

## **Infective and Inflammatory Eyelid Disorders: Conventional and Unconventional Therapies to Maintain Eye Health and Avoid Lid Surgery**

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### **Abstract**

Infective and inflammatory eyelid disorders arise frequently in pediatric age due to a minor control of the hygiene. Usually such disorders are treated with local therapeutic procedures to resolve itching and ocular hyperemia and reduce the risk of chronicity and corneal complications. If the pathology has recurring elements, or an aesthetic manifestation, then other examinations are performed to place the problem in a context of general health. In fact, disorders of immune system are revealed in eyelid disorders, in particular of the mucous membrane immune system (lungs, intestine, liver). The environment, nutrition and family life style, play an important role in eyelid disorders. Prophylaxis, conventional and unconventional therapies (homeopathy) are proposed to prevent chronic conditions, avoid lid surgery and reduce the risk of sight problems due to corneal damage.

**Keywords:** *Eyelid; Homeopathy; Pediatric; Immunity; Microbiota*

### **Abbreviations**

MALT: Mucose-Associated Lymphoid Tissue; IgA: Immunoglobuline A; CH: Centesimale Hahnemannienne

### **Introduction**

The child is an organism still in development [1]. It follows that, the fewer pharmaceuticals taken throughout the period of growth, the more harmonious the development of the child's organs and immune system will be [2,3]. Infectious or inflammatory diseases that arise on the eyelid have a variable incidence in childhood, depending on the overall level of health and the lifestyle of the family of origin. Certain conditions, such as herpes or molluscum contagiosum, being infectious, are typical of the child's inter human contact, as socialization with other children can result in contamination and clinical manifestations typical of the specific virus on the skin or the eyelids [4,5]. The pathogenesis of bacterial infections, such as styes or chalazia, is different, seeing that they are generally caused by an underlying acute or chronic blepharitis. Chalaziosis of the eyelid can be sporadic or recurring; in the latter form especially, it can give rise to acute inflammation and obvious concern on the part of the parents [6], who may be advised to opt for surgery to rapidly resolve the eyelid condition or possible complications affecting the cornea, should there be localized secondary trichiasis. The eventuality of surgery is not only unwelcome to parents of children at any pediatric age, but especially if the child is younger than three, it poses a potential problem for neurocognitive development. During this period neuronal development is not yet complete, and certain anesthesiological studies still underway recommend abstaining from general anesthesia with children less than three years of age, unless it proves indispensable. A number of authors see a correlation between the risk of developing dyslexia or neurocognitive alterations and precocious exposure of children to general anesthesia for pathologies that make it necessary [7,8]. Thus the need to view infectious and inflammatory pathologies

of the eyelid, seemingly banal conditions, in a broader context, in order to understand why these manifestations appear in an organ of the senses, such as the eye, and how best to prevent and treat them, drawing not only on conventional antibiotic and antiviral therapies, but also on unconventional treatments, taking an integrated approach to the child, who is not a small adult but rather an individual with his or her own clinical characteristics. The process that the parents go through once they understand that the problem is not only a local disturbance of the eyelid, but frequently the sign of a more general pathological context, potentially capable of compromising the child's sight, leads them to an increased awareness of all the different facets of health, giving them a better understanding of their child's condition. Even allergic pathologies of the eyelid, which can arise at an early age in children as part of a broader allergic condition (asthma, rhinitis, eczema), should be managed by viewing them as part of the overall clinical history and genetic predisposition of the family of origin [9]. Awareness that the embryogenesis of both the respiratory and intestinal tracts can be traced to the same germinative layer (the endoderm) is of key importance in the therapeutic management of the child. Especially in early infancy, he or she exhibits the condition in equivalent fashion in both organs, the respiratory and intestinal tracts, with the result that other mucous and related tissues, such as the conjunctival membrane and the nasal mucosa, are also affected by the condition.

## **An analysis of the scientific literature**

### **The eyelid diseases in the field of non-conventional medicine**

The eye, the organ of sight, originating from the neuroectoderm, can manifest numerous illnesses in the course of a lifetime, in remembrance of its embryogenesis. Its nervous portion behaves, in terms of both physiology and nutrition, like an organ with terminal circulation, in direct contact with the central nervous system, while its ectodermic portion gives full expression to manifestations of other tissues originating from the same layer, such as the skin and the exocrine secretion glands (the lipidic lacrimal glands, both accessory and primary). Non-conventional medicine, and especially homeopathy, focuses much attention on these fundamentals, basing a large part of its medical reasoning on the physical constitution of the individual, traditionally divided among the short, the normal and the tall, which correspond, in homeopathy, to the carbonic, the sulfuric or muriatic and the phosphoric constitutions of individual subjects. Each physical constitution, which begins to express itself after the first twelve months of life, guided by the child's genetics, is influenced by numerous other elements: the endocrine component, in which the thyroid plays a key role for the entire metabolism; the immune component, which begins to mature once the infant is weaned; the neuropsychic component, which involves all the organs of the senses; the environmental component, meaning the latitude, the amount of sunshine and air pollution. Indeed, a noteworthy difference of homeopathic semiotics, as compared to the conventional approach, is that it evaluates the reactive processes of the patient (whether the condition worsens or improves in cold or hot temperatures, whether there is a preference for sweet, salted or acidic food, an assessment of the rhythm of sleep-wakefulness etc.) [10,11]. These clinical evaluations of the processes of reaction, in both children and adults, enable homeopathic semiotics not only to take a more complete approach to the etiopathogenesis of the eyelid condition, but also to act in a number of different areas to modify its clinical manifestation, moving in the opposite direction of its causes. Depending on the subject, it can be best to work on the environmental component (respiration, oxygenation, absorption of the vitamin D- found in tears and with specific receptors on the cornea) [12,13], on eating with its influence on the gut microbiota [14,15], on the immune or endocrine components or, finally, on the psychic component. The concept of "epigenetics" was recently introduced, according to which the environment in which we live and our lifestyle able to modify the phenotypic expression of our genetic code. It follows that even genes capable of giving rise to serious illnesses can remain in a state of latency, due in most cases to mechanisms of enzymatic methylation, if the lifestyle of the subject, and especially the nutritional regime and tissue oxygenation, are suitable to keeping the dangerous genes from leaving their state of latency. Furthermore, in infancy, primarily up to the age of eight, there are close ties between the mental and emotional components and the physical body, and so a mental or emotional condition can easily manifest itself somatically, just as a physical trauma can become a mental problem [16]. Further on, the mental and physical spheres begin to separate, and the capacity to filter life and relations with others increases. Not all individuals develop this capacity in the same way, however, with the eyelid pathologies of some adolescents representing manifestations of unexpressed anxiety or aggressiveness.

In smaller children, we can identify three different types of respiration: 1) air 2) digestive 3) through the organs of the senses.

**Air Respiration:** The key feature of the respiratory process is its rhythmic pace. As with any rhythmic movement, this is a result of a polarity governed by nerve stimuli. On the one hand we have the organism's need for oxygen, on the other the need to eliminate carbon dioxide, the waste product of the exchange, in order to maintain the equilibrium. Normal respiration, with the exchange of  $O_2/CO_2$ , "fuels" the process of renewal, which is why the lungs are the most extensive surfaces of our bodies in direct contact with the outside environment. In terms of pathologies of the surface of the eye, it is interesting to note that the lungs and the cornea are the only two organs that act as an interface between oxygen and blood. As a result of this similarity, it is not rare to observe pulmonary conditions appearing following those of the cornea or, vice versa, pathologies of the cornea disappearing when a respiratory condition suffered at the same time is resolved. Pathologies of viral (i.e. herpetic) or bacterial origin (such as staphylococcus aureus) are significantly affected by such restorations of balance, both in children and adults.

**Digestive respiration:** The digestive tract, the point of encounter between the human being and external substances, in addition to absorbing nutritional substances from food, also fills an important defensive role, thanks to its ties to the lymphatic and immune system. Given its noteworthy metabolic activity, it generates significant levels of energy and heat, with the intestinal metabolism receiving key contributions from the liver and the gallbladder. The liver, which has not yet reached maturity in a child, is an organ that functions primarily at night, operating slowly and deliberately, with its chief concern being the quality of the food ingested. Non-conventional medicine places less importance on the calorie intake of the food eaten than on the vitality of the food and the intensity of the resulting digestive process. If the metabolism of glucides and lipids, which is handled by the liver, does not function properly, then the problem can manifest itself, from early infancy, as a condition in the peripheral site of the eyelid like: blepharitis, meibomitis, the formation of styes and chalazia, representing acute and chronic localized expressions of the condition. Even if these pathologies make their appearance in a peripheral organ of the senses, they point to more than just a lipid lacrimal secretion, and should give rise to considerations of a more general metabolic problem, as they are often a sign of: a food intolerance, intoxication, a failure to absorb nutrients, insufficient absorption of vitamin D or gluten intolerance [17]. The eyelid is a "bile bladder" where stress, tension and anger are frequently expressed. Phlogistic reactions signal that something must come out: toxins from the intestine, the liver, hydrocarbons etc. It is the physician who must figure out what should be modified for each individual patient.

**Sensory respiration:** The sensory organs of a small child are extremely open and receptive to the surrounding environment. They are especially sensitive to noises (hearing – the organ of social relations), odors and scents (if an excess is channeled through the skin, the child can suffer an intoxication), to touch, the true primary sensory organ of infants. Touch becomes a mode of communication for the child, a way of getting to know others and the surrounding environment, seeing that he or she cannot speak yet. Touch also allows adults to communicate with the child's psyche, transmitting calm of anxiety, protection or fear. The ultimate purpose of sight, the adult's primary sense organ, is movement, but in infancy it is an organ still in development, and so it lets the other senses take precedence while slowly maturing in the course of the development of the central nervous system. The circulatory system ensures a harmonious connection among all the organs of a healthy individual, bringing the small intestine into contact with the central nervous system, all in harmony with the respiratory rhythm, which mediates either adequate or inadequate quantities of oxygen.

### **Maturation of immunity in the nursing infant and the young child**

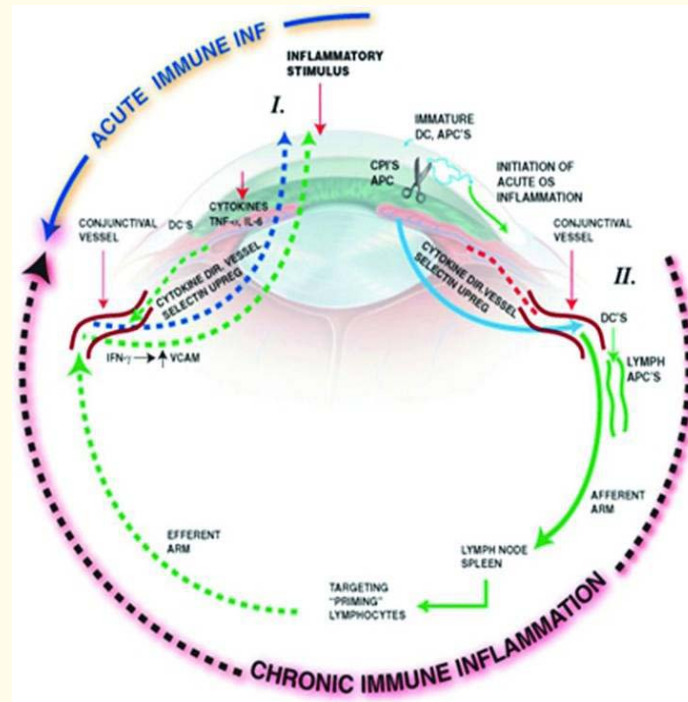
Immunity in children can be subdivided between the immediate function carried out by the antibodies already circulating in the blood and long-term immunity, which needs a few days to take effect. In terms of the phases in the maturation of a child's immune system, it can be noted that the thymus, the organ that produces antibodies, begins to atrophy once the child starts eating solid food, meaning after weaning, when bacterial flora starts to form in the intestine. This flora, together with the lymphatic system of the mucous membranes (the M.A.L.T., found in the intestine, the respiratory and genitourinary tracts and in the conjunctival membrane), activates the lymphocytes,

which gradually develop as the weaning proceeds. The intestinal lymphocytes migrate by means of the lymph, arriving at the regional lymph nodes, where they produce antibodies. The antibodies then reach the peripheral M.A.L.T. systems in zones connected with the outside environment. Here, when triggered by the immune system, the lymphocytes tied to the mucous membranes, having been activated, produce inflammatory mediators, first of all cytokines, which carry information to both the afferent and efferent portions of the system, stimulating the other stations of the immune system (Figure 1) [18]. In this scenario, it is important that the levels of mucous and lactobacilli be correct, seeing that the IgA lives in the mucous that covers and protects the mucous membranes, while the lactobacilli become co-producers of IgA. A shortage of secretory IgA can facilitate the passage of antigenic molecules, while certain bacterial proteases produced by *Haemophilus*, *Neisseria*, *Streptococcus* can attack the  $\alpha 1$  chains of the IgA. All the factors capable of altering or damaging the production of mucous (such as NSAIDs) reduce the level of IgA antibodies. Should this condition occur in the intestine, it modifies the contact between the food and the bacterial antigens, resulting in absorption of antigenic or bacterial molecules [19]. These occurrences are of significant importance, because degradation of the proteins by the hydrochloric acid, together with the pancreatic and intestinal enzymes, should be handled by the intestinal microvilli, with the proteins being hydrolyzed into amino acids; during this process, some antigenic molecules, including some of large size, manage to pass through the intestinal epithelium intact, arriving in the lymph through the enterocytes, giving rise to processes of exocytosis and pinocytosis. Toxins produced by bacteria or viruses, or catabolic products of intestinal bacterial flora, can also interact with the antigenic molecules, resulting in the change in pH that is responsible for the “intestinal dysbiosis” found in approximately 80% of all adults. The end result is a state of chronic immune inflammation, which explains the variability of the symptoms of intolerance to foods. What is more, given that the lymphocytes of the M.A.L.T. system are sent back in circulation, the pathological effects can appear even at a distance from the intestinal lumen, meaning at the conjunctival or nasal mucous membranes, resulting in full-fledged, chronic manifestations of allergies in these sites. In immunological terms, the conjunctival membrane behaves like a lymph node opened up and turned inside out [18]. The correlation between inflammatory conditions of the conjunctival membrane, lacrimal dysfunctions and an intestinal immune condition featuring dysbiosis, intolerances or allergies are pathophysiological issues still under study, given the importance of such factors on human health. The possibility that the nutrients in addition to their nutritional role, could influence the expression of the genes, activating or inhibiting metabolic channels, with synthesis or degradation of proteins, falls under the purview of the study of nutrigenomics. With this in mind, individuals who present polymorphism in the IL6 and TNF genes, to the point where inflammation and apoptosis are activated and an underlying phlogosis is facilitated, increasing susceptibility to conditions of chronic inflammation [20], require supplementary doses of Omega 3, at a quantity of 3 g/day, as opposed to the normal dose of 1.6 g/day. Finally, there is increasing evidence of the key role played by vitamin D in the immune control of processes of phlogosis and in the cell memory of infection [21-27]. The cornea has specific receptors for that vitamin, as do the nervous cells. This could explain why it is so effective in treating chronic forms of keratitis, especially of the herpetic and neurotrophic type, as well as recurring chalazia.

### Conventional medicine and homeopathy

The main principle of homeopathy, a unique scientific system of medicine established by Samuel Hahnemann two centuries ago, is that of ‘*similia*’ or ‘*simile*’ (similarity), which means ‘let likes be cured by likes’. In other words, when a substance is capable of inducing a series of symptoms in a healthy living system, low doses of the same substance can cure these symptoms under certain circumstances (‘*similia similibus curentur*’) [28].

Homeopathic stocks are substances, product or preparations used as a starting material for the production of homeopathic medicines. A stock is usually one of the following: a mother tincture or a glycerol macerate, for raw materials of botanical, zoological or human origin; or the substance itself, for raw materials of chemical or mineral origin. Homeopathic medicines are prepared through consecutive dilutions of a chosen substance in alcohol (ethanol 70% V/V in the major part of cases) or distilled water (in other cases), followed by forceful striking on an elastic device (Succession) [29].



**Figure 1:** Cytokine, mediators in afferent and efferent component of acute and chronic eyelid phlogosis RIF.

Once obtained the dilutions, an inert support is impregnated with the final active substance, where in homeopathy “active substance” meaning a homeopathic stock and its dilution [30]. Usually these pharmaceutical forms are called *pillules* (meaning with this term both *pillules* in single and multidose container). They are composed by lactose (15%) and sucrose (85%) [31]. *Pillules* are not the only pharmaceutical dosage forms in homeopathy but they are the most common. In addition, it is possible to have: tablets, ovules, oral drops, oral and cutaneous solutions, ointments, gels, creams and so on.

Homeopathic medicine and immunology have historical and conceptual ties. Both disciplines trace their origins back to the late 18<sup>th</sup> century: at the same time as Jenner was administering the first smallpox vaccinations, the German physician Samuel Hahnemann was performing his first homeopathic *proving*. Homeopathic remedies are substances prescribed in extremely low doses (or high dilutions/dynamizations, also known as “potencies”) to treat the same specific syndromes they are known to cause in overdose, by mimicking and augmenting the patient’s immune response and natural defenses [32]. Although western immunology is part of modern biomedicine, while homeopathy has always been considered an “alternative” medicine, in recent decades the two disciplines have come into closer contact.

### Homeopathic medicines used to treat a number of infectious or viral pathologies in infancy

In ophthalmology homeopathic medicines can be chosen, when treating acute pathological conditions, as an alternative to allopathic pharmaceuticals, due to [33-35]: the patient’s preference; subacute but chronic pathological conditions on account of allergies to pharmaceuticals or their components; altered immunological state; in complex situations where the ocular condition is part of an organic disorder involving the entire patient; in conditions where the objective is prophylaxis, as when an organism is being prepared for a surgi-

cal procedure. A typical condition in which homeopathic medicines can be of use in prophylaxis is the molluscum contagiosum infection. As an alternative to surgery, or after an operation, *MEDORRHINUM 200 CH* can be used at a dose of one tube per month for 6 months. Medorrhinum, a biotherapy medicine made from a lysate of purulent, urethral, blennorrhagicum secretions, is especially recommended for skin subject to boil-like, itchy eruptions [36-39]. In the specific case of molluscum contagiosum, it modifies the immune state of the subject, keeping him or her from being infected anew upon returning to the same living environments. Infected individuals typically seek acidic food, a preference that ceases when they no longer have need of the remedy. Two other homeopathic medicines frequently used in day-to-day clinical practice are Thuja occidentalis and Causticum. Thuja occidentalis L, of the Cupressaceae family, is the “tree of life”, widely found in Canada and North America. The mother tincture, prepared from the branches, consists of: Tannins (5%), plus Flavonoids and essential oils (1%), of which the main ingredient, Thujone, has shown a number of noteworthy properties [36,40-44]. The Causticum got its name from its method of preparation: it is a complex chemical substance obtained by distilling a mix of spent lime and potassium bisulphate, used most frequently for chronic clinical conditions, though it is often applied to acute conditions as well [36,45]. As ophthalmological treatments, these medicines can be supplemented, for children undergoing surgery for papilloma in the anophthalmic cavity, with *THUJA 200 CH* at a dose of: one tube on the 7<sup>th</sup> and 21<sup>st</sup> day of the month, for a number of months, together with *CAUSTICUM 7 CH* granules, at a dose of: 5 granules 2 times a day for two months.

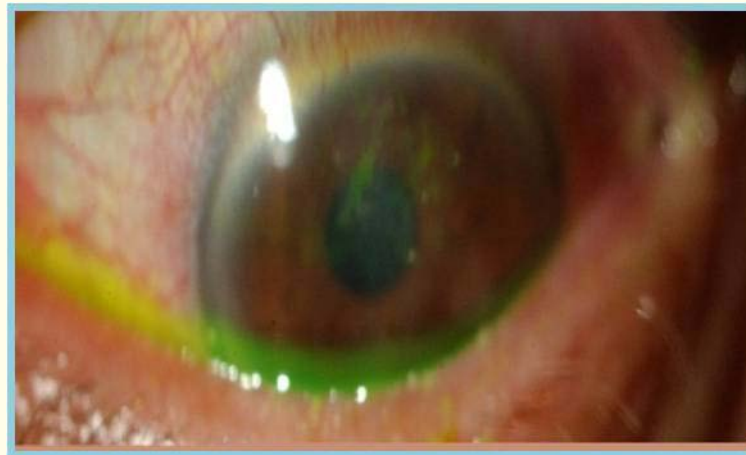
For multiple and recurring chalazia, normally managed with topical antibiotics or surgery, and whose pathogenesis has already been described, *HEPAR SULFUR 7-9 CH* can prove beneficial, at a dose of: 5 granules for 10-15 days, or gradually diminishing weekly doses of *SULFUR 9-15-30 CH* can be taken. Hepar sulfur is a medicine made from a mix of purified sulfur flowers and oyster-shell lime and is generally used to treat inflammatory conditions with a marked tendency towards acute and, at times, in chronic skin, respiratory tract mucous membranes and lymphoid tissues suppuration [36,46]. Sulfur, on the other hand, is obtained from sublimed and washed sulfur and it is also used for acute inflammatory states of the skin, the mucous membranes, the serous membranes and the connective tissues [36,47]. If a subject with multiple chalazia exhibits latent aggressiveness, then a useful substance is *STAPHYSAGRIA 7 or 9 CH*, also known as the lice herb, whose plant of origin belongs to the Ranunculaceae family. The mother tincture is obtained from the seeds, whose content of alkaloids is approximately 1.3%, with the most important being delphinia and staphysagria. This homeopathic medicine is normally recommended for use on a number of major skin conditions: standard itching, surgical sores, recurring styes and chalazia [36,48]. In cases of ocular allergy, whose pathogenesis was indicated earlier, an exact identification of the allergen is not important. The condition originates from a metabolic problem, and so what matters is reorganizing the intestine and its metabolism. Along with membrane stabilizers (spaglumic acid, ectoine), topical antihistaminic and steroids, we could use *EUPHRALIA EYE DROPS* at a dose of: 2 drops per eye 3-4 times a day, or more often when needed [49] and *MANGANESE* micro-elements vials taken orally. Euphrasia is a homeopathic eye drop that contain Euphrasia Officinalis and Chamomilla vulgaris, both homeopathic medicines used to treat clinical conditions in which swelling plays a major role [36,49, 50-51]. Herpetic infections of the eyelid, and especially cases involving the cornea, are suffered primarily by small children (younger than 5); there are two ages of peak incidence: 0-5 years and late adolescence, when sexual activity begins. In homeopathy, not much of a distinction is made between the two type of herpes: simplex and zoster. Homeopathic medicines can be used both in the acute phase and to alleviate post-herpetic pain. The referred medicine is *RHUS TOXICODENDRON 9 or 15 CH*, at a dose of 5 granules a number of times a day, for the first week, then 1 tube every 10 days for a month. This homeopathic medicine is obtained from the poisonous sumac of a shrub of the Anacardiaceae family and it can be chosen for all reactions involving boils or erythema, such as: eczema, pink acne, scrofulous conjunctivitis, rheumatic iritis [36,52-53]. Naturally, the medicine is not equally effective for all patients. The closer the reactive mode of the individual is to a remedy, the more effective the treatment (Figures 2-3). Infections of the tear ducts are a frequent problem with newborns, and one generally not treated with surgery before the child’s first birthday [54]. At this stage of life, the baby’s physical constitution has yet to be differentiated, and so the child suffering from dacryocystitis can benefit from a homeopathic medicine made from the Crasostrea angulata, *CALCAREA CARBONICA OSTREARUM 30 CH*, at a dosage of: one tube a month, up until the 12<sup>th</sup> month for maturation of the bone component. Apart from benefitting young children and adolescents, this medicine is particularly recommended for ENT infections (acute and recurring) and eczema and in vivo and in vitro studies can show its efficacy [36,55]. As a valid



alternative or supplement to topical antibiotic therapy (frequently extended for lengthy periods), the single-dose eye drops *HOMEOPTIC* can be used, at a dosage of: 1- 2 drops in each eye 2-6 times a day, *ARGENTUM NITRICUM 7CH* tube of granules, 5 granules 2 times a day for 15 days (pediatric homeopathy) or *SILICEA 9 -15 CH*, when more extensive problems of rhino-sinus infection are present. Homeoptic is a homeopathic eye drops made from *Euphrasia officinalis 3DH*, *Calendula officinalis 3DH* and *Magnesia carbonica 5CH*, which are especially effective on inflammations with sharp pain, copious tearing and reddening of the eyes [36,50]. *Argentum nitricum* is a homeopathic medicine made from silver nitrate and generally used in case of excretions [36,56], while *Silica* is made from colloidal anhydrous silica and it is generally used in pediatric age [36,57]. At the end, it should be remembered that antibiotic therapy below one year of age means opening the way for allergy later in the child's life.



**Figures 2:** Herpetic corneal infection: Time 0 and 5 days later *Rhux Toxicodendron 15CH* granules.



**Figures 3:** Herpetic corneal infection: Time 0 and 5 days later *Rhux Toxicodendron 15CH* granules.

## Conclusion

For any individual, but especially for a growing child, the term health should not be viewed in absolute terms, as the absence of illness, but rather as a balance to be restored constantly, amidst processes that, were they to act on their own, would be unopposed and would cause illness. The child's immune system is a virgin mechanism that easily responds when prompted to reorder itself. Homeopathy can provide the prompting in certain pathologies of the eyelid and the eye. Conventional and non-conventional therapies are merely two different ways to practice the same art of medicine.

## Conflict of Interest

The author declares that she has no competing interests.

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## Bibliography

1. Burgio GR. "Practicing a Culture of Pediatric Immunogenetics". *American Journal of Medical Genetics* 100.4 (2001): 257-263.
2. Sterkers G. "Immune defenses of newborn infants". *La Revue du Praticien* 41 (1991): 1341-1344.
3. Yin S. "Malicious use of pharmaceuticals in children". *The Journal of Pediatrics* 157.5 (2010): 832-836.
4. CDC "Molluscum Contagiosum: Risk of Factor". 2015.
5. Pinninti S. "Pediatric Herpes Simplex Virus Infection".
6. Duss DN, et al. "Management of Recurrent Chalazia". *Journal of Pediatric Ophthalmology and Strabismus* 49.6 (2012): 327-328.
7. Di Maggio C, et al. "Early childhood exposure to anesthesia and risk of developmental and behavioral disorders in a sibling birth cohort". *Anesthesia and Analgesia* 113.5 (2011): 1143-1151.
8. Sun L. "Early childhood general anaesthesia exposure and neurocognitive development". *British Journal of Anesthesia* 105.Suppl 1 (2010): i61-i68.
9. Margo CE and Harman Le. "Autoimmune Disease: Conceptual History and Contributions of Ocular Immunology". *Survey of Ophthalmology* 61.5 (2016): 680-688.
10. Montfort-Cabello H. "Chronic diseases: what are they? How are they inherited?". *Homeopathy* 93.2 (2004): 88-93.
11. Guajardo G, et al. "Homeopathic terminology: a consensus quest". *British Homeopathic Journal* 88.3 (1999): 135-141.
12. Hong J, et al. "Ambient air pollution, weather changes, and outpatient visits for allergic conjunctivitis: A retrospective registry study". *Scientific Reports* 6 (2016): 23858.
13. Shetty R, et al. "Corneal Dendritic Cell Density Is Associated with Subbasal Nerve Plexus Features, Ocular Surface Disease Index and Serum Vitamin D in Evaporative Dry Eye Disease". *Biomed Research International* 13 (2016): 4369750.
14. Rokhsefat S, et al. "Mucin-Microbiota Interaction During Postnatal Maturation of the Intestinal Ecosystem: Clinical Implications". *Digestive Diseases and Sciences* 61.6 (2016): 1473-1486.



15. Ohnmacht C. "Intestinal microbiota, evolution of the immune system and the bad reputation of pro-inflammatory immunity". *Cellular Microbiology* 13.5 (2011): 653-659.
16. Cole J., et al. "The therapeutic potential of epigenetic manipulation during infectious diseases". *Pharmacology & Therapeutics* S0163-7258.16 (2016): 30138-3.
17. Anania C. et al. "Liver involvement in pediatric celiac disease". *World Journal of Gastroenterology* 21.19 (2015): 5813-5822.
18. Stern ME., et al. "Dry Eye as a Mucosal Autoimmune Disease". *International Reviews of Immunology* 32 (2013): 19-41.
19. Nurkic J., et al. "Diagnostic Significance of Reduced IgA in Children". *Medical Achieves* 69.4 (2015): 236-239.
20. Menezes V. et al. "Cytokine gene polymorphisms involved in chronicity and complications of anterior uveitis". *Cytokine* 35.3-4 (2006): 200-206.
21. Sethu S., et al. "Correlation between tear fluid and serum vitamin D levels". *Eye Vision (London)* 3.1 (2016): 22.
22. Yin Z., et al. "Vitamin D enhances corneal epithelial barrier function". *IOVS* 52.10 (2011): 7359-7364.
23. Reins RY., et al. "Effects of Topically Applied Vitamin D during Corneal Wound Healing". *PLoS One* 11.4 (2016): e0152889.
24. Reins RY., et al. "Vitamin D Activation and Function in Human Corneal Epithelial Cells During TLR-Induced Inflammation". *IOVS* 56.13 (2015): 7715-7727.
25. Lu X and Watsky MA. "Effects of Vitamin D Receptor Knockout on Cornea Epithelium Gap Junctions". *IOVS* 55.5 (2014): 2975-2982.
26. Elizondo RA., et al. "Effect of Vitamin D Receptor Knockout on Cornea Epithelium Wound Healing and Tight Junctions". *Investigative Ophthalmology & Visual Science* 55.8 (2014): 5245-5251.
27. Suaini NH., et al. "Immune Modulation by Vitamin D and Its Relevance to Food Allergy". *Nutrients* 7.8 (2015): 6088-108.
28. Bellavite P., et al. "Immunology and Homeopathy. 1. Historical Background". *Evidence-Based Complementary and Alternative Medicine* 2.4 (2005): 441-452.
29. European Pharmacopoeia. "Homeopathic preparations"; Monograph 1038.
30. Bellavite P., et al. "High-dilution effects revisited. 1. Physicochemical aspects". *Homeopathy* 103.1 (2014): 4-21.
31. European Pharmacopoeia. "Homeopathic preparations"; Monograph 2153.
32. Bellavite P., et al. "Advances in homeopathy and immunology: a review of clinical research". *Frontiers in Bioscience* 3 (2011): 1363-1389.
33. Ghosh S., et al. "An open label pilot study testing the role of classical homeopathy in chronic allergic rhinitis". *International Journal of Pharmaceutical Sciences and Research* 4 (2013): 1475-1484.
34. Witt CM., et al. "How healthy are chronically ill patients after eight years of homeopathic treatment? Results from along term observational study". *BMC Public Health* 8 (2008): 413.
35. Beghi GM and Morselli-Labate AM. "Does homeopathic medicine have a preventive effect on respiratory tract infections? A real life observational study". *Multidisciplinary Respiratory Medicine* 11 (2016): 12.

36. Demarque D, *et al.* "Farmacologia e materia medica omeopatica". *Milano: Tecniche nuove* (2005): 270-272.
37. Abdel-Hadi OB, *et al.* "Case reports of the use of Medorrhinum in three patients suffering from exfoliative dermatitis and one patient with porphyria". *British Homoeopathic Journal* 69.2 (1980): 105-107.
38. Mercaldo M. "How to prescribe Medorrhinum: the frequency of symptoms and signs in homeopathic patients". *British Homoeopathic Journal* 88.2 (1999): 69-77.
39. Erickson K, *et al.* "Case Study in Integrative Medicine: Jared C, A Child with Recurrent Otitis Media and Upper Respiratory Illness". *Explore (NY)* 2.3 (2006): 235-237.
40. Mukherjee A, *et al.* "Ethanol extract of Thuja occidentalis blocks proliferation of A549 cells and induces apoptosis *in vitro*". *Zhong Xi Yi Jie He Xue Bao* 10.12 (2012): 1451-1459.
41. Mukherjee A, *et al.* "Homeopathic Thuja 30C ameliorates benzo(a)pyrene-induced DNA damage, stress and viability of perfused lung cells of mice *in vitro*". *Journal of Integrative Medicine* 11.6 (2013): 397-404.
42. Naser B, *et al.* "Thuja occidentalis (Arbor vitae): a review of its pharmaceutical, pharmacological and clinical properties". *Evidence-Based Complementary and Alternative Medicine* 2.1 (2005): 69-78.
43. Oliveira JF, *et al.* "Effect of Thuya occidentalis on the labeling of red blood cells and plasma proteins with technetium-99m". *Yale Journal of Biology and Medicine* 69.6 (1996): 489-494.
44. Torres A, *et al.* "Pro-apoptotic and anti-angiogenic properties of the a/b-thujone fraction from Thuja occidentalis on glioblastoma cells". *Journal of Neuro-Oncology* (2016).
45. De Araújo Prado Neto J, *et al.* "Action of Causticum in inflammatory models". *Homeopathy* 93.1 (2004): 12-16.
46. Cavalcanti AM, *et al.* "Effects of homeopathic treatment on pruritus of haemodialysis patients: a randomised placebo-controlled double-blind trial". *Homeopathy* 92.4 (2003): 177-181.
47. Eizayaga JE and Eizayaga JI. "Prospective observational study of 42 patients with atopic dermatitis treated with homeopathic medicines". *Homeopathy* 101.1 (2012): 21-27.
48. Daoudi A, *et al.* "Screening of immunomodulatory activity of total and protein extracts of some Moroccan medicinal plants". *Toxicology & Industrial Health* 29.3 (2013): 245-253.
49. Aragona P, *et al.* "Use of homeopathic eye drops for the treatment of ocular surface irritation". *Euvision* (2011).
50. Paduch R, *et al.* "Assessment of eyebright (euphrasia officinalis L.) extract activity in relation to human corneal cells using *in vitro* tests". *Balkan Medical Journal* 31.1 (2014): 29-36.
51. Srivastava JK, *et al.* "Chamomile: A herbal medicine of the past with bright future". *Molecular Medicine Reports* 3.6 (2010): 895-901.
52. Lee KJ and Yeo MG. "Homeopathic Rhus toxicodendron has dual effects on the inflammatory response in the mouse preosteoblastic cell line MC3T3-e1". *Homeopathy* 105.1 (2016): 42-7.
53. Dos Santos AL, *et al.* "In vivo study of the anti-inflammatory effect of Rhus toxicodendron". *Homeopathy* 96.2 (2007): 95-101.
54. Tanenbaum M and McCord Jr CD. "Lacrimal drainage system". In: Tasman W, Jaeger EA, eds. *Duane's Ophthalmology*. 2013 ed. Philadelphia, PA: Lippincott Williams & Wilkins 4.13 (2013).

55. Saha S., *et al.* "Calcarea carbonica induces apoptosis in cancer cells in p53-dependent manner via an immuno-modulatory circuit". *BMC Complementary and Alternative Medicine* 13 (2013): 230.
56. Graf H., *et al.* "Reaction of the anterior eye segment to preventive Credé treatment". *Zentralbl Gynakol* 116.11 (1994): 639-42.
57. Dalla Libera D., *et al.* "Complementary and alternative medicine (CAM) use in an Italian cohort of pediatric headache patients: the tip of the iceberg". *Neurological Sciences* 35 Suppl 1 (2014): 145-148.

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