
- Sclerodermia (IL17-IL6)
- HIV
The concept of BALANCE and the use of the cytokines.

Th1
Hyperactivation Diseases

• Psoriasis  (IL12, IL23)
• Crohn D.  (IL12→IL6, TNF-α, IL18)
• Alopecia  (IL1, TNF-alfa, IL8)

Th2
Hyperactivation diseases

• …
Trial Design Issues

• Choice of an appropriate methodology
• Internal and external validity
• Even qualitative changes can be subjected to validated methods of quantification
Trial Design Issues

• Clinical outcome measures must reflect the ‘whole person’ approach
• Quality of Life assessment is as important as physical health determinants.
• Qualitative studies followed by pilot studies and RCT.
Summary

• We have explored a new frontier in terms of the use of PNEI and biological molecules
• New techniques are becoming available to study a possible mechanism of action
• Further research is needed, trial design must have rigor and reflect CAM aims
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