

# Traumatic Myiasis: A Neglected Disease in a Changing World

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#### Abstract

Traumatic myiasis, the parasitic infestation by fly larvae in traumatic lesions of the tissues of living vertebrates, is a serious medical condition in humans and a welfare and economic issue in domestic animals. New molecular studies are providing insights into its evolution and epidemiology. Nevertheless, its incidence in humans is generally underreported, particularly in tropical and subtropical regions. Myiasis in domestic animals has been studied more extensively, but continuous management is difficult and expensive. A key concern is the inadvertent introduction and global spread of agents of myiasis into nonendemic areas, facilitated by climate change and global transport. The incursion of the New World screwworm fly (*Cochliomyia hominivorax*) into Libya is the most notable of many such range shifts and demonstrates the potential risks of these parasites and the costs of removing them once established in a geographic area. Nevertheless, the insect agents of myiasis can be of societal benefit to forensic science and in medicine as an aid to wound treatment (larval therapy).

#### WHAT IS TRAUMATIC MYIASIS?

Although the term myiasis was first proposed by Hope (65) to group animal diseases caused by the larvae of flies, the most clear and frequently used definition is that of Zumpt (164, p. xi): "the infestation of live human and vertebrate animals with dipterous larvae which, at least for a certain period, feed on the host's dead or living tissue, liquid body-substances, or ingested food." The definition thereby excludes the great range of parasitisms of invertebrates made by fly larvae as parasitoids (38).

The term traumatic, or wound, myiasis was first used by James (68) and it is used by us after the definition of Zumpt (164, p. xiii) as "a condition in which dipterous larvae live as obligatory or facultative parasites in traumatic lesions." Zumpt (164, p. xii) expands on this under the heading of dermal/subdermal myiasis, defining traumatic myiasis as when larvae "invade pre-existing wounds and enlarge them, or form wounds after having actively gained access to the tissue." The latter situation is important because although infestations, especially by facultative species, can occur at sites of preexisting wounds, wounding is not a prerequisite for infestation, especially by obligate species (55). Thus, the range of anatomical sites infested can be very broad, but infestations are limited either to the skin surface or to deeper invasions of the body orifices, sinuses, and sites of wounding. Traumatic myiasis can include conditions defined in the anatomical sense as aural, ophthalmic/ocular, rectal, and genital, and Singh & Singh (123) provide a useful compilation of human cases categorized in that way. Traumatic myiasis does not usually include dermal infestations by single larvae in subdermal furuncles. Hence, it excludes myiasis due to Oestridae (bot flies) (25), including the subdermal infestations caused by Dermatobia hominis and Cuterebra species (30) in Central and South America. It also excludes similar forms of furuncular myiasis caused by Calliphoridae of the genus Cordylobia in sub-Saharan Africa (149) and southwestern Saudi Arabia (95). Although all Oestridae are obligate parasites, only three of the species that cause traumatic myiasis of mammals are truly obligate and the majority are facultative ectoparasites. Traumatic myiases cause significant pain and suffering to the affected host and therefore are a major human/animal health and welfare and social/economic problem (Figure 1).

#### TRAUMATIC MYIASIS: A DIVERSE AND NEGLECTED PARASITISM

Extensive studies of the New World screwworm fly (NWSF), *Cochliomyia hominivorax* (Diptera: Calliphoridae), were undertaken in the middle decades of the twentieth century in relation to the use of the sterile insect technique (SIT) to achieve its successful eradication from the United States and Central America (74). Interest was rekindled when NWSF was first detected in Libya in 1988 some 6,700 km beyond the nearest edge of its natural distribution. An eradication program was initiated and lasted three years, with nine months of sterile fly release, at a cost of approximately US\$78 million (42, 78). Studies of Old World screwworm fly (OWSF), *Chrysomya bezziana*, have been less extensive and associated largely with concern about the potential invasion into Australia and its likely impact on the Australian livestock industry (9, 12). Myiasis due to OWSF was a serious medical and veterinary problem in India in the early twentieth century (98) and it remains today the most common form of myiasis there, where it is one of the most widespread clinical problems in veterinary practice (23) and human cases are routinely reported (e.g., 4, 110), the sight, smell, and stigma of which can lead to patients being turned out of their homes (128).

Nevertheless, it is fair to say that traumatic myiasis remains largely a neglected disease, particularly in humans and especially in the tropics and subtropics (92). The incidence of myiasis in humans is probably underreported generally (70), especially in situations where humans are crowded in refugee camps as a result of war or political disorder (17) or natural disasters (79). A





Figure 1

The impact of traumatic myiasis illustrated in cartoon form and in reality. (*Left*) A cartoon from the New Zealand serial *Footrot Flats* illustrating the horror and disgust engendered by traumatic myiasis (*Lucilia* blow fly strike) in even hardened livestock professionals (© Murray Ball). (*Right*) Larvae-infested wound in a sheep's limb in Hungary attracting at least 21 adults of species of *Lucilia* (Calliphoridae) and Muscidae and a single larvipositing female of *Wohlfabrtia magnifica* (Sarcophagidae, *yellow arrow*). Despite the adult composition, 100% of larvae were *W. magnifica* (© The Natural History Museum, London, photograph by Martin Hall).

review of neglected tropical diseases of Oceania reports human myiasis only from New Zealand (73), although it also occurs in Australia (81) and is likely to occur elsewhere in the region, especially in Papua New Guinea, where OWSF occurs naturally (96). Myiasis of humans is often encountered in situations of low economic and educational development, and a report on NWSF cases in Brazil concluded that it was a "neglected zoonosis.... attacking the poorest people and mutilating them in a serious or even permanent way" (10, p. 6). However, in countries with a high standard of health care, myiasis might also be underreported as a result of "cultural, social and medicopolitical reasons" (81, p. 240) or simply because few health care providers consider it worthy of reporting (118). Myiasis is sometimes overlooked in an initial diagnosis and the delay in appropriate treatment can cause unnecessary distress for the patient (114). Estimates of the occurrence of traumatic myiasis in humans are rare, but it was recorded in 5.1% of 450 patients with septic wounds presenting at a hospital in Ain-Shams, Egypt (115). Diaz (31, p. 1) concluded, "Ectoparasitic diseases [including myiasis] are no longer infestations of children and socioeconomically disadvantaged populations in tropical countries; they have re-emerged as unusual, but not uncommon, infectious diseases worldwide." Heukelbach et al. (64) highlight that one problem in tackling these diseases is that reliable data on epidemiology, immunology, and therapy of ectoparasitic infestations, as well as on parasite biology, remain scarce.

Aside from the human health problems, the major economic impact of traumatic myiasis is due to infestation of large domesticated animals, particularly in sheep-rearing areas of the world, such as Australasia and northern and central Europe. Infestation of sheep by *Lucilia cuprina* and *L. sericata* has been studied extensively (152) and may be a significant impediment to livestock husbandry. Myiasis has been estimated to cost the Australian sheep industry on average A\$280 million per year (148). The infestation of small companion animals, such as pet rabbits, may also be an animal welfare issue (27). Such infestations are distressing for the animal and its owner and, if not treated promptly, can lead to extensive tissue destruction necessitating euthanasia.

Traumatic myiasis of wildlife is an understudied issue, yet is probably more widespread than a review of the literature would suggest, owing to predation of infested animals or their shelter-seeking behavior in which they, and in many cases their demise, are not observed (51). The potential impact of the disease on wildlife is suggested by the two- to threefold increase in deer populations following NWSF eradication in southern United States (93). Obanda et al. (94) provided a rare report on the severe effects of traumatic myiasis on free-ranging eland (*Taurotragus oryx*) in Kenya.

Although veterinary agencies may be aware of the potential for spread of these species into new areas, and some countries have detailed preparedness plans (e.g., 9), in those countries where screwworm flies are endemic, treatment of traumatic myiasis is frequently left to the livestock owner to manage. Local veterinary knowledge of the distribution and impact of traumatic myiasis can be slight and a lack of knowledge and a lack of records of infestations can be misleading. For example, it was suspected that OWSF might have been introduced into Morocco in 2001 (53). However, investigations showed that the species responsible for a reported rise in traumatic myiasis was *Wohlfahrtia magnifica* (Diptera: Sarcophagidae), Wohlfahrt's wound myiasis fly, the third of the important obligatory traumatic myiasis agents (OTMAs) (140). This myiasis-causing species still remains a serious pest for the livestock industry, even though the damaging effects of its developing larvae on healthy tissues were first described almost 250 years ago, in 1770 (125). Human aural myiasis due to *W. magnifica* was commonly reported during the last century (100) and can still be a significant problem for children (163). This species was recently described from Sicily, where surveys suggested it had probably been endemic for at least 20 years, despite the lack of any previous records (46).

The initial misidentification of the outbreak in Morocco as OWSF reflects the much reported decline (or inadequacy at least; 141) of morphological taxonomy and of those able to apply it with competence (e.g., 66). Even relatively straightforward identifications of larvae from cases of traumatic myiasis might not be attempted for numerous reasons (e.g., lack of taxonomic expertise, larvae not collected or, if collected, poorly preserved and thus in poor condition), significantly limiting the value of otherwise interesting case reports (e.g., 3, 60, 67, 101). Indeed, Sherman (118) showed that larvae from 17% (23/127) of patients reported to have US-acquired myiasis were either never seen or not identified, and he advised that larvae from myiasis cases should not be "hastily discarded" (118, p. 2012). These problems are compounded when misidentification potentially causes unnecessary alarm over the spread of pest species (e.g., 2, 40, 48, 106: all describe autochthonous OWSF cases in single humans outside the normal geographic distribution of that fly species in the absence of reports of animal cases).

#### TRAUMATIC MYIASIS RESEARCH: MOLECULAR METHODS

Molecular methods are increasingly used in myiasis research in a variety of largely applied contexts. Usage falls under four main topic areas: (a) taxonomy, phylogenetics, and identification; (b) epidemiology and population biology; (c) the development of genetic sexing strains for SIT applications; and (d) elucidation of the molecular basis of insecticide resistance. There is considerable overlap between many of these themes.

## Taxonomy, Phylogenetics, and Identification

Molecular methods in myiasis research (at least in terms of the number of recent publications) are used mostly in forensic entomology. Since the landmark publication by Sperling et al. (129), an ever-increasing stream of publications has documented efforts to identify blow fly specimens

and tissues by the use of single gene markers, predominantly the mitochondrial DNA (mtDNA) CO1 gene (82), as used in barcoding studies (62). As the number and geographic coverage of CO1based studies of myiasis-causing flies have expanded, regional patterns of genetic variation between populations of commonly utilized species of forensic value have become apparent (e.g., 59, 155, 162), a trend reflected in studies employing a range of other genetic markers, e.g., random amplified polymorphic DNA (RAPDs) (132) and 28S rRNA (131, 135), though not in all species/marker systems, e.g., amplified fragment length polymorphisms (AFLPs) (99). A survey of publications in the field suggests that the preoccupation of forensic entomologists with elucidating global intraspecific variation in CO1 sequences does not look set to diminish anytime soon, with papers on flies from previously understudied regions [e.g., China (7) and India (117)] now being published in numbers. With the advent of genome-wide scanning techniques, e.g., restriction site associated DNA sequencing (RAD-Seq), and the imminent arrival of the genome of at least one species of myiasis and forensic importance—L. cuprina—it will be interesting to see how long a classification system based on a maternally inherited, single gene marker continues to be deemed of sufficiently high resolution for biological and legal purposes. Finally, scientists have used molecular methods to analyze insect gut contents in a forensic capacity (e.g., 19) and to survey mammal diversity (e.g., 75).

Molecular methods (using a variety of genetic markers) have elucidated the evolution and taxonomy of myiasis-causing flies (85, 88, 124, 131, 155), including the origins of the parasitic trait (see 88, 131, 134, 137, 138, 155; and references therein). Genetic analyses have been instrumental in clarifying evolutionary relationships within the Calliphoridae and Sarcophagidae and overcoming problems of homoplasy in morphology-based systematic and evolutionary studies (105, 131, 161).

Molecular methods also provide powerful tools that help researchers resolve taxonomic questions that have not been resolved by morphology. For example, the flesh flies *Wohlfahrtia vigil* and *W. opaca* of the New World and *W. meigeni* of the Old World have been synonymized as *W. vigil* because reliable morphological characters that distinguish these species are lacking. However, molecular studies have identified a difference between Nearctic and Palearctic specimens; there are also differences in parasitic habits of the species in the two regions that deserve further study (54). Molecular methods have also proven valuable in unraveling the status of apparently hybrid forms of *L. sericata* and *L. cuprina* (133, 136, 145) from Hawaii and South Africa.

## **Epidemiology and Population Biology**

Genetic methods offer robust tools to track fly populations of medical and veterinary importance and to clarify patterns of contemporary and historical gene flow. The elucidation of such patterns is vital for accurate epidemiological analysis. To date, such approaches have been used mainly to explore gene flow and movement of NWSF populations in South America, ostensibly as a precursor to possible SIT releases (e.g., 44, 45, 87, 143); however, although several studies have been undertaken, it is not yet feasible to undertake a sustained NWSF SIT release outside of North and Central America. Nonetheless, a number of microsatellite panels are available to analyze in detail the gene flow and population structure in NWSF (e.g., 49, 143, 144), and mitochondrial single nucleotide polymorphisms (in the *Cyt-b* gene) have been used to explore intraspecific and population variation in OWSF (102, 158).

A variety of markers useful for studying population-level variation exist for a range of other myiasis-causing species. These include microsatellite loci (41), RAPDs (132), and inter-simple sequence repeat markers (61) for the sheep blow fly, *Lucilia sericata*, and AFLPs for the black blow fly, *Phormia regina* (99). At the time of writing, however, researchers appear to make little use of population genetic methods when studying the epidemiology of myiasis-causing Diptera.

## Use of Molecular Methods in Sterile Insect Technique Applications

Genetic methods have played a significant role in SIT research in NWSF and look likely to make a still more extensive contribution in the future. For example, in the application of conventional SIT, ionizing radiation is typically used for insect sterilization, but this is often highly detrimental to the fitness of released male flies in the wild; transgenic insect techniques offer opportunities to replace and/or augment this method, providing a safer, more cost-effective alternative (5, 57). Genetic sexing strains (e.g., 5, 57, 77) have been developed to modify the sex ratio of flies released into the environment at the point of release; in some systems genetic modifications directly confer sterility (113), while in others male and female flies (often at the pupal stage) can be distinguished so that female flies can be eliminated prior to release (57, 77). Molecular methods have also been employed to evaluate fly population/strain compatibility for SIT releases and as a part of post-release monitoring to assess the effectiveness of release programs (e.g., 44, 87, 142, 143). NWSF SIT releases continue in the region of the Darién Gap in southern Panama (103) as part of an ongoing program to prevent reinvasion from Colombia.

#### The Genetic Basis of Insecticide Resistance

Molecular methods have significantly advanced our understanding of the genetic basis of insecticide resistance in blow flies. Research into this topic has been driven largely by the rise of resistance to organophosphates (OPs) in the Australian sheep blow fly, *L. cuprina*. Resistance was apparent by 1965, with polymorphisms for two forms (diazinon and malathion resistance) detected in Australia by 1968 (58). Molecular studies have identified two single nucleotide mutations in the  $\alpha E7$  gene (which encodes esterase 3) that confer the two forms of OP resistance in *L. cuprina* (18, 91). In a subsequent study, Hartley et al. (58) compared the incidence of diazinon and malathion resistance in museum specimens of *L. cuprina* with contemporary specimens of both *L. cuprina* and its sister species *L. sericata* from Australia and further afield. Significantly, in specimens collected after the widespread use of OPs began, the diazinon-resistance change was rare outside of Australia, whereas malathion resistance-associated mutations were widespread. Furthermore, analysis of *L. cuprina* museum specimens collected pre-OP usage showed no cases of the diazinon-resistance change but several cases of the malathion-associated changes, suggesting that mutations conferring malathion resistance were already present in Australian *L. cuprina* before the widespread use of OPs.

Subsequently, Carvalho et al. (20) have demonstrated a similar basis for OP resistance in NWSF. Thus, it appears that esterase-based OP resistance in Calliphoridae (and *Musca domestica*; 24) is characterized by parallel evolution and a limited range of evolutionary solutions. Finally, a recent expressed sequence tag-based study (76) has begun to map gene usage and location in *L. cuprina* against known gene structures of *Drosophila melanogaster*; a number of the mapped gene locations, including  $\alpha E7$ , are associated with insecticide resistance. Such work is part of a fast-growing catalog of genomic resources available for this economically important pest species, a repertoire likely to be completed in the near future with the release of the Australian sheep blow fly genome (see https://www.hgsc.bcm.edu/arthropods/sheep-blowfly-genome-project).

#### TRAPPING TOOLS FOR SURVEILLANCE AND CONTROL

Traps for adult flies, usually baited with semiochemicals, provide distribution and abundance data in a controlled, repeatable, and comparable manner, and trapping is a fundamental part of myiasis-monitoring programs for NWSF and OWSF (42, 52). New trap designs with improved semiochemical baits for OWSF caught more flies with greater selectivity than previous traps (130),

but OWSF still made up only 9.1% of the trap catches at the Malaysian study site (146). However, development of a real-time PCR assay enables scientists to detect one OWSF mixed in a sample of 1,000 nontarget species (69); the trap can therefore be used to monitor populations in endemic situations with high populations of OWSF and also to monitor spread of the fly into areas with low or zero prevalence. Greater confidence in negative results has been achieved with an internal amplification control in a multiplexed assay (90).

The control of myiasis using nonreturn traps and targets has been widely considered, but for traps to accomplish this goal in a cost-effective manner they must be highly efficient and sustain a period of effectiveness in both attracting and killing flies. This combination is usually difficult to achieve because a high number of traps per unit area are required to overcome the high rates of reproduction of most traumatic myiasis species. The use of more effective semiochemical baits could increase efficiency (26), but such developments are slow. The bait most commonly used for NWSF remains the long-established Swormlure-4 (83). Although various studies, for example, those examining the waste media in which NWSF larvae have been reared (22), have identified novel compounds, none have supplanted Swormlure-4. A unique study of sticky traps baited with lures used for tsetse flies (POC: P, 3-n-propylphenol; O, racemic 1-octen-3-ol; C, 4-methylphenol) combined with those for OWSF (Bezzilure B) showed the potential for synergism and the benefits of combining lures that target different behavioral responses (139).

A number of traps have been developed to control *Lucilia* blow flies. For example, the LuciTrap, which incorporates Lucilure, a bait composed of butyric acid, 2-mercaptoethanol, indole, and 20% sodium sulfide solution (147), can reduce *L. cuprina* populations and associated fly strike of sheep in Australia if used at the recommended rate of one trap per 100 sheep (148); reductions in incidence of fly strike of up to 46% have been reported (156, 157). Similarly, Broughan & Wall developed a trap baited with rehydrated freeze-dried liver for *L. sericata* in Europe and showed that incidence of fly strike in flocks for which trapping was used was on average five times lower than in flocks without traps present (16).

The bluebottle blow fly, *Calliphora vicina*, is considered mainly a carrion breeder but it can cause traumatic myiasis, usually in necrotic tissues (29). Development of an efficient mass-trapping program for this species in Norway, where it is a major economic pest of drying fish stock (1), has been proposed as a viable long-term approach to minimizing fish-stock losses and should stimulate trapping studies of other traumatic myiasis species.

For some species, no effective trapping system exists, which is a major handicap to surveys. For example, *W. magnifica* does not respond to Swormlure-4, unlike OWSF and NWSF (56). Sotiraki et al. (125) reviewed studies that suggest odors that attract gravid females to hosts, especially to the undamaged genitalia of male and female sheep (36), could be identified by gas chromatography combined with electroantennography (GC-EAG) (e.g., 13) for use in traps.

## CHANGES IN THE DISTRIBUTION OF TRAUMATIC MYIASIS SPECIES IN A CHANGING WORLD

Climate change, habitat modification, and growing global trade and travel (of people and domestic animals) all increase the probability that novel agents of myiasis will be introduced into and establish in nonendemic areas. The introduction of NWSF into Libya is the most well-known example, with potentially extreme economic consequences (42, 78), but numerous smaller-scale introductions have occurred and each can have a significant impact on the individuals concerned, whether animal or human. For example, OWSF was first reported in Hong Kong as a problem in dogs in 2003 and soon afterward it became a problem for human health, with several cases associated with elderly nursing home patients who were unable to care for themselves. These cases

raised awareness of this new problem and of the need to introduce measures (e.g., fly screening over windows and doors) to reduce the risk (21).

Predicting the distribution of a pest species on the basis of existing distribution data can help show where a species occurs and also highlight where it might occur following dispersal or climate change (107). Nevertheless, care is needed because simplistic climate-driven models ignore many important parameters, such as farmer behavior and animal management practices as well as the biology of the parasite (154). The inclusion of many aspects of parasite biology, host biology, and the environment through agent-based modeling within a Geographic Information System platform in relation to the spread of OWSF if introduced into Australia has been explored with success (160). Factors introduced into the model include OWSF survivorship, development and dispersal, ambient temperatures, soil suitability for pupal development, vegetation cover, and the availability of hosts and wounds.

The likely impact of climate change on blow fly strike in sheep in England, which is due mainly to *L. sericata*, was modeled by Wall & Ellse (153). In addition to the effects due to changes in seasonality and distribution of *L. sericata*, the authors speculated that significantly greater myiasis problems could result if *W. magnifica* were able to establish following climate warming. This species dominates in the Mediterranean Basin (125, 126), appears to outcompete *L. sericata* (37) (**Figure 1**, right), and likely has a great impact on naïve populations of sheep. This is indicated by its greater impact on imported than local breeds in areas where it naturally occurs, e.g., in Hungary, where indigenous breeds had an infestation rate of 5.8% compared with 28.8% for imported breeds (36).

All three major obligate agents of traumatic myiasis have been involved in relatively recent range expansions; the most reported case is the incursion of NWSF into Libya (42, 78). However, OWSF has also extended its range in the Gulf region of the Middle East to Iraq (122), where it persists at low levels, potentially vulnerable to SIT (6). In addition, *W. magnifica* became newly established in Crete and more prominent in Morocco (125); it appears to be spreading in southern Italy (47), and it remains to be seen whether this is a natural or human-assisted phenomenon.

#### RISK, PREVENTION, AND TREATMENT OF TRAUMATIC MYIASIS

Predisposing factors for human traumatic myiasis include a combination of clinical (e.g., open wounds, peripheral vascular disease, diabetes, physical and mental disability, advanced age) and social (e.g., homelessness, alcoholism, poor hygiene, bad housing conditions) factors (10, 110, 116, 120). In domestic animals, particularly sheep, two groups of factors, those that influence sheep susceptibility and those that affect fly abundance, determine the incidence of ovine cutaneous myiasis by *Lucilia* blow flies. However, it is often difficult to disentangle the various individual factors that act together to influence the overall pattern of myiasis incidence, particularly because different risk factors affect the position on the body (breech, body, or foot), the age class of animal (lamb or ewe), or the time of year when it occurs. Furthermore, the importance of the various risk factors changes dynamically over the year (152). Important contributors include physical conformation of the sheep's body, particularly wrinkles in the skin surrounding the tail; diarrhea and the accumulation of feces in the wool; open wounds; and warm, humid weather, which facilitates oviposition and larval survival.

The treatment of choice for myiasis in malignant cutaneous wounds in humans has not changed for many years. Francesconi & Lupi (43) review for clinicians the treatment of wound myiasis, which briefly comprises (a) mechanical removal of larvae, after local anesthesia if necessary; (b) surgical excision and debridement of necrotic tissues in the lesion; and (c) thorough rinsing of the affected area with antiseptic and/or antibiotic solutions (complemented with oral antibiotics: 3, 116).

In livestock, myiasis is controlled primarily through the prophylactic and therapeutic use of the OP diazinon; the pyrethroids high-cis cypermethrin, alpha-cypermethrin, and deltamethrin; the tetracyclic-macrolide compound spinosad; and, of increasing importance over recent decades, the insect growth regulators cyromazine, dicyclanil, and diflubenzuron (14, 152). In England, cyromazine provides a 90% reduction in fly strike in lambs for up to 9 weeks and an 80% reduction for 10-12 weeks (80). Dicyclanil is ten times more active than cyromazine or diflubenzuron and provides substantially longer protection against myiasis (111). In the Netherlands, sheep treated with dicyclanil showed a 100% reduction in blow fly strike for up to 16 weeks after application (111). Even 22 weeks after application, the number of fly strikes in a dicyclanil-treated flock was reduced by 89% (80). Dicyclanil provided effective protection against wohlfahrtiosis for at least 12 and 20 weeks for male and female sheep, respectively (127), and, when applied to just 15-20% of a flock, incidence in the untreated animals was significantly reduced. There are few recent developments in the use of insecticides for control of obligate agents of traumatic myiasis (159). One major problem with obligate traumatic myiasis is that reinfestations at sites of treated infestations are common within the same season (55), if not with the obligate species then with secondary parasites, e.g., L. sericata and Chrysomya albiceps (126).

The role of dogs in the epidemiology of wohlfahrtiosis of livestock may be important (32, 35, 112). In dogs, infestations can occur at body orifices and at sites of wounding due to fighting, but they often go untreated because of ignorance, negligence, and lack of funds, or because they have no owner. Therefore, dogs can act as reservoirs of infestation, which could be of significance in countries with large populations of stray dogs. Indeed, during the unsuccessful eradication campaign against NWSF in Jamaica, one important complicating factor was urban hot spots of incidence in unmanaged and stray dogs (104).

Despite much effort, scientists have made little progress on vaccines against agents of traumatic myiasis (109). In 2007, Elkington & Mahony (34) argued that a successful vaccine against fly strike required a reappraisal of strategies and that immunosuppression together with the induction of cellular immunity should be emphasized, unlike the standard approaches that aim to induce humoral immunity.

#### SOCIETAL BENEFITS OF TRAUMATIC MYIASIS

Although this review emphasizes traumatic myiasis as a disease, brief consideration is given to two areas where an understanding of the disease and of the life cycle of the disease agents can benefit humans and animals. These areas are larval therapy, the carefully controlled use of facultative myiasis species to bring about wound healing, and the prosecution of cases of human or animal neglect, in which knowledge of larval development can indicate the minimum period of neglect.

## Advances in the Therapeutic Application of Traumatic Myiasis

The historical use of facultative myiasis-causing fly larvae in wound therapy in a carefully controlled, deliberate myiasis has been reviewed comprehensively (120). Larval therapy, or maggot debridement therapy (MDT), has value not only in human medicine but also in veterinary medicine (28, 71). Sherman (119) has reviewed the evidence for the effectiveness of MDT in debridement (removal of necrotic tissues), disinfection (microbial killing), and hastened wound healing (tissue growth stimulation). Clear and substantial support exists for the role of larvae in debridement, but support for disinfection and wound healing is more equivocal. Nonetheless, blow fly larvae produce some potent antimicrobial compounds (72) that can even reduce bacterial biofilms, and a number of studies have demonstrated the disinfectant potential of MDT (see 119). Some evidence

exists that MDT promotes wound healing, but studies are complicated by the difficult environment of chronic wounds and the ongoing problems of reinfection and tissue death, suggesting a need for maintenance debridement (119).

## Traumatic Myiasis and Forensic Investigation of Neglect

Although traumatic myiasis is frequently a consequence of ignorance, it can be an indicator of wound care neglect, either self-neglect or neglect by care givers. In such cases traumatic myiasis can indicate a minimum period of neglect, which can be used to prosecute those at fault (8, 33). Hospital-acquired (nosocomial) myiasis is not uncommon (89) but is probably underreported in many regions (e.g., Latin America and the Caribbean; 108) because notification is not compulsory. Myiasis in a health care situation can have complications that extend well beyond the medical consequences for the patient, e.g., a serious psychological impact on the patient and the patient's family and significant harm to the reputation of the health care facility and all that implies (121). Even fly species usually associated with rural areas such as NWSF have been reported to cause nosocomial traumatic myiasis (11, 108).

Medical staff in all geographic locations must be reminded of the possibility of myiasis during the relevant fly season. It can be challenging for them to recognize and treat such rarely encountered conditions in a timely and efficient manner. Medical staff and health care providers need to be aware that traumatic myiasis can complicate healing when a wound resulting from a medical procedure, such as the use of fixation devices (97, 150) and the insertion of tracheostomy tubes (11, 15, 63), becomes infested.

#### **FUTURE PROSPECTS**

Agents of traumatic myiasis continue to constrain sustainable livestock production, undermine national and international trade in livestock, and present a public health risk. Successful demonstrations of localized eradication remain the removal of NWSF from North and Central America and from Libya using SIT as a component of area-wide integrated pest management, including robust efforts on the ground to treat infestations and control movements of infested animals, especially their rapid transport by vehicles. The northern limit of NWSF is now the Darién Province of eastern Panama (159), where a barrier is maintained to prevent incursion of the fly from Colombia. The use of SIT is now under consideration in South America, and a pilot project was conducted near the Brazil-Uruguay border in 2009; any future campaign might include the release of sterilized flies of a Jamaican strain, which was compatible with Brazilian strains (86). The failure of an NWSF campaign in Jamaica, however, highlights the complex combination of management and technical difficulties that need to be overcome to achieve eradication (151). Hence, for most species, particularly where they are nonobligate agents of myiasis, eradication is not an option owing to cost, the ability of flies to use a wide range of hosts and to breed in carrion, and the presence of contiguous populations. Therefore, myiasis must be managed at a local scale. However, the growth in insecticide resistance in some areas and the slowdown in the rate of development of novel insecticides, coupled with environmental and health concerns associated with the continued use of some of the older neurotoxic insecticides, all within a scenario of "changing climates, changing markets and changing parasites" (109, p. 888), mean that more sophisticated approaches to the integrated management of myiasis need to be identified and applied.

In the future, climate change is likely to influence the distribution and seasonal incidence patterns of a range of myiasis species in a manner that is difficult to predict. The continuing rise in international travel and trade will also inevitably result in the inadvertent introduction of species

into nonendemic areas and the exposure of travelers to exotic species of myiasis-causing flies (e.g., 84). The latter emphasizes the important need for recognition and treatment of myiasis in the home country of the traveler, by medical and veterinary professionals who might not be familiar with the symptoms and methods of treatment (50).

One outcome of the incursion of *C. hominivorax* in Libya was the investment in research on screwworm flies by the Joint Food and Agriculture Organization (FAO) and International Atomic Energy Agency (IAEA) Division of Nuclear Techniques in Food and Agriculture (39, 103). It is hoped that such programs and new ones (e.g., IAEA Technical Cooperation Programme Regional Latin America 5067, Supporting Capacity Building for Evaluation of Feasibility of a Progressive Control Programme for New World Screwworm) will continue to raise awareness of the importance of traumatic myiasis-causing flies as agents of transboundary animal diseases with significant zoonotic importance. We are neglecting them to our peril.

#### DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

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