

# Haemangioma Successfully Treated in a Bitch with *Mercurius solubilis*: A Case Report

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## Abstract

Conventional medical therapy for haemangioma usually consists of corticosteroids through oral administration, intralesional injection or topical application. This benign vascular tumour is not always so complicated to have to be removed surgically and many others remit without treatment. However, sometimes the unexpected can happen and evolve unfavourably. For these situations, homeopathy can also be evaluated. Here is a case report of an elderly bitch that developed a haemangioma on the pad of the left fifth toe. Complete remission of the vascular tumour and improvement of behavioural and physical complaints was achieved with a high dilution of *Mercurius solubilis*. The homeopathic remedy *Phosphorus*, a phytotherapeutic ointment of *Calendula officinalis*, and the application of topical antibiotics did not have the efficacy of the previous one. Although homeopathy does not yet have a specific mechanism of action for each remedy, the pathogenesis of *M. solubilis* is compatible with a negative regulation of glutamine synthetase. Given that it has been shown that ultra-dilutions can stimulate gene expression, it is theoretically hypothesised here that *Mercurius* could stimulate glutamate-ammonia ligase gene, which expresses the aforementioned enzyme, and solve or improve diseases whose symptoms are due to their underexpression or inhibition (at gene and protein level). Hence, the aim of this article is to show the results of homeopathy in the clinical practice and to propose a line of research on the mechanism of action of the remedies.

## Keywords

- haemangioma
- infected wound
- suppuration
- *Mercurius solubilis*
- GLUL gene
- glutamine synthetase

## Introduction

Haemangioma is a vascular benign tumour that can develop anywhere in the body. When it is cutaneous, therapy is necessary when it causes discomfort. Other times it remits without treatment.<sup>1</sup> Children suffer from more complications and for this reason various drugs have been evaluated to solve haemangiomas. Corticosteroids are well known among them,<sup>2</sup> although their adverse effects sometimes suggest a replacement with better alternatives like propranolol.<sup>3</sup> In veterinary medicine, these tumours have a similar pathophysiology and treatment.<sup>4</sup> In any case, surgery is considered if the patient does not respond to conservative

therapy, the tumour enlarges causing discomfort, it has a visceral location or exists risk of laceration and infection.<sup>5</sup> On the other hand, homeopathy is also an option present in the scientific literature, with numerous remedies for addressing haemangiomas.<sup>6</sup>

## Patient Information

A 12-year-old half-blood bitch had a haemangioma on the pad of the left fifth toe. The injury was discovered during hairdressing in a veterinary clinic. The location made movement difficult and caused a limp. A treatment with corticosteroid ointment did not work well. The pet's owner

testified that the tumour grew rapidly after its application, taking the shape of a pepper. This fact could also be promoted by the continuous trauma of the footfall when walking. The bitch's reaction was to bite the tumour and tear off a piece, developing an oozing infection and worsening the lameness.

## Clinical Findings

The inability to plant the foot on the ground due to pain was evident in the consultation room. After removing a home-made bandage, the affected finger was seen to be wet and had the smell of infection (►Fig. 1). The inspection of the sole of the foot revealed the remaining haemangioma after self-injury (►Fig. 2).

Furthermore, the old bitch used to complain a lot and tolerate little physical contact in any part of the body, but without immediate aggression. It was rather anxiety, impatience and psychophysical hypersensitivity. The owner added that her pet also drank a lot of water, woke up frequently at night, had mild urinary incontinence and tended to cough. The physical examination showed normal cardiorespiratory sounds through auscultation, but evidenced a reaction to pain under pressure on lumbosacral region and the hips (signs of osteoarthritis in old age<sup>7</sup>).

## Diagnosis

A haemangioma is an accumulation of extra blood vessels due to the benign proliferation of vascular cells.<sup>8</sup> As discussed above, there is a tendency to suggest observation of its

evolution before medical treatment because this type of injury seems to recede on its own. In cases where it causes functional or aesthetic discomfort, tissue growth inhibitors are administered, or the mass is surgically removed if appropriate.

From a homeopathic point of view, diagnosis is based on the Law of Similars, which consists in relating the clinical picture of the patient with the pathogenesis of a medicine experimented in toxicological trials, but considering the mental and physical symptoms as a whole.<sup>9</sup> Then, the ultra-diluted remedy can be used to heal diseases with analogue characteristics. Thus, diagnosis has the name of the prescribed medicine.<sup>10</sup>

The holistic approach of homeopathy gives priority to the individual disease as a mirror image of the total harmful effects of a drug before it becomes a remedy (healing high dilution). There is a symptomatic hierarchy, which puts mental and general symptoms before local ones.<sup>11</sup> This is important because a patient can respond to a constitutional medicine, which is the one that fits with his/her psychophysical features and tendency to get sick.<sup>12</sup> In words of Dr James Tyler Kent, if mental and general symptoms of a drug are present, its high dilution should work well on an injury in a part of the body even though the lesion is not literally mentioned in the pathogenesis.<sup>13</sup> The present case report is in line with this statement. However, specific lesions such as haemangioma are listed in repertory books to facilitate the choice of the most similar to the clinical case (►Table 1).

*Phosphorus* was the diagnosis initially. This medicine had previously good results in relieving joint pain in the bitch. It is present in the list in ►Table 1 and works well on ageing discomfort. Despite the general improvement in symptoms



**Fig. 1** Appearance of the left foot due to suppuration of the vascular tumour after the self-induced bite by the bitch.



**Fig. 2** Remaining haemangioma on the pad of the left fifth toe. The picture was taken after cleaning the wound.

**Table 1** Homeopathic remedies of many uses (polychrests) indicated for vascular injuries such as haemangioma<sup>6</sup>

| Some polychrests for haemangioma according to Kent's Repertory                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                              |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>- <i>Apis mellifica</i></li> <li>- <i>Arnica montana</i></li> <li>- <i>Arsenicum album</i></li> <li>- <i>Bryonia alba</i></li> <li>- <i>Calcarea carbonica</i></li> <li>- <i>Calcarea fluorica</i></li> <li>- <i>Carcinosin</i></li> <li>- <i>Causticum</i></li> <li>- <i>Graphites</i></li> <li>- <i>Hepar sulphur</i></li> <li>- <i>Lachesis mutus</i></li> </ul> | <ul style="list-style-type: none"> <li>- <i>Lycopodium clavatum</i></li> <li>- <i>Natrum sulphuricum</i></li> <li>- <i>Nitricum acidum</i></li> <li>- <i>Nux vomica</i></li> <li>- <i>Phosphorus</i></li> <li>- <i>Plumbum metallicum</i></li> <li>- <i>Pulsatilla nigricans</i></li> <li>- <i>Secale cornutum</i></li> <li>- <i>Silicea terra</i></li> <li>- <i>Sulphur</i></li> <li>- <i>Thuja occidentalis</i></li> </ul> |

and infection, a second diagnosis and prescription were made. The repertorisation showed that *Mercurius solubilis* fits with the clinical picture due to the following set of symptoms:

- Signs of senile dementia in the form of hypersensitivity, anxiety, night restlessness, urinary incontinence and tendency to cry
- Self-mutilation of the haemangioma
- Excessive thirst
- Cough
- Bone pain

Considering that the pathogenesis of *Mercurius* does not tell anything about vascular tumours,<sup>14</sup> it is candidate to be the constitutional remedy. This is the one that restores homeostasis and boosts the general well-being of the bitch.<sup>15</sup>

## Treatment

**First attempt:** *Phosphorus* 200 CH, one granule diluted in 2 mL of water orally once a day for 10 days. Daily wound healing with *Calendula officinalis* ointment + bandage. After that period of time, the treatment was no longer effective.

**Second and definitive attempt:** *Mercurius solubilis* 30 CH, one granule diluted in 2 mL of water twice a day till the total remission of the infected haemangioma. Daily wound healing with *C. officinalis* ointment + bandage.

The decision of adding *Calendula* for topical application was due to its indication for painfully oozing wounds.<sup>16</sup> It is important to know that the owner decided on her own to use different ointments to cure, since she did not always have the one with *C. officinalis*. For this reason, she applied some with antibiotics. These conventional products did not show a significant improvement respecting the rest of the treatment, as they were used from the beginning. *Calendula* by itself did not work better maybe because it was used together with *Phosphorus*, so *Mercurius* made the difference. The potency of 30 CH of this last medicine was chosen because in my daily practice it shows the best results in animals together with 200 CH. The former's ultra-dilution is more appropriate to start the treatment in elderly pets than the latter's due to its lower intensity with a view to possible symptomatic exacerbations. In short, it gives more security.

## Follow-Up and Outcomes

After administering *Mercurius*, the bitch's complaints were significantly reduced. The animal seemed to live a second



**Fig. 3** Aspect of the lesion 9 days after the beginning of the treatment with *Mercurius solubilis* 30 CH.

youth, having more energy. The tumour and infection improved day by day.

Day 9: remarkable reduction in the size of the lesion. After a little over a week, it measured a quarter of a part. The smell of infection was fading (► **Fig. 3**).

Day 34: the injury was healed completely. The owner did not come before because she was travelling (► **Fig. 4**).

#### **Possible Mechanism of Action of *Mercurius solubilis***

Since its inception, homeopathy has been conceived as a therapy with the ability to stimulate the body to resolve the symptoms of disease.<sup>17</sup> For this goal, high dilutions should work through protein expression because body functions depend on them.<sup>18</sup> In absence of enough molecules below C12 and without Avogadro's number above the same



**Fig. 4** Aspect of the lesion 34 days after the beginning of the treatment with *Mercurius solubilis* 30 CH. Only the scar remains.

potency,<sup>19</sup> a biological effect over cells seems difficult to explain. However, homeopathic remedies have nanoparticles<sup>20</sup> and demonstrate that they can produce gene expression.<sup>21,22</sup> On the other hand, experiments not related to homeopathy show that nanoparticles provoke gene expression,<sup>23,24</sup> which leads to protein activity. Taking all together, the stimulatory action of high dilutions to improve health should involve gene and protein expressions. Some publications oppose this possibility,<sup>25,26</sup> but they cannot give answers to the results in clinical practice<sup>27</sup> and cell cultures.<sup>28</sup> Furthermore, the referenced refusal experiments do not consider the idiosyncrasy in the way to get sick, nor use all the remedies for a specific disease when they try to evidence the effect of high dilutions on sick cells (cancer in citations). Maybe the clue of the controversies is in a specific gene that could explain the pathological condition of a patient. This key gene could be the first to be inhibited or underexpressed to limit its protein expression, allowing the development of a pathophysiology analogue to the pathogenesis of a homeopathic remedy. Thus, a disease can be understood as a functional disability and each high-diluted medicine may stimulate its key gene to improve protein expression. Other genes and proteins would be regulated through biochemical cascade to restore homeostasis. Given that the pathogenesis of homeopathic remedies assembles symptoms recorded in humans<sup>29</sup> and the medicines work on animals,<sup>30</sup> key genes for each one must be common in all species. This theoretical mechanism of action needs further investigation and experimental evidence, but the reader should know that application of this hypothesis in veterinary practice enhances diagnostic accuracy and therapeutic efficacy.

*Mercurius solubilis* has a pathogenesis characterised by destructiveness. The behaviour is aggressive and even violent, with possible attempts to kill and commit suicide. Self-harm is another form of overt destruction, as is the tendency for tissue ulceration on the physical plane. Furthermore, the symptoms have common features with neurodegenerative processes (Alzheimer's, Parkinson's, senile dementia and so on) and infectious diseases (mainly venereal, such as syphilis or chlamydia).<sup>14</sup> All this makes *Mercurius* an important medicine for serious illnesses that can lead to death. Thus, its mechanism of action should be related to a body function whose deficiency or inhibition can explain the loss of integrity of the patient at all levels (emotional, mental, physical). However, mild symptoms can also develop since the severity of the clinical picture could be directly proportional to the severity of the functional blockade.

Glutamate-ammonia ligase (GLUL) could be the key gene underexpressed to explain the pathogenesis of *M. solubilis*. This gene has a high RNA expression in the skeletal muscle, brain and adipose tissue, encoding the enzyme glutamine synthetase.<sup>31</sup> This one binds glutamate and ammonia to form glutamine,<sup>32</sup> which is the most abundant amino acid in the body and acts as a nitrogen carrier.<sup>33</sup> The function of glutamine synthetase is crucial to control glutamate signalling as an excitatory neurotransmitter<sup>34</sup> and to remove in astrocytes the excess of ammonia produced by neurons.<sup>35</sup> If these processes are not performed, glutamate and ammonia exert

excitotoxicity that can lead to neurodegeneration.<sup>36,37</sup> In addition, glutamate constitutes the glutamatergic pathway together with acetylcholine,<sup>38</sup> so co-expression of both excitatory neurotransmitters leads to anxiety and restlessness as mental symptoms. In the same line, other potentiated cholinergic responses, which figure as general symptoms in *Mercurius*, are perspiration,<sup>39</sup> thirst<sup>40</sup> and tremors.<sup>41</sup> Interestingly, the mercurial patient tends to have the mouth wet.<sup>14</sup> According to Inenaga and Ono,<sup>40</sup> thirst and salivation are compatible conditions. Precisely, the secretion of the salivary glands depends on muscarinic acetylcholine receptors.<sup>42</sup> On the other hand, glutamate catabolism leads to the production of pyrroline-5-carboxylate and subsequently ornithine and polyamines (putrescine, spermidine, spermine) in the so-called arginine metabolism.<sup>43</sup> The latter along with ammonia can explain the unpleasant smell of the patient's body. Both glutamate excess and glutamine synthetase disability cause circadian rhythm disorders,<sup>44,45</sup> explaining why the patient in need of *Mercurius* worsens at night.

Tendency to tissue ulceration and suppuration is linkable to the importance of glutamine for body integrity and the immune system. Although glutamine is not an essential amino acid, it seems to be it during pathological conditions such as sepsis, trauma or burns.<sup>46</sup> Its consumption will alleviate tissue destruction, but it is important to know that too much exogenous glutamine during the above clinical situations inhibits glutamine synthetase (so homeostasis will not be restored).<sup>47</sup> The amino acid is basic for cells as a fuel, especially enterocytes, neutrophils, macrophages and lymphocytes. Epithelial cells also depend on this nutrient for their structural integrity.<sup>48</sup> *Mercurius solubilis* covers inflammatory ulcerative processes in the proximal digestive tube (oral cavity, tongue, pharynx, salivary glands), genitals and skin, along with adenopathies and bone disorders (pain, infection, fragility). There seems to be a correlation between these highlighted tissues in the pathogenesis of the remedy and the expression of glutamine synthetase and transglutaminases<sup>31</sup> (both connected through glutamate metabolism, even in the brain<sup>49</sup>). These latter enzymes bind amino acids to form structural proteins, glutamine being indispensable to make possible this glue function for the stability of mucous membranes.<sup>50</sup>

Regarding haemangioma, glutamate promotes angiogenesis through its receptors (GRM1, NMDA).<sup>51,52</sup> For its part, glutamine synthetase participates in endothelial cells migration during neovascularisation.<sup>53</sup> Therefore, the balance between glutamate and glutamine metabolism is necessary for a proper distribution of the vasculature. In the case of *M. solubilis*, it is proposed here that the hypothetic stimulation of GLUL (gene)/glutamine synthetase (protein) stops the proliferative activity of glutamate and ameliorates cicatrisation. This is in line with the production of interleukin 4 (IL-4) by mice-activated macrophages when they are exposed to *Mercurius* high dilutions.<sup>54</sup> Something similar has been seen in a case report of human leprosy treated with this homeopathic remedy.<sup>55</sup> IL-4 also derives from lymphocytes T helper 2 cells for macrophage differentiation into morphotype 2 cells, which are involved in anti-inflammation and tissue repair. This process needs glutamine and glutamine synthetase activity.<sup>56</sup>

## Discussion

This case report shows the healing process of a haemangioma with a homeopathic high dilution of *M. solubilis*. Other drugs combined throughout the treatment, such as *Phosphorus*, *C. officinalis* or antibiotic ointments, were not effective regardless of the time of inclusion. A possible mechanism of action has been proposed to explain how *Mercurius* could work to solve clinical pictures similar to its pathogenesis. Glutamine could be involved in the imbalance, with a suggested limited bioavailability related to low glutamine synthetase activity. This would affect transglutaminases and lead to a pathophysiology where ammonia, glutamate and acetylcholine would be upregulated. Considering that glutaminase catalyses the opposite reaction of glutamine synthetase, increasing the pool of glutamate, maybe this enzyme is also overexpressed. This is in line with the role of glutamine in the development of chlamydia,<sup>57</sup> a venereal disease similar to mercurial injuries. In this sense, the reader should know that the image of *Mercurius* as the faithful representation of Syphilis (Hahnemann's chronic disease) gave way to the term Luesis to cover more pathological conditions characterised by destructiveness (states of depression with self-injury and risk of suicide, neurodegenerative processes, drug addiction, sexual illnesses with ulcerative lesions and so on).<sup>12</sup>

Furthermore, glutamine and its synthetase enzyme are essential for a proper immune response.<sup>58</sup> This could justify why *Mercurius* modulates reactive oxygen species like superoxide and hydrogen peroxide, reactive nitrogen species such as nitric oxide, and the cytokines interferon gamma and IL-4 in the experiment with mice macrophages.<sup>54</sup> The patient in need of *Mercurius* seems to be sensitive to everything and susceptible to all kind of pathogens,<sup>59</sup> so the stimulation of glutamine synthetase will boost the immune system. However, the enzyme does not only have a role in liberation of glutamine, but also it is involved in angiogenesis apart from the production of the amino acid.<sup>53</sup>

Two main handicaps can be pointed out for a hypothetical mechanism of action involving GLUL gene expression: (1) glutamine synthetase deficiency is considered a rare genetic disease<sup>60</sup> (although changes in glutamine synthetase activity in relation to *Mercurius*-linked neurological disorders have been described according to Ref.<sup>32</sup>), and (2) the effect of a homeopathic remedy seems to be different according to its potency or dilution<sup>61</sup> (also seen in Ref.<sup>54</sup>). However, the involvement of glutamine and glutamine synthetase in illnesses with destructive features such as neurodegenerative processes and venereal diseases, which are mentioned or described with similar symptoms in the pathogenesis of *M. solubilis*, invites to propose a line of research that clarifies the specific gene that could stimulate the aforementioned homeopathic remedy to explain its mechanism of action.

## Conclusion

Homeopathic remedies are options for treatment of haemangioma and many other diseases. Their biological effects go beyond placebo and could be positive or negative depend-

ing on the force of the drugs and the sensitivity of the patient. Getting better or worse could occur through the same gene and protein expression when the stimulation is appropriate or excessive, respectively. Here, it is theoretically proposed that *M. solubilis* could cause the expression of GLUL gene to improve glutamine synthetase activity. Further investigation is necessary to clarify this issue.

### Note

A.M.M. is the collaborator of the Andalusian Association of Homeopath Physicians (Asociación de Médicos Homeópatas de Andalucía, AMHA).

### Conflict of Interest

The author has no conflict of interest.

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