



## MYIASIS – PATHOLOGY OR TREATMENT?

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**Abstract:** Myiasis is the infestation of live vertebrates with arthropod larvae of the order Diptera. The increase in the number of tourists in endemic areas, with the appearance of new cases in risk-free geographical areas, has increased the interest of doctors in knowing the insects that cause myiasis. The most common cases of myiasis are found in tropical and subtropical areas, the temperate zone being of interest in the warm season. In dermatological practice, there are cases of skin myiasis, especially at the level of skin ulcers. The appearance of ulcers myiasis is favoured by the poor socio-economic status, poor hygiene conditions or associated debilitating general pathologies. Performing a correct treatment of ulcers is the main factor in preventing the larval infestation of ulcers.

### INTRODUCTION

Myiasis, a term derived from Greek (mya = to fly), represents the infestation of live vertebrates with arthropod larvae of the order Diptera. This term was proposed by Hope in 1840 and highlights the difference from larval infestation by other insects.(1)

The order Diptera has about 150,000 species of insects, distributed on all continents. These, with a few exceptions (Mycetophilidae, Tipulidae, Phoridae and Hippoboscidae), have wings and are active fliers. In the larval stage, they do not have real legs, but they do have a locomotor system, which differs depending on the species, having the appearance of worms.(2)

The order Diptera is divided into 2 suborders: Nematocera (includes most families of blood-eating insects - it infects the host with viruses, protozoa, helminths) and Brachycera (includes the infraorder Muscomorpha which contains all the species that cause myiasis).

Ulcers myiasis is the infestation of ulcers of various etiologies with larvae of the order Diptera. The most common species of flies that oviposit ulcers are: *Cochliomyia hominivorax*, *Chrysomya bezziana* and *Wohlfahrtia magnifica*.

Zumpt made an anatomical classification of the myiasis, namely:

- sanguinivorous,
- cutaneous - which may be furuncular or migratory,
- myiasis of ulcerations,
- cavitory myiasis (cerebral, sinonasal, otic, ophthalmic, etc.).(3)
- From an ecological point of view, in myiasis, parasites can be:
  - Specific/ obligate parasite - depends on the host to survive,
  - Semispecific/ facultative parasite: primary, secondary, tertiary - can affect the host when it is or is not infested by other parasites or when it is with a general condition affected,

- Accidental parasite (pseudomyiasis) - can affect the host by accidental contact (can infest the host by ingestion, migration into the urethra, rectum, vagina, etc.).(3)

Obligate parasites destroy the healthy infested tissues, invade deep tissues, superinfect the host. Facultative parasites do not destroy healthy tissues, clean the necrotic tissue, produce antibacterial substances and stimulate granulation.

The upward trend in the number of tourists in areas with epidemic risk has increased the global interest in knowing the insects that cause myiasis, this being classified as the 5<sup>th</sup> dermatological disease among tourists.

The triggers for the appearance of myiasis in ulcers are:

- poor socio-economic condition,
- unsatisfactory hygiene,
- old age,
- associated pathologies (psychiatric, alcoholism, diabetes),
- physical disabilities that restrict care,
- certain climatic conditions (heat, humidity), natural disasters,
- rural environment (contact with domestic animals).

Favourable conditions for larval development are related to excess heat and humidity, thus, larval infestation has an increased incidence in tropical and subtropical areas, in temperate areas with a seasonal variation.(3,4) A very important role is played by veterinarians in the recognition and treatment of myiasis in domestic or pet animals, as they are a possible source of larvae that can be transmitted to humans.(5)

Performing a correct treatment of ulcers with antiseptic solutions, sterile dressings changed periodically allows the prevention of larval infestation. The treatment of ulcerative myiasis consists of irrigation to eliminate larvae, debridement, local application of disinfectants and antibiotic treatments in case of bacterial superinfection. Despite a favourable prognosis, the mental impact on the patient and even on the medical staff is extremely important.(3)

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### CASE REPORTS

We present two clinical cases that were diagnosed and treated in the Dermatovenerology Ward of the Clinical County Emergency Hospital of Sibiu in the summer of 2019. Elderly patients, aged 70 years and 74 years, respectively, known with florid venous ulcers, presented to the emergency department, afterwards, being referred to our clinic for the presence of larvae at the level of chronic ulcerations.

The risk factors identified in our patients were:

- old age,
- the precarious social condition with the lack of domicile and of the persons to take care of them,
- inadequate hygiene and improper care of ulcers,
- physical disability,
- addiction to tobacco and alcohol,
- favourable climatic conditions (summer) for larval infestation.

At admission, the patients had multiple live yellow, spindle-shaped larvae, which came out and entered the ulcer bed (figures no. 1,2).

As a general pathology, patients presented with venous pathology (chronic venous insufficiency stage CEAP 6, (obliterating arteriopathy of the lower limbs), respiratory pathology (chronic obstructive pulmonary disease), cardiac pathology (permanent atrial fibrillation with medium AV, dilated cardiomyopathy with moderate/ severe systolic dysfunction, chronic NYHA IV, grade II mitral regurgitation) and insulin-dependent type II diabetes.

**Figure no. 1. Myiasis of venous ulcers in the first case**



**Figure no. 2. Myiasis of venous ulcers in the second case**



The treatment consisted in the mechanical removal of the larvae, compressed with antiseptic solutions (3% borax solution). After 2 days the destruction of the larvae was obtained then the daily dressing of the ulcerations with epithelializing ointments was performed.

### DISCUSSIONS

Some dermatological conditions can be associated with myiasis according to data from the literature, namely: ulcers (venous, neuropathic, arterial, lymphatic etc.), psoriasis, seborrheic keratosis, onychomycosis, B-cell skin lymphoma, basal cell carcinoma, Shingles, pediculosis, genital warts, impetigo etc.(3)

In dermatological practice, the most common forms of myiasis are the furuncular and cutaneous migratory ones.

In the furuncular myiasis, *Dermatobia hominis* and *Cordylobia anthropaga* (present in tropical America) cause skin-like lesions, most commonly, furuncular-like. Other clinical variants of this form are: vesicular, bullous, pustular, erosive, ecchymotic or ulcerative form. Upon contact of the larva with the intact skin of the exposed areas, it penetrates it and forms an erythematous-edematous lesion, hardened, 1-2 cm in diameter, with a central microulceration, covered with crusts with purulent or bloody appearance, intensely itchy and painful (especially at night). In association, it may have local lymphadenopathy, fever, altered general condition, insomnia, sensation of movement at the site of contact. Without intervention, the larva will come to the surface in a few days to a few weeks to turn into a pupae or an abscess will form, causing its death.

The differential diagnosis of furuncular myiasis includes insect bites, prurigo lesions, inflamed cysts, pyodermitis, cellulite. The anamnesis and the clinical examination are in the vast majority of cases sufficient to establish a positive diagnosis. In atypical cases, dermatoscopy or ultrasonography are useful tools in diagnosing furuncular myiasis.(6)

Dermatoscopically, the presence of *D. hominis* larva is described as a yellowish structure with black barb-like spines cantered by a microulceration and surrounded by small dilated blood vessels.(3)

Ultrasonography is useful in atypical cases for diagnosing furuncular myiasis and for complete extraction of the larva. The furuncular myiasis with *D. hominis* is described as a well-defined echogenic zone, surrounded by a hypoechoic zone, with segmentations in the longitudinal sections and posterior acoustic shadow.(3)

From a therapeutic point of view, furunculoid myiasis can benefit from surgical treatments - extraction of the larva with tweezers, application of dressings or occlusive substances (vaseline, plaster) that asphyxiate or cause the larvae to migrate to the surface, then their manual extraction. If the occlusion treatment is chosen, it must be maintained for at least 24 hours. In this situation, there is a risk that the larva instead of coming to the surface, will suffocate subcutaneously and cause a local inflammatory response. Local injection of lidocaine 1%, and application of ivermectin 1% are other therapeutic variants that immobilize the larvae and allow their extraction. Surgical treatment is rarely chosen, but in some cases it is required for extraction or perilesional debridement. After sterilization of ulcers from larvae, the therapeutic approach is similar to that applied to any ulcer. With proper treatment, the lesions heal without complications, but sometimes residual hyperpigmentation or scars may persist.

Cutaneous migratory myiasis are not caused by fly larvae, but by worm larvae of animals. For example, infestation of ulcers with larvae of the species *Gasterophilus* (horseflies) or *Hypoderma* (cattle flies) is clinically similar to cutaneous

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migratory myiasis, causing serpiginous rash, with indication for surgical treatment. In humans, this occurs accidentally, the larvae not being able to end their life cycle.(6)

The myiasis of ulcers represents their infestation by flies (obligate or facultative parasites). *Cochliomyia hominivorax*, *Chrysomya bezziana* and *Wohlfahrtia magnifica* are the most common species of flies that colonize ulcers. Other common agents are: *Diptera hominis*, *Musca domestica*, *Chrysomya megacephala*, *Calliphora vicina*, *Lucilia sericata*, *Chrysomya albiceps*, *Phormia regina*, *Parasarcophaga argyrostoma*, *Lucilia cuprina*, *Sarcodexia lambens*.

In America, *Lucilia sericata* (green fly) and *Phormia regina* (black fly) of the *Calliphoridae* family are the most common sources of ulcers myiasis. *Lucilia sericata*, a species of the genus *Lucilia* (green-metallic colour) lives in many temperate areas, including Europe, North America, where it is an important source of ulcerative myiasis. *Lucilia* females infest humans, sheep, horses and cattle.(1)

In general, members of the *Muscidae* family do not have an increased prevalence in myiasis, but are involved as secondary parasites. Cases of myiasis caused by the *Musca domestica* (common fly) are reported, but frequently, they are involved as vectors for various pathogens.(1)

The etiology of ulcers involved in myiasis is diverse: venous ulcers, post-traumatic, diabetic ulcers, eschars, persistent surgical ulcers etc.(6) A microulceration caused by an insect bite can promote the attraction of flies, as well.(3) The alkaline pH of the secretions (7.1-7.5) at the level of ulcers forms a favourable environment for attracting flies, thus, the fly ovoposites the ulcerations. Adult flies of *Cochliomyia hominivorax* or *Phaenicia sericata* lay eggs in ulcers. They develop and become pink, spindle-shaped and segmented larvae.(7) Locally, *Cochliomyia hominivorax*, *Chrysomya bezziana* destroy the healthy tissues, feeding with them, forming caverns, necrotic tissue, perilesional swelling with superinfection and the formation of fetid purulent secretions. The patient has significant local pain, itching, sensation of movement, but may also have fever, chills, fatigue. In some cases, the pain is absent because the sensitive nerve endings are destroyed during the invasion.(8)

Most fly species involved in myiasis cause superficial ulcer infestations, but *Cochliomyia hominivorax* (blue-green fly, commonly found in Central and South America, with pink larvae that can reach 2 cm in length) and *Chrysomya bezziana* (blue-green fly), 18-22 mm in length, with 2 lines on the thorax, found in Africa, regions of Asia, including Indonesia and the Philippines, New Guinea) infest the deep tissues, mucous membranes, cavitary organs, with a more important pathological involvement.(9) *Wohlfahrtia magnifica* is responsible for the myiasis caused by several flies, causing significant local destruction. Most cases of infestations are recorded in summer because it is the favourable season for the life cycle of flies.

The identification of the species is useful in knowing the pathogenesis, respectively of the invasiveness.(10) The clinician, with the help of the anamnesis, finds information regarding the area in which the patient travelled, thus, being able to document the insects that colonize that geographical area. The identification of the species requires knowledge of morphology, being often impossible to perform in the hospital, being very rarely documented. The diagnosis is established by clinical examination – macroscopically, the stage of the larva can be determined depending on the shape, colour, size; paraclinical - neutrophilia with or without eosinophilia can be observed, and imaging and biopsy are very rarely indicated.

Prevention of ulcers infestation with larvae requires the correct treatment of ulcers with antiseptic solutions, sterile dressings changed periodically, proper hygiene of food, housing

(use of insect nets), clothing and footwear (drying in sunlight, ironing them), periodic inspection of pets.

Myiasis treatment consists of surgical debridement of necrosis, irrigation to remove larvae, especially if tunnels and cavities have been formed, local application of antiseptic solutions, daily change of dressings, antibiotic treatment in case of bacterial superinfection.

In the case of extraction, it is mandatory to remove the remains of larvae and eggs because they are highly allergenic and have a risk of superinfection and eczema.(3) Chloroform 50% in olive oil or other type of oil or a thin layer of petrolatum are therapeutic variants in that they immobilize the larvae and allow an easier extraction. Ivermectin 1% applied locally for 2 hours then cleaned with saline can be a treatment solution. Siddharth Singh et al highlighted the superiority of topical ivermectin over Turpentine oil, with Ivermectin-treated patients recovering faster (4-5 hours after application), having a shorter hospital stay, less pain, reduced use of staff resources because manual extraction was not required.(8)

There is no consensus on the systemic treatment in ulcerative myiasis. Ivermectin 200 µg / kg may be used in case of damage to other organs. It acts on the muscle and nerve cells of invertebrates, causing their apoptosis. Because myiasis can be a gateway for *Clostridium tetani*, tetanus vaccination of affected people is encouraged.(7)

Myiasis is a self-limiting pathology with low mortality and morbidity. The prognosis for this condition is favourable, but the mental impact is extremely high.

In some medical centers, maggot debridement therapy (MDT) are available, ie the application of fly larvae grown in the laboratory in chronic ulcers, with debridement, disinfectant and epithelialization effect. Chronic ulcers are a public health problem with a significant psychological impact, with major treatment costs, with physical disability due to their recurrence, with difficult healing and possible complications (superinfections). Therefore, therapy with laboratory-grown larvae has reappeared as a therapeutic option, having been known since the 16<sup>th</sup> century. MDT is not yet widely used worldwide, but it is a promising therapeutic option because the literature supports its effectiveness and safety in the treatment of ulcers of different etiologies (diabetic, venous, post-traumatic, infectious, vascular, eschars etc.), even if there are no large clinical trials. Myiasis, in a controlled environment, is performed with certain species of safe flies (most commonly, breed LB-01, genus *Phaenicia* (*Lucilia*) *sericata*), grown in special laboratories, sterile and applied under special dressings that do not allow migration. 5-10 larvae / cm<sup>2</sup> of ulceration are applied and are kept under dressing for 2-3 days. Patients may experience discomfort and pain 24 hours after applying the larvae as they grow, but it can be controlled with painkillers.(11) The larvae mechanically debride the necrotic tissue, due to the rough morphology, and biochemically, through the secretion of proteolytic enzymes (trypsin, chymotrypsin-like collagenase, dextroribonuclease, lipase etc.), which have the effect of lysis and ease of digestion by them. Debridement with the help of larvae has the advantage of causing minimal injury to the healthy tissue. Recently, the increase in antibiotic resistance makes the antibacterial effect of larvae on Gram-positive and Gram-negative bacteria (including Methicillin-sensitive or Methicillin-resistant *Staphylococcus aureus*, *Pseudomonas aeruginosa*, etc.) and their antifungal effect increasingly appreciated. Bacteria are destroyed by the digestive tract of larvae by bactericidal substances (eg. ammonia) secreted. Fly larvae have an epithelializing, neovascularizing and tissue-forming role due to gamma-interferon, secreted interleukins, reduced complement (anti-inflammatory effect), stimulating the production of growth factors, especially liver growth factor (HGF).(12,13)

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They play a role in the migration of keratinocytes and fibroblasts that promote ulcer healing. The substances secreted by the larvae stimulate the production of vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF), which stimulate endothelial cell migration and local proliferation.(14) Larval debridement therapy is a promising therapeutic option for persistent ulcers due to their low cost, efficacy and safety.

### CONCLUSIONS

- Myiasis is a pathology with a favourable prognosis, but with an important emotional impact for patients and medical staff.
- In the temperate zone, summer is the season in which patients with myiasis address mostly the medical services.
- Poor social conditions, old age, improper care of ulcers are triggering factors that allow the infestation of ulcers with larvae.
- Proper management of ulcers is the key to prevention of myiasis.
- Debridement therapies with larvae raised in the laboratory are therapeutic options applied in specialized centres abroad with promising results.

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