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REVIEW

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The history of leishmaniasis

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Abstract

In this review article the history of leishmaniasis is discussed regarding the origin of the genus *Leishmania* in the Mesozoic era and its subsequent geographical distribution, initial evidence of the disease in ancient times, first accounts of the infection in the Middle Ages, and the discovery of *Leishmania* parasites as causative agents of leishmaniasis in modern times. With respect to the origin and dispersal of *Leishmania* parasites, the three currently debated hypotheses (Palearctic, Neotropical and supercontinental origin, respectively) are presented. Ancient documents and paleoparasitological data indicate that leishmaniasis was already widespread in antiquity. Identification of *Leishmania* parasites as etiological agents and sand flies as the transmission vectors of leishmaniasis started at the beginning of the 20th century and the discovery of new *Leishmania* and sand fly species continued well into the 21st century. Lately, the Syrian civil war and refugee crises have shown that leishmaniasis epidemics can happen any time in conflict areas and neighbouring regions where the disease was previously endemic.

Keywords: Leishmaniasis, *Leishmania*, History

Background

Leishmaniasis is a vector-borne disease caused by flagellated protozoans of the genus *Leishmania*. The disease is widespread in the tropical and subtropical areas and found in 98 countries in Europe, Africa, Asia and America [1]. However, over 90% of new cases occur in just 13 countries (Afghanistan, Algeria, Bangladesh, Bolivia, Brazil, Columbia, Ethiopia, India, Iran, Peru, South Sudan, Sudan and Syria). It is estimated that between 0.9 and 1.7 million people are newly infected every year, but only a small fraction of them will develop the disease and 20,000–30,000 will eventually die [2].

Leishmania parasites are transmitted by the bite of infected phlebotomine sand flies and 98 species of the genera *Phlebotomus* and *Lutzomyia* have been described as proven or suspected vectors for human leishmaniasis [2]. Only female sand flies attack mammals to take blood meals required for the completion of egg development. Some sand flies have a wide host range including canids, rodents, marsupials and hyraxes while others are mainly feeding on humans. Accordingly, human leishmaniasis can have zoonotic or anthroponotic transmission patterns.

In their mammalian host, *Leishmania* parasites live and multiply intracellularly in phagocytic cells within so-called phagolysosomes. Currently, there are 18 different *Leishmania* species described that are pathogenic for humans (Table 1) [4–6]. Although the different *Leishmania* species are morphologically very similar, they cause two main clinical forms, cutaneous leishmaniasis (CL)¹ and visceral leishmaniasis (VL)², depending on which types of phagocytic cells are invaded. In CL, the parasites infect macrophages resident in the skin. When the host cell is full of parasites, it bursts and the released amastigotes will infect neighbouring macrophages. In VL, however, the re-leased amastigotes are spread by the blood circulation and infect cells of the mononuclear phagocyte system (reticulo-endothelial system) of liver, spleen, bone marrow, lymph nodes and the intestine.

The most common form of leishmaniasis is CL with 0.7–1.3 million new cases occurring annually worldwide [2]. CL occurs in three different forms, localised cutaneous leishmaniasis (LCL), diffuse cutaneous leishmaniasis (DCL) and mucocutaneous leishmaniasis (MCL). LCL is characterised by skin lesions and ulcers on exposed parts of the body, leaving permanent scars. DCL is a less common and distinguished from LCL by the development of multiple, slowly progressing nodules without ulceration involving the entire body. MCL is restricted to Latin America. After the initial skin lesion has healed, the disease spreads to the mucou

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Table 1 Species of *Leishmania* causing leishmaniasis in humans (adopted and modified according to references [4–6])

Subgenus	Species	Old/New World	Clinical disease	Distribution
Leishmania	<i>L. aethiopica</i>	OW	LCL, DCL	East Africa (Ethiopia, Kenya)
	<i>L. amazonensis</i>	NW	LCL, DCL, MCL	South America (Brazil, Venezuela, Bolivia)
	<i>L. donovani</i>	OW	VL, PKDL	Central Africa, South Asia, Middle East, India, China
	<i>L. infantum</i> (syn. <i>L. chagasi</i>)	OW, NW	VL, CL	Mediterranean countries (North Africa and Europe), Southeast Europe, Middle East, Central Asia, North, Central and South America (Mexico, Venezuela, Brazil, Bolivia)
	<i>L. major</i>	OW	CL	North and Central Africa, Middle East, Central Asia
	<i>L. mexicana</i> (syn. <i>L. pifanoi</i>)	NW	LCL, DCL	USA, Ecuador, Venezuela, Peru
	<i>L. tropica</i>	OW	LCL, VL	North and Central Africa, Middle East, Central Asia, India
	<i>L. venezuelensis</i>	NW	LCL	Northern South America, Venezuela
	<i>L. waltoni</i>	NW	DCL	Dominican Republic
Viannia	<i>L. braziliensis</i>	NW	LCL, MCL	Western Amazon Basin, South America (Guatemala, Venezuela, Brazil, Bolivia, Peru)
	<i>L. guyanensis</i>	NW	LCL, MCL	Northern South America (French Guinea, Suriname, Brazil, Bolivia)
	<i>L. lainsoni</i>	NW	LCL	Brazil, Bolivia, Peru
	<i>L. lindenbergi</i>	NW	LCL	Brazil
	<i>L. naiffi</i>	NW	LCL	Brazil, French Guinea
	<i>L. panamensis</i>	NW	LCL, MCL	Central and South America (Panama, Columbia, Venezuela, Brazil)
	<i>L. peruviana</i>	NW	LCL, MCL	Peru, Bolivia
Mundinia	<i>L. shawi</i>	NW	LCL	Brazil
	<i>L. martiniquensis</i>	NW, OW	LCL, VL	Martinique, Thailand

Abbreviations: DCL diffuse cutaneous leishmaniasis, LCL localised cutaneous leishmaniasis, MCL mucocutaneous leishmaniasis, NW New World, OW Old World, PKDL post-kala-azar dermal leishmaniasis, VL visceral leishmaniasis

membranes of the nose, mouth and throat. Subsequently, the mucosal ulcers cause destruction of the nasal septum, lips and palate leading to extensive facial disfiguring. VL is the most severe form of leishmaniasis with an estimated 0.2–0.4 million new cases occurring worldwide each year [2]. Without treatment, VL is fatal in over 95% of cases. The symptoms of VL included irregular fever, weight loss, hepatomegaly, splenomegaly (sometimes hepatosplenomegaly) and anaemia.

Origin of the genus *Leishmania*

Fossil evidence

The existence of *Leishmania*-like species in prehistorical times is documented in two fossil ambers. The first *Leishmania*-like fossil was found in the proboscis and alimentary tract of a blood-filled female of the extinct sand fly *Palaeomyia burmitis* preserved in a 100 million-year-old Cretaceous Burmese amber [7, 8]. The *Leishmania*-like species was described in a new, collective fossil genus *Paleoleishmania* and named *P. proterus* [8]. Alongside promastigotes and paramastigotes, amastigotes were also found indicating that the sand fly acquired the parasite from blood of a vertebrate during feeding [8]. The presence of amastigotes is suggestive of a digenetic life-cycle of *P. proterus*. The blood cells were subsequently identified as being of a reptile [9]. The second *Leishmania*-like fossil was described

as *Paleoleishmania neotropicum* and was found in the extinct sand fly *Lutzomyia adiketis* in a 20–30 million-year-old Dominican amber [10]. Promastigotes, paramastigotes and amastigotes were observed in the gut and proboscis of the sand fly; however, no vertebrate blood cells were found [10]. Nevertheless, the presence of amastigotes and the fact that no monogenetic flagellates colonise sand flies suggest a digenetic life-cycle of *P. neotropicum* with a vertebrate host. This fossil record also provides evidence that Neotropical sand flies were vectors for *Leishmania*-like parasites in the mid-Oligocene to early-Miocene.

Geographical origin of *Leishmania* species

The genus *Leishmania* has probably evolved in the Mesozoic era (252–66 MYA) prior to the breakup of the supercontinent Pangaea [11]. However, the particular geographical origin of the different *Leishmania* species is a matter of ongoing debate. Three hypotheses are currently discussed.

The Palaearctic hypothesis

In 1971, Lysenko [12] suggested that *Leishmania* originated in the Palaearctic region, an area encompassing Europe, Asia north of the Himalayas, northern Arabia and Africa north of the Sahara, in the Palaeocene (66–56 MYA) [13, 14]. This hypothesis is supported by fossil records indicating that ancestral phlebotomine sand flies and murid rodents also

evolved in the Palaearctic region during the Palaeocene [15, 16]. Murid rodents were probably important mammalian reservoir hosts as their burrows offered high humidity and shelter from cold for sand flies [13]. Presumably along with its vector and murid host, the parasite spread to the Nearctic region, an area comprising most of North America, including Greenland, Central Florida and the highlands of Mexico, in the Eocene (56–34 MYA) when the Bering land bridge was intact [13]. After the Bering isthmus vanished, *Lutzomyia* sand flies, the vectors of *Leishmania* species in the New World, evolved in the Nearctic during the Oligocene (34–23 MYA) [13]. When the Panama land bridge was formed about 3 million years ago, sigmodontine rodents and *Lutzomyia* sand flies colonised the Neotropical region, an area including South and Central America, the southern Mexican lowlands, the Caribbean islands and southern Florida, in the Pliocene (5.33–2.86 MYA) [12–14, 17]. However, there is evidence that *Leishmania* may have been introduced into the Neotropical region during the Miocene (23–5.33 MYA) before the uplift of the Panama isthmus [11, 14]. Increasing temperature may have been the reason why sand flies began to inhabit the forest canopy with the consequence that arboreal mammals became new hosts for *Leishmania* parasites. Climate change and the adoption of new hosts by the vector may explain the greater diversity of *Leishmania* in the New World compared to the Old World.

The Neotropical hypothesis

The speculation that the genus *Leishmania* had originated in the Neotropical region was first suggested by Lainson & Shaw in 1987 [18] and further elaborated by Noyes in 1998 [19]. It was argued that the greater diversity of New World *Leishmania* compared to that of Old World *Leishmania* was evidence for a Neotropical origin of the species [18, 20]. However, the formation of new species may not always appear at a constant rate which would give rise to a larger number of species over longer residence time. In fact, speciation of *Leishmania* in the New World may be attributed to accelerated evolution in the Neotropical region due to climate change, increased host range and geographical isolation. It was suggested that sloths served as the first vertebrate host for *Leishmania* and that during the Eocene the parasite adapted to porcupines [19]. It was further hypothesised that the parasite was introduced into the Nearctic by infected porcupines and into the Palaearctic by an unspecified mammal during the Miocene [19, 21]. However, this hypothesis is incompatible with at least two scientifically established facts. First, fossil records indicate that porcupines did not appear in the Nearctic until the late Pliocene after the Panama isthmus had formed [16, 22], thus about 30–50 million years later than postulated by the hypothesis. Secondly, *Lutzomyia* sand flies, the only vectors of *Leishmania* in the Neotropical, evolved during the

Oligocene in the Nearctic and thus about 30 million years too late to serve as insect carrier for the parasite [13].

The Supercontinent hypothesis

In 2000, Momen & Cupolilli [23] provided a third hypothesis suggesting that with the breakup of the supercontinent Gondwana in the Mesozoic the subgenera *Leishmania* and *Sauroleishmania*³ evolved in Africa while the subgenus *Viannia* developed in South America. The subgenus *Leishmania* includes all the Old World species: *L. aethiopica*, *L. donovani*, *L. infantum*, *L. major* and *L. tropica*. As *L. aethiopica* occurs only in Ethiopia and Kenya, it was reasoned that this species originated in Africa [23]. Based on the restricted habitat of the primitive *Arvicornes-Phlebotomus* system in sub-Saharan Africa, it was presumed that *L. major* most likely also originated on this continent [24]. An East-African origin for *L. donovani* and *L. infantum* has been postulated based on a cladistic analysis of isoenzymes [25]. As humans evolved in East Africa, it was suggested that the anthroponotic transmission of *L. tropica* indicates that this species may also have originated in this part of Africa [23]. In accordance with the first hypothesis it was postulated that the New World species *L. mexicana*, which belongs to the subgenus *Leishmania* and shares many characteristics with *L. major* [18], dispersed into the Nearctic together with its rodent hosts during the Eocene. After entering South America, climatic and ecological factors probably caused further speciation giving rise to *L. venezuelensis*, *L. amazonensis* and *L. waltoni* [5, 23]. *Leishmania chagasi*, another New World species that belongs to the subgenus *Leishmania*, is meanwhile considered to be synonymous with *L. infantum* which was brought to South America in historical times (about 500 years ago by European settlers or their dogs) [26, 27]. With respect to *Leishmania* parasites of the subgenus *Viannia* (*L. braziliensis*, *L. guyanensis*, *L. lainsoni*, *L. lindenbergi*, *L. naffi*, *L. panamensis*, *L. peruviana* and *L. shawi*), which exclusively occur only in the Neotropical, it was hypothesised that these species evolved in South America after the separation of Gondwana [23]. The supercontinent hypothesis reflects much better the available molecular phylogenetic data and was recently corroborated by phylogenomic reconstruction using new bioinformatics methods (SISRS, Site Identification from Short Read Sequences) to identify over 200,000 informative sites across the genome from newly sequenced and publicly available *Leishmania* data [28]. This new study and two recently published analyses also suggest that sloth- and porcupine-infecting *Leishmania*-like trypanosomatids derived from a clade long separated from *Leishmania* species [6, 28, 29]. Consequently, all *Leishmania*-like sloth and porcupine parasites have now been grouped in the genus *Endotrypanum*⁴ and in the new genus *Porcisia*⁵, respectively [6, 29]. In addition, the worldwide distribution of *L. martiniquensis* supports an ancient global dispersal of the

genus *Leishmania* predating the breakup of Gondwana [28]. This suggestion is corroborated by phylogenetic analyses showing that *L. martiniquensis* belongs to the *L. enriettii*⁶ complex [30], a clade basal to the clade comprising the subgenera *Leishmania*, *Viannia* and *Sauroleishmania* [6]. Considering the uniqueness of the *L. enriettii* complex, it was proposed to create a new subgenus *Mundinia* for the *L. enriettii* complex that includes *L. martiniquensis* [6].

Based on available data, it can be concluded that leishmanine trypanosomatids originated in mammals in the Mesozoic on the supercontinent Gondwana. Presumably, a monoxenous insect flagellate established itself in mammals and developed into a dixenous species [6, 31]. It is reasonable to assume that with the diversification of mammals, the genera *Endotrypanum*, *Porcisia* and *Leishmania* initially evolved. After the breakup of Gondwana, the genera *Endotrypanum* and *Porcisia* ended up together with their mammalian hosts on the South American continent. During the separation of Gondwana, the genus *Leishmania* was divided and subsequently evolved into the subgenus *Viannia* in South America and into the subgenera *Leishmania*, *Mundinia* and *Sauroleishmania* in Africa. The absence of leishmanial infections in New World lizards and the phylogenetic proximity of the subgenera *Leishmania* and *Sauroleishmania* is probably an indication that *Sauroleishmania* represent a mammalian line that subsequently became adapted to lizards [6, 31]. Finally, in the Eocene, a species of the subgenus *Leishmania* spread from Asia to the Nearctic together with its rodent hosts via the Bering land bridge and evolved into American *L. (Leishmania)* species.

Ancient times

Only a few accounts exist reporting on the occurrence of leishmaniasis in ancient human history. There are descriptions of lesions reminiscent of Oriental sore on tablets in the library of the Assyrian King Ashurbanipal from the 7th century BCE [32]. It is even thought that they were derived from earlier texts dating back to 1500–2500 BCE [32]. A paleoparasitological study of 42 Egyptian mummies from a Middle Kingdom tomb in West Thebes (2050–1650 BCE) found leishmanial mitochondrial DNA in four specimens [33]. Direct sequencing of the amplified DNA fragment revealed that the four mummies were infected with *L. donovani*, suggesting that VL was present in ancient Egypt. Leishmaniasis is also mentioned in the Ebers Papyrus, a collection of ancient Egyptian medical documents dating back to 1500 BCE [34]. This scripture reports a skin condition, known in English as “Nile Pimple”, which supposedly refers to CL. Using immunological analysis, *Leishmania*-infected macrophages were detected in a Peruvian mummy of a 6-year-old girl dated from 800 BCE [35].

Further evidence for the presence of leishmaniasis during antiquity was the knowledge of ancient Arabic societies that individuals with healed Oriental sores were protected from further infections [36]. This insight was used by the people in the Middle East and Central Asia for active immunisation against Oriental sore. They inoculated exudates from active lesions into the buttocks of young children, particular girls or exposed the bottoms of babies to sand flies in order to prevent the development of disfiguring facial scars.

Middle ages

Arabic scientists were the major chroniclers in the description of CL during medieval times. In 930, the Persian polymath Rhazes (Abū Bakr Muhammad ibn Zakariyyā al-Rāzī, 854–935) described the occurrence of cutaneous sores in the Baghdad region [37]. The first accurate description of Oriental sore was by the great Persian philosopher and physician Avicenna (Abū ‘Alī al-Ḥusayn ibn ‘Abd Allāh ibn Al-Hasan ibn ‘Alī ibn Sīnā, 980–1037). He described a dermal condition known as Balkh sore from northern Afghanistan suggestive of dry skin lesions caused by *L. tropica* [32]. In the New World, disfiguring facial conditions reminiscent of MCL are depicted on Pre-Columbian ceramics since the 5th century [17, 38]. In addition, four female skulls dating back to the 11th century discovered in the archaeological cemetery of Coyo Oriente in the desert of San Pedro de Atacama, northern Chile, provided morphological and molecular evidence of leishmaniasis in South America [39]. The presence of leishmaniasis at high-altitude (note that the Atacama Desert is 2400 m above sea level) where the disease is normally not found, was explained by migration of lowlanders infected with the diseases to the desert highland [39].

Modern times

16th–19th century

From the 16th century onwards, several accounts of skin infections suggestive of Oriental sore were recorded from various places in the Middle East. In many of the reports the conditions described were named according to the place they were acquired and by which they are still known today (e.g. Aleppo boil, Baghdad boil, Jericho boil)

[32]. In 1756, the Scottish physician and naturalist Alexander Russell (1715–1768) published a detailed clinical account of both dry and wet forms of Oriental sore when he was practising in Aleppo [40]. He described how the local people distinguished between a ‘male’ and a ‘female’ form of the disease, which most likely correspond to wet zoonotic CL caused by *L. major* and dry anthroponotic CL caused by *L. tropica*, respectively. He provided a detailed description of the development of lesions and mentioned that the diseases heal within 8 months and 1 year. With respect to treatment, he stated “from what I observed, it is infinitely better to apply nothing, than any

of the numberless medicines they make use of" but also wrote that he found that a mercurial plaster was most efficacious.

With the Spanish colonisation of the Americas at the beginning of the 16th century, reports appeared by conquistadors and missionaries describing disfiguring facial conditions reminiscent of MCL [39]. One of the first account of MCL was given by the Spanish chronicler Pedro Pizarro (1515–1602) in 1571. He wrote of coca growers working in the lower eastern slopes of the Peruvian Andes who suffered from the destruction of the nose and lips [41].

There are no convincing reports about VL before the 19th century. One of the earliest account of kala-azar was by the military surgeon William Twining (1790–1835) when he published an article in 1827 about patients in Bengal, India, who appeared emaciated with enlarged spleens, acute anaemia and intermittent fever [42]. In 1832, Twining published a book in which he described in more detail the symptoms of kala-azar including the dried-up and scaly appearance of the skin [43]. The first outbreak of kala-azar was already recorded in 1824/25 in the village of Mahomedpore, thirty miles east of Jessore in Lower Bengal, India [44]. From there, the disease spread westwards and reached Burdwan in West Bengal in 1860

[44]. Kala-azar became epidemic and spread to the north of Bengal and to Assam in the following years [44]. The mortality of kala-azar patients in the affected areas was reported to be about 30% [44]. The disease remained endemic in many areas for the next decades. The word kala-azar⁷ was coined in the late 19th century and literally means 'back disease'. The naming of the disease as kala-azar refers to the greyish discolouration of the skin of light coloured people in the course of the infection.

Although the search for the causative agents responsible for the different forms of leishmaniasis began at the end of the 19th century, it was not before the turn of the century that Leishmania parasites were definitively described. However, already in 1885 the Scottish doctor David Douglas Cunningham (1843–1914) saw Leishmania parasites in a Delhi boil but did not realise what they were [45]. Subsequently, the Russian army doctor Piotr Fokich Borovsky (Петр Фокич Боровский) (1863–1932) was the first to recognise that the bodies present in Oriental sore lesions were protozoans [46]. Because he published his findings in an obscure Russian journal in 1898, his observation remained unnoticed.

20th century

In November 1900, the Scottish pathologist William Boog Leishman (1865–1926) (Fig. 1), who served with the British Army in India, discovered ovoid bodies in smears taken post-mortem from the spleen of a soldier who died from emaciation and splenomegaly while stationed at Dum



Fig. 1 Lieutenant General Sir William Boog Leishman. The genus Leishmania was named after the Scottish pathologist who is credited together with Charles Donovan for the discovery of the parasite that caused visceral leishmaniosis (VL). Photo Wellcome Library, London, used according to the Creative Commons Attribution only licence CC BY 4.0

Dum, a town near Calcutta [47]. Subsequently, he found similar bodies in an experimentally infected white rat. He published his findings in 1903 and suggested that the ovoid bodies were degenerated forms of trypanosomes and therefore proposed that the illness which he termed 'Dum-dum fever' was a form of trypanosomiasis [47]. A few weeks later, the Irish doctor Charles Donovan (1863–1951) (Fig. 2), who was professor of physiology at the Madras Medical College, published a paper reporting that he had found similar bodies in splenic samples taken during life and at autopsy from native Indian subjects with remittent fever and enlarged spleens [48]. As Donovan did not think that the ovoid bodies were degenerated trypanosomes, he sent a slide of the parasite to the French Biologist Félix Étienne Pierre Mesnil (1868–1938) in Paris asking him to show the specimen to his fellow countryman Charles Louis Alphonse Laveran⁸ (1845–1922) who was an authority on protozoan parasites that time. Laveran thought that it was a new parasite of the genus Piroplasma [49]. Meanwhile, the British medical doctor Ronald Ross (1857–1932), who was ordered by the Indian government in 1898 to investigate kala-azar,

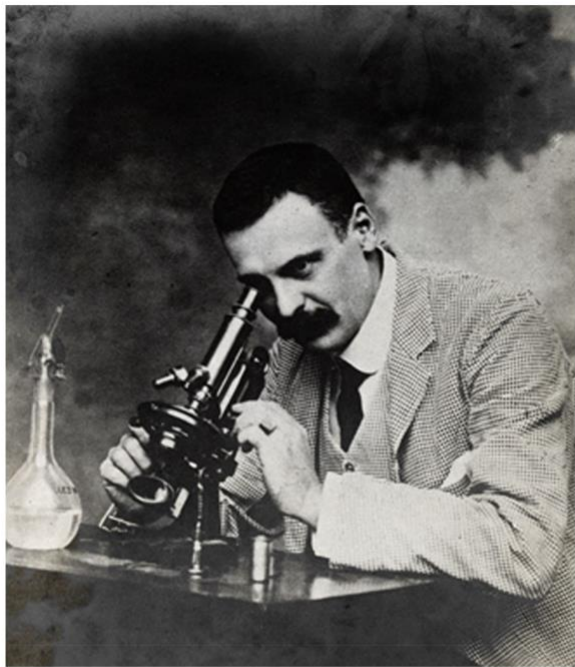


Fig. 2 Major Charles Donovan. The species *L. donovani* was named after the Irish doctor who independently of William Leishman discovered the parasite in spleens of patients with kala-azar. Photo Wellcome Library, London, used according to the Creative Commons Attribution only licence CC BY 4.0

published a paper in November 1903 commenting on the discovery of the ovoid bodies found by Leishman and Donovan in spleen pulp of patients with chronic pyrexia and splenomegaly [50]. He concluded that the ovoid bodies were not degenerated trypanosomes but a novel protozoan organism and that the clinical picture of the cases resembled that of kala-azar. In a follow-up paper, Ross also disagreed with Laveran's suggestion that the ovoid bodies were parasites of the genus *Piroplasma* but that they belonged to a new genus and proposed to name them *Leishmania donovani* [51]. The discussion on the nature of the Leishman's bodies continued for another year but by the end of 1904 the term *Leishmania donovani* was generally adopted [44]. The related VL causing species *Leishmania infantum* was first described by the French bacteriologist Charles Jules Henry Nicolle (1866–1936) in children in Tunisia suffering from splenic anaemia in 1908 [52]. In the same year, together with his colleague Charles Comte (1869–1943), he also found the parasite in dogs in Tunis [53]. Since then, dogs have been implicated as important reservoir hosts for VL [54].

As already mentioned above, Cunningham and Borovsky were the first who saw leishmanial parasites in Oriental sore lesions but it was the American pathologist James Homer Wright (1869–1928) who was credited for the discovery of *L. tropica*. In 1903, he published a detailed

description of the organism from a specimen of a sore of an Armenian girl and named the parasite *Helcosoma*¹⁹ *tropicum* [55]. In 1906, the German physician and zoologist Max Lühe (1870–1916) changed the name into *Leishmania tropica* [56]. In 1914, the Russian physicians Wassily Larionovich Yakimoff (Василий Ларионович Якимов) (1870–1940) and Nathan Isaakovich Schokhor (Натан Исаакович Шохор) (1887–1941) suggested that *L. tropica* should be divided into the two subspecies *L. tropica minor* and *L. tropica major* based on the size of the parasites found in skin lesions (*L. t. minor*, smaller amastigotes; *L. t. major*, larger amastigotes) [57]. This classification of *L. tropica* became the standard for the next 60 years. Meanwhile, it was discovered that the two subspecies of *L. tropica* were associated with two types of lesions and differences in epidemiology: *L. t. minor* was found to cause dry nodular lesions and to occur in urban environments while *L. t. major* was discovered to produce wet ulcerating lesions and to appear in rural regions [58]. Based on these differences, Bray et al. [59] proposed to classify the two subspecies as *L. tropica* and *L. major*, respectively, in 1973. In the same publication they reported the discovery of a new *Leishmania* species causing a different form of CL in Ethiopia which they named *L. aethiopica* [59].

New World leishmanial parasites were first described independently by the Brazilian doctor Adolpho Carlos Lindenberg (1872–1944) [60] and the Italian physician Antonio Carini (1872–1950) together with his Brazilian colleague Ulysses de Freitas Paranhos (1880–1954) [61] in skin lesions of patients with 'Bauri ulcers' from the State of São Paulo, Brasil, in 1909. Two years later, the Italian physician and bacteriologist Alfonso Splendore (1871–1953) found the parasite in mucocutaneous lesions of espundia patients [62]. Initially it was thought that the New World parasites were identical with *L. tropica*. In 1911, the Brazilian clinician and scientist Gaspar de Oliveira Vianna (1885–1914) studying leishmanial specimens obtained from a skin lesion of a patient resident in São João de Além Paraíba, Minas Gerais, concluded that the parasite was different from *L. tropica* [63]. He based his decision on apparent morphological differences [41] and named the new species by a lapsus calami *Leishmania brazilienses* [63], which was corrected to *Leishmania braziliensis* by Vianna's colleague Alfredo Augusto da Matta (1870–1954) in 1916 [64]. Although *L. peruviana* was already described in 1913, all other New World *Leishmania* species causing LCL and MCL were characterised much later: *L. mexicana* in 1953, *L. guyanensis* in 1954, *L. amazonensis* and *L. panamensis* in 1972, *L. venezuelensis* in 1980, *L. lainsoni* in 1987, *L. naffi* and *L. shawi* in 1989, *L. lindenbergi* in 2002 and *L. waltoni* in 2015 [5, 41]. Another species that previously was associated with leishmaniasis in humans and animals in Colombia and Panama, *L. colombiense* [65], has been recently reclassified as *Endotrypanum colombiense* [6].

VL was first recorded in Latin America in the 1930s. Because Aristides Marques da Cunha (1887–1949) and Evandro Serafim Lobo Chagas¹⁰ (1905–1940) were, for unknown reasons, unable to infect laboratory animals with the parasite from Brazilian cases of VL while that was usually no problem with both *L. donovani* and *L. infantum* causing Old World VL, they thought that they had discovered a new species responsible for VL in the New World and named it *Leishmania chagasi* in 1937 [66]. However, 1 year later, Cunha reported that he succeeded in infecting animals with cultures isolated from cases of American VL and thus concluded that the agent of VL in Latin America is identical to *L. infantum* [67]. More recently, this notion has been supported by modern molecular analysis techniques showing that *L. chagasi* strains could not be distinguished from *L. infantum* strains [68].

The species *L. martiniquensis* was only recently discovered. It was first isolated in 1995, its taxonomical position established in 2002 and named in 2014 [69]. Since 2009, the name '*L. siamensis*' popped up repeatedly in the literature. This 'new' species has been associated with leishmaniasis in horses and cattle in Europe and the USA [70–72], and with VL in humans in Thailand [73, 74]. However, as this species has not been properly characterised and described, the name '*L. siamensis*' should not be used [6]. In addition, recent DNA sequence analysis showed that most parasite isolates previously identified as '*L. siamensis*' were identical with *L. martiniquensis* [75]. Thus, '*L. siamensis*' should be regarded as a synonym of *L. martiniquensis* [6].

Although sand flies were suspected early on to be the vectors for transmission of *Leishmania* parasites, it was not until 1921 that this was proven when the French brothers and biologists Edmond Sergent (1876–1969) and Étienne Sergent (1878–1948) demonstrated that scarifying a suspension of ground sand flies into the skin of volunteers resulted in the development of typical Oriental sore lesions [76]. However, the result of this experiment was not generally accepted as proof that sand flies are the vectors of Oriental sore. The actual mode of transmission through the bite of the sand fly was finally demonstrated by the British-Israeli parasitologist Saul Adler (1895–1966) in 1941 when he successfully infected five volunteers with sand flies experimentally infected with *L. tropica* in the laboratory [77]. One year later, it was also conclusively proven that sand flies are the vector of kala-azar [78]. In 1922, the Brazilian doctor Henrique de Beaurepaire Rohan Aragão (1879–1956) showed that sand flies are responsible for the transmission of leishmaniasis in South America [79]. Later it was found that the sand flies transmitting leishmaniasis in the New World belong to the genus *Lutzomyia*. Meanwhile 42 *Phlebotomus* species and 56 *Lutzomyia* species have been implicated in the transmission of leishmaniasis in the Old and New World, respectively [3].

Current situation

Leishmaniasis still remains a major health problem in many endemic countries. The total number of annually reported VL cases in the 14 VL high-burden countries (Brazil, China, Ethiopia, Georgia, India, Kenya, Nepal, Paraguay, Somalia, South Sudan, Spain, Sudan and Uganda) has fallen from 60,000 in 2006 to 30,000 in 2014 [80]. This drop in numbers is mainly due to a 5-fold decline in VL cases in India [80]. On the other hand, the total number of yearly reported CL cases in the 12 CL high-burden countries (Afghanistan, Algeria, Brazil, Colombia, Iran, Morocco, Pakistan, Peru, Saudi Arabia, Syria, Tunisia and Turkey) remained unchanged at the high level of about 150,000 over the same period [80].

The increase in the number of leishmaniasis cases observed during the last 25 years throughout the world is due to several factors. Globalisation and climate change are two factors that contribute to the spread of leishmaniasis to non-endemic areas [81]. For example, over the last decades, the number of cases of leishmaniasis in international travellers (tourists and businesspeople) has increased [82]. In addition, the international traffic of blood products has resulted in *Leishmania* infections of patients who never travelled to leishmaniasis endemic regions [81]. The problem here is that no blood bank screens blood preservations for the presence of anti-leishmanial antibodies. There is also evidence that global warming will lead to an extension of the distribution of sand flies more northwards which could result in the transmission of leishmaniasis in hitherto non-endemic regions in the future [81, 83].

Other risk factors for the emergence and spread of leishmaniasis are war and unrest [81]. Currently, of great concern is the outbreak of Old World CL in the Middle East and North Africa. This CL epidemic was triggered by the Syrian civil war and refugee crisis and now affects hundreds of thousands of people living in refugee camps or caught in conflict zones [84, 85]. Before the outbreak of the civil war, the annual incidence of Old World CL in Syria was estimated to be around 23,000 cases [84]. This number has now more than doubled: 53,000 and 41,000 cases were reported in 2012 and in the first half of 2013, respectively [84]. A similar crisis seems to be unfolding in eastern Libya and in Yemen [84]. In addition, outbreaks of leishmaniasis have been recorded from refugee camps in Turkey, Lebanon, Jordan and Tunisia and may soon be reported from Saudi Arabia due to refugee fleeing the current Yemeni conflict [84–86].

Conclusions

From the history of leishmaniasis it is clear that the evolution of the disease is intrinsically tied with human activity. Although the disease probably already affected early hominids, leishmaniasis was not a selection factor

in the evolution of humans as was, for example, African trypanosomiasis [87]. Nevertheless, leishmaniasis was spread throughout the world by man during early human migration. In addition, domesticated dogs, one of the main reservoir hosts for VL, seem to have played an important role in the early epidemiology of the disease [88]. The more recent history of leishmaniasis has shown that new *Leishmania* species pathogenic for humans are still to be discovered. The emergence of new forms of leishmaniasis is probably linked to human activity at the edge of or within woodlands. This brings people in closer contact with sand flies that usually feed on wild animals which increases the risk that previously undetected *Leishmania* species may be transmitted to humans. In fact, deforestation and penetration of forests by humans can lead to the adaptation of sand flies to feed on people and their domestic animals near human dwellings and settlements

[89]. In many endemic regions, leishmaniasis is an epidemiologically unstable disease that shows a tendency for unpredictable fluctuations in the number of cases. The reasons for this are probably manifold but cultural, environmental and socio-economic factors play an important role. The recent outbreak of CL in conflict zones of the Middle East indicates that war, ecological disasters and forced migration are other factors that are associated with leishmaniasis epidemics.

Endnotes

¹In the Old World, CL is known as Oriental sore, Aleppo boil, Jericho boil, Baghdad boil, Balakh sore, Penjeh sore, Briska button (clou de Briska), Bouton de Crete and Bouton D'Orient. In the New World, the disease is known as Uta, Espundia, Chiclero's ulcer, Pain bois and forest yaws

²Visceral leishmaniasis is also known as kala-azar, black fever and Dumdum fever

³The subgenus *Sauroleishmania* includes all reptile-infecting *Leishmania* species

⁴Parasites of the genus *Endotrypanum* are restricted to Neotropical tree sloths and infect erythrocytes of their mammalian host

⁵The genus *Porcisia* includes the Neotropical porcine parasites originally described as *L. hertigi* and *L. deanei*

⁶*Leishmania enriettii* is a leishmanial parasite exclusively found in guinea pigs

⁷The word kala-azar was derived from the Hindi/Urdu word for black (kala) and the Persian word for disease (azar)

⁸Laveran won the Nobel Prize for Physiology or Medicine in 1907 for his discovery of protozoan parasites as causative agents for infectious diseases

⁹For the generic name Homer Wright used the Greek word for ulcer, ἑλκος

¹⁰Evandro Chagas was the eldest son of Carlos Chagas, who is renowned for the discovery of the causative agent of American trypanosomiasis or Chagas disease, *Trypanosoma cruzi*. Tragically, Evandro Chagas died in an air crash on the 8th of November 1940, aged 35

Abbreviations

BCE: before common era; CL: cutaneous leishmaniasis; DCL: diffuse cutaneous leishmaniasis; LCL: localised cutaneous leishmaniasis; MCL: mucocutaneous leishmaniasis; MYA: million years ago; VL: visceral leishmaniasis

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LEISHMANIASIS AND LEISHMANIA/HIV CO-INFECTION

Background of the disease

Leishmaniasis

Leishmaniasis is a parasitic infection transmitted by the bite of an infected female sandfly whose hosts are animals, such as dogs or rodents, or human beings. Leishmaniasis is a highly focal disease with widely scattered foci. The parasite may survive for decades in asymptomatic infected people, who are of great importance for the transmission since they can spread visceral leishmaniasis indirectly through the sandflies. The parasites can also be transmitted directly from person to person through the sharing of infected needles which is often the case with the *Leishmania*/HIV co-infection. The disease has four main forms, depending on the parasite species and the cellular immune system of the patient:

Cutaneous leishmaniasis produces skin lesions mainly on the face, arms and legs. Although this form is often self-healing, it can create serious disability and permanent scars. After recovery or successful treatment, cutaneous leishmaniasis induces immunity to re-infection by the species of *Leishmania* that caused the disease.

Diffuse cutaneous leishmaniasis is difficult to treat due to disseminated lesions that resemble leprosy and do not heal spontaneously. This form especially is related to a defective immune system and it is often characterized by relapses after treatment.

Mucocutaneous leishmaniasis, also called 'espundia' in South America, causes disfiguring lesions to the face; it destroys the mucous membranes of the nose, mouth and throat. Reconstructive surgery of deformities is an important part of therapy.

Visceral leishmaniasis, also known as 'kala azar', is characterized by irregular fever, weight loss, swelling of the liver and spleen and anaemia. It is the most severe form of Leishmaniasis, and is usually fatal if left untreated. The incubation period can be months or years and, unlike the cutaneous forms of leishmaniasis, it involves the internal organs. After treatment and recovery, patients may develop chronic cutaneous leishmaniasis that requires long and expensive treatment.

Leishmaniasis has a long history. Designs on pre-Colombian pottery and the existence of thousand-year old skulls with evidence of leishmaniasis prove that the disease has been present in the Americas for a long time. It has also been present in Africa and India since at least the mid-eighteenth century.⁴ Today, an estimated 12 million cases of leishmaniasis exist worldwide with an estimated number of 1.5 - 2 million new cases occurring annually; 1 - 1.5 million cases of cutaneous leishmaniasis and 500 000 cases of visceral leishmaniasis.⁵

The geographical distribution of leishmaniasis is restricted to tropical and temperate regions, the living area of the sandfly. The leishmaniasis are considered to be endemic in 88 countries (16 developed countries and 72 developing countries) on four continents. Ninety percent of cases with cutaneous forms of leishmaniasis occur in Afghanistan, Algeria, Brazil, Iran, Peru, Saudi Arabia and Syria, while ninety per cent of visceral leishmaniasis cases are found in Bangladesh, Brazil, India, Nepal and Sudan.

Visceral leishmaniasis can cause large-scale epidemics with high case fatality. For example, Western Upper Nile State in South Sudan experienced a major outbreak of visceral leishmaniasis between 1984 and 1994. This was the first epidemic in this area and therefore people were very susceptible to the disease. Because of an accumulation of risk factors such as civil unrest, disruption of health systems, malnutrition, underlying diseases and due to absence of diagnostic facilities and first line drugs at local level, the mortality rate was very high and 40 000 people were reported to have died due to the disease. Studies indicate that in some villages up to half of the population succumbed to the disease;⁶ one study suggests that during this ten-year period visceral leishmaniasis claimed 100 000 lives in a population of around 300 000 in Western Upper Nile State.⁷

There is reason to believe that the number of cases of leishmaniasis is increasing.⁸ This is partly due to man-made environmental changes which increase human exposure to the sandfly vector. Extracting timber, mining, building dams, widening areas under cultivation, new irrigation schemes, road construction in primary forests such as the Amazon, widespread migration from rural to urban areas and fast urbanization worldwide are among the main causes for an increased exposure to the sandfly. According to agencies operating clinics in the city of Kabul, Afghanistan, an estimated 270 000 cases of cutaneous leishmaniasis occurred in 1996 among the less than 2 million inhabitants of the city. ⁹ Kabul is a city where a lot of movement of people from rural to urban areas takes place. Another risk factor is the movement of susceptible populations into endemic areas, including large-scale migration of populations for economic reasons such as the development of agro-industrial projects.

Interaction between surveillance and response

Early case detection and treatment are the most important control measures for leishmaniasis. In anthroponotic leishmaniasis in which humans are the only reservoir, early detection and treatment reduces morbidity and mortality. Treatment reduces or eliminates parasite loads, and this in turn reduces transmission. Thus surveillance and control are directly linked. The main limitations to treatment are high cost and the relatively long treatment period. In severe situations such as epidemics and highly endemic areas vector control is also used. It consists of house spraying or the use of insecticide-impregnated bed nets.

For zoonotic visceral leishmaniasis, which is usually fatal if left untreated, priority is also given to the detection and treatment of human cases. Other control measures include large-scale screening and testing of dogs, the main reservoir, spraying of houses and animal shelters, and individual protection. Environmental management measures such as destroying breeding and resting sites of the vector have been recommenced for zoonotic cutaneous leishmaniasis control.

With the use of insecticide-impregnated bed nets and new tests for serological diagnosis, progress has been made in the prevention and control of leishmaniasis infection. However, better methods are still needed such as more affordable drugs with shorter treatment periods.

Generally How can I prevent leishmaniasis?

There's no vaccine or prophylactic medication available. The only way to prevent leishmaniasis is to avoid getting bitten by a sand fly.

Follow these steps to help prevent being bitten by a sand fly:

- Wear clothing that covers as much skin as possible. Long pants, long-sleeved shirts tucked into pants, and high socks are recommended.
- Use insect repellent on any exposed skin and on the ends of your pants and sleeves. The most effective insect repellants contain DEET.
- Spray indoor sleeping areas with insecticide.
- Sleep on the higher floors of a building. The insects are poor fliers.
- Avoid the outdoors between dusk and dawn. This is when sand flies are most active.
- Use screens and air conditioning indoors when possible. Using fans might make it more difficult for the insects to fly.
- Use a bed net tucked into your mattress. Sand flies are much smaller than mosquitos, so you need a tightly woven net. Spray the net with insecticide containing pyrethroid if possible.

Buy bed nets, insecticides, and repellents before traveling to high-risk areas.

House fly: Scientific name: *Musca domestica* Linnaeus (Insecta: Diptera: Muscidae)

Introduction - Distribution - Description and Life Cycle - Damage and Medical Importance - Economic Threshold - Management

Introduction

The house fly, *Musca domestica* Linnaeus, is a well-known cosmopolitan pest of both farm and home. This species is always found in association with humans or the activities of humans. It is the most common species found on hog and poultry farms, horse stables and ranches. Not only are house flies a nuisance, but they can also transport disease-causing organisms. Excessive fly populations are not only an irritant to farm workers but, when there are nearby human habitations, a public health problem could occur.

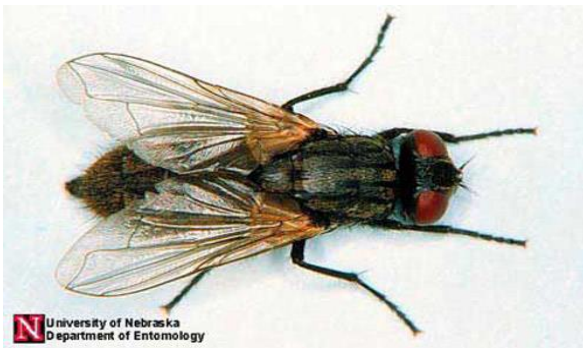


Figure 1. Adult house fly, *Musca domestica* Linnaeus. Photograph by Jim Kalisch, University of Nebraska-Lincoln.

Distribution

This common fly originated on the steppes of central Asia, but now occurs on all inhabited continents, in all climates from tropical to temperate, and in a variety of environments ranging from rural to urban. It is commonly associated with animal feces, but has adapted well to feeding on garbage, so it is abundant almost anywhere people live.

Life Cycle and Description

The house fly has a complete metamorphosis with distinct egg, larval or maggot, pupal and adult stages. The house fly overwinters in either the larval or pupal stage under manure piles or in other protected locations. Warm summer conditions are generally optimum for the development of the house fly, and it can complete its life cycle in as little as seven to ten days. However, under suboptimal conditions the life cycle may require up to two months. As many as 10 to 12 generations may occur annually in temperate regions, while more than 20 generations may occur in subtropical and tropical regions.

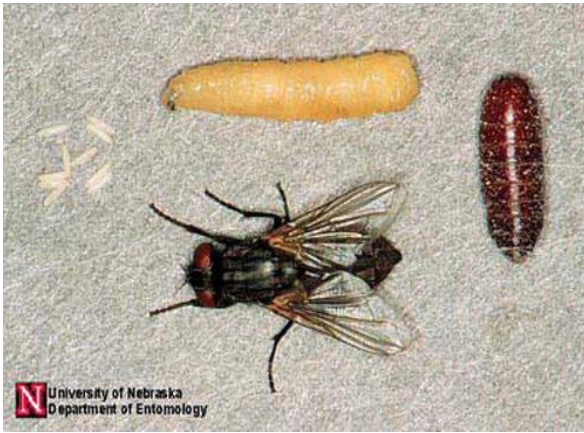


Figure 2. Life cycle of the house fly, *Musca domestica* Linnaeus. Clockwise from left: eggs, larva, pupa, adult. Photograph by Jim Kalisch, University of Nebraska-Lincoln.

Egg: The white egg, about 1.2 mm in length, is laid singly but eggs are piled in small groups. Each female fly can lay up to 500 eggs in several batches of 75 to 150 eggs over a three to four day period. The number of eggs produced is a function of female size which, itself, is principally a result of larval nutrition. Maximum egg production occurs at intermediate temperatures, 25 to 30°C. Often, several flies will deposit their eggs in close proximity, leading to large masses of larvae and pupae. Eggs must remain moist or they will not hatch.



Figure 3. Adult and eggs of the house fly, *Musca domestica* Linnaeus. Photograph by [Jerry F. Butler](#), University of Florida.

Larva: Early instar larvae are 3 to 9 mm long, typical creamy whitish in color, cylindrical but tapering toward the head. The head contains one pair of dark hooks. The posterior spiracles are slightly raised and the spiracular openings are sinuous slits which are completely surrounded by an oval black border. The legless maggot emerges from the egg in warm weather within eight to 20 hours. Maggots immediately begin feeding on and developing in the material in which the egg was laid. The larva goes through three instars and a full-grown maggot, 7 to 12 mm long, has a greasy, cream-colored appearance. High-moisture manure favors the survival of the house fly larva. The optimal temperature for larval development is 35 to 38°C, though larval survival is greatest at 17 to 32°C. Larvae complete their development in four to 13 days at optimal temperatures, but require

14 to 30 days at temperatures of 12 to 17°C. Nutrient-rich substrates such as animal manure provide an excellent developmental substrate. Very little manure is needed for larval development, and sand or soil containing small amounts of degraded manure allows for successful belowground development. When the maggot is full-grown, it can crawl up to 50 feet to a dry, cool place near breeding material and transform to the pupal stage.

Pupa: The pupal stage, about 8 mm long, is passed in a pupal case formed from the last larval skin which varies in color from yellow, red, brown, to black as the pupa ages. The shape of the pupa is quite different from the larva, being bluntly rounded at both ends. Pupae complete their development in two to six days at 32 to 37°C, but require 17 to 27 days at about 14°C). The emerging fly escapes from the pupal case through the use of an alternately swelling and shrinking sac, called the ptilinum, on the front of its head which it uses like a pneumatic hammer to break through the case.



Figure 4. Prepupa and sequence of puparia by age for the house fly, *Musca domestica* Linnaeus. Photograph by Jim Kalisch, University of Nebraska-Lincoln.

Adult: The house fly is 6 to 7 mm long, with the female usually larger than the male. The female can be distinguished from the male by the relatively wide space between the eyes (in males, the eyes almost touch). The head of the adult fly has reddish-eyes and sponging mouthparts. The thorax bears four narrow black stripes and there is a sharp upward bend in the fourth longitudinal wing vein. The abdomen is gray or yellowish with dark midline and irregular dark markings on the sides. The underside of the male is yellowish.



Figure 5. Adult house fly, *Musca domestica* Linnaeus. Photograph by Matt Aubuchon, University of Florida.

The house fly is often confused with the stable fly, *Stomoxys calcitrans* (Linnaeus), and the false stable fly, *Muscina stabulans* (Germar). All three are in the same family.

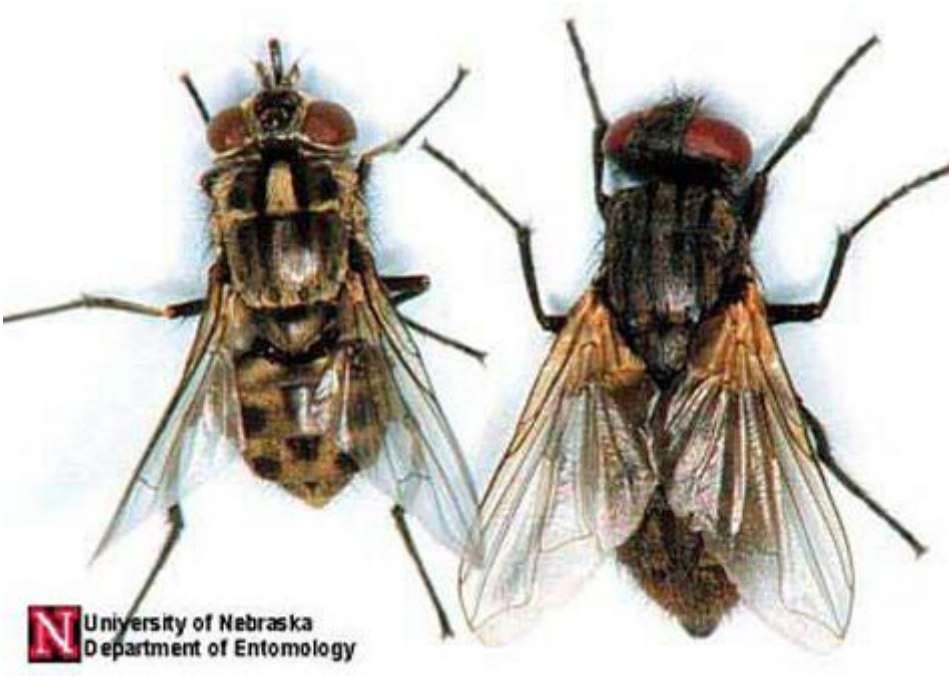


Figure 7. A dorsal comparison of adult stable fly, *Stomoxys calcitrans* (Linnaeus) (left), and house fly, *Musca domestica* Linnaeus (right). Photograph by Jim Kalisch, University of Nebraska-Lincoln.

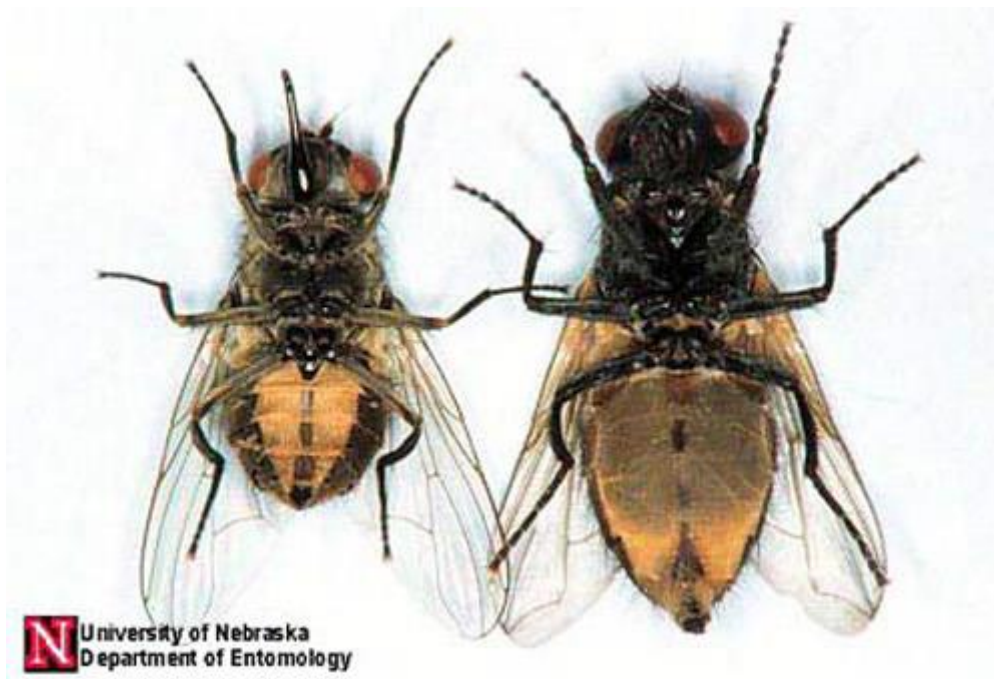


Figure 8. A ventral comparison of adult stable fly, *Stomoxys calcitrans* (Linnaeus) (left), and house fly, *Musca domestica* Linnaeus (right). Photograph by Jim Kalisch, University of Nebraska-Lincoln.

Adults usually live 15 to 25 days, but may live up to two months. Without food, they survive only about two to three days. Longevity is enhanced by availability of suitable food, especially sugar. Access to animal manure does not lengthen adult life and they live longer at cooler temperatures. They require food before they will copulate, and copulation is completed in as few as two minutes or as long as 15 minutes. Oviposition commences four to 20 days after copulation. Female flies need access to suitable food (protein) to allow them to produce eggs, and manure alone is not adequate. The potential reproductive capacity of flies is tremendous, but fortunately can never be realized. Scientists have calculated that a pair of flies beginning reproduction in April may be progenitors, under optimal conditions and if all were to live, of 191,010,000,000,000,000 flies by August.

The flies are inactive at night, with ceilings, beams and overhead wires within buildings, trees, and shrubs, various kinds of outdoor wires, and grasses reported as overnight resting sites. In poultry ranches, the nighttime, outdoor aggregations of flies are found mainly in the branches, and shrubs, whereas almost all of the indoor populations generally aggregated in the ceiling area of poultry houses. According to a study conducted in Texas, USA, breeding site suitability (in descending order), was horse manure, human excrement, cow manure, fermenting vegetable matter, and kitchen waste. However, another study found that structures containing swine, horse, sheep, cattle, and poultry varied in fly abundance, with swine facilities containing the most and poultry the least. Fruit and vegetable cull piles, partially incinerated garbage, and incompletely composted manure also are highly favored sites for breeding.

Damage and Medical Importance

Flies commonly develop in large numbers in poultry manure under caged hens, and this is a serious problem requiring control. Although this fly species does not bite, the control of *Musca domestica* is vital to human health and comfort in many areas of the world. The most important damage related with this insect is the annoyance and the indirect damage produced by the potential transmission of pathogens (viruses, bacteria, fungi, protozoa, and nematodes) associated with this fly. Pathogenic organisms are picked up by flies from garbage, sewage and other sources of filth, and then transferred on their mouthparts, through their vomitus, feces and contaminated external body parts to human and animal food.

Of particular concern is the movement of flies from animal or human feces to food that will be eaten uncooked by humans. Also, when consumed by flies, some pathogens can be harbored in the mouthparts or alimentary canal for several days, and then be transmitted when flies defecate or regurgitate. In situations where plumbing is lacking, such as open latrines, serious health problems can develop, especially if there are outdoor food markets, hospitals, or slaughter houses nearby. Among the pathogens commonly transmitted by house flies are *Salmonella*, *Shigella*, *Campylobacter*, *Escherichia*, *Enterococcus*, *Chlamydia*, and many other species that cause illness. These flies are most commonly linked to outbreaks of diarrhea and shigellosis, but also are implicated in transmission of food poisoning, typhoid fever, dysentery, tuberculosis, anthrax, ophthalmia, and parasitic worms.

Economic Threshold

The threshold density for determining when to control flies depends on the area where the control measures will be taken. In general, in homes the threshold is very low and control actions are taken with few flies. The complaint threshold density of the house fly at waste management sites may be 150 individuals per flypaper per 30 minutes. House flies are monitored with baited traps, sticky ribbons, or spot cards on livestock facilities. Spot cards are 3-inch by 5-inch white index cards attached to fly resting surface. A minimum of five cards should be placed in each animal facility and left in place for seven days. A count of 100 or more fecal or vomit spots per card per week indicates a high level of fly activity and a need for control. Tolerance of flies depends greatly on circumstances. In sensitive environments such as food preparation and packing facilities, restaurants, and hospitals, even small numbers of flies cannot be tolerated. In the context of livestock or poultry production, however, some flies are inevitable. Serious problems occur when cities or suburban development occur near poultry production facilities, as residents usually will not tolerate the large numbers of flies emanating from such facilities.

Management

The more commonly used control measures for house flies are sanitation, use of traps, and insecticides, but in some instances integrated fly control has been implemented. The use of biological control in fly management is still at a relatively early stage.

Sanitation or cultural control. Good sanitation is the basic step in any fly management program. Food and materials on which the flies can lay eggs must be removed, destroyed as a breeding medium, or isolated from the egg-laying adult. Since the house fly can complete its life cycle in as little as seven days, removal of wet manure at least twice a week is necessary to break the breeding cycle. Wet straw should not be allowed to pile up in or near buildings. Since straw is one of the best fly breeding materials, it is not recommended as bedding. Spilled feed should not be allowed to accumulate. Ordinarily, fly control from 1 to 2 km around a municipality prevents house fly infestations. Killing adult flies may reduce the infestation, but elimination of breeding areas is necessary for good management. Garbage cans and dumpsters should have tight-fitting lids and be cleaned regularly. Dry garbage and trash should be placed in plastic garbage bags and sealed up. All garbage receptacles should be located as far from building entrances as possible.

For control at waste disposal sites, refuse should be deposited onto the same area as inorganic wastes to deteriorate the capacity of breeding resources, or the disposed refuse should be covered with inorganic wastes (15 cm thickness). Around homes and businesses, screening or covering of windows, doors or air doors, and trash containers proves useful in denying access of flies to breeding sites. Packaging household trash in plastic bags, and burying trash under at least 15 cm of soil and in sanitary landfills also helps to eliminate breeding.

In agricultural areas, manure can be scattered over fields so that it quickly dries and becomes unsuitable for egg and larval survival. Composting of manure can be effective if the compost is properly maintained, including regular turning. Manure can also be liquefied and stored in lagoons anaerobically, though at some point the solids need to be separated.

Traps. Fly traps may be useful in some fly control programs if enough traps are used, if they are placed correctly, and if they are used both indoors and outdoors. House flies are attracted to white surfaces and to baits that give off odors. Indoors, ultraviolet light traps collect the flies inside an inverted cone or kill them with an electrocuting grid. One trap should be placed for every 30 feet of wall inside buildings, but not placed over or within five feet of food preparation areas. Recommended placement areas outdoors include near building entrances, in alleyways, beneath trees, and around animal sleeping areas and manure piles. Openings to buildings should be tightly screened with standard window screen, thereby denying entrance to flies.

Traps can be baited with molasses, sugar, fruit or meat, and often are used in combination with a device that captures the attracted flies. The sex pheromone (Z)-9-tricosene also functions as an aggregation pheromone, and is called muscalure. Muscalure is formulated with sugar as a

commercially-available fly bait for local population suppression, as well as an enhancement for population monitoring.

Ultraviolet light traps can be used to assess population levels, but also serve as a non-chemical control technique that can be used indoors in both agricultural and non-agricultural areas. They normally function by electrocuting flies that enter the trap, though those used in restaurants typically have a sticky panel. Flies do not orient to traps from a great distance, so several are normally needed for them to be effective. Placement should include within 4 to 8 m of entryways, and within 1.5 m of the floor, to take advantage of fly flight behavior. They should be operated continuously, although they are most effective when the room lights are off.

Biological control. With the increasing incidence of insecticide resistant house fly populations, rising costs of insecticides and a growing public concern about actual or potential problems associated with insecticides, interest in alternative house fly control strategies has increased.

Natural biological suppression of the house fly results primarily from the actions of certain chalcidoid wasps (Hymenoptera: Pteromalidae), of which many species have been associated with house fly around the world. Among the more important are *Muscidifurax* and *Sphalangia* spp. Ichneumonids and other parasitoids, as well as some predatory insects (especially histerids [Coleoptera: Histeridae] and staphylinids [Coleoptera: Staphylinidae]), also contribute to fly mortality, but under optimal fly breeding conditions the house fly quickly builds to high numbers. The more important in poultry facilities are the wasps *Muscidifurax raptor* and *Sphalangia cameroni*. Leaving a layer of old manure in the pits when manure is removed might enhance or stabilize the suppression of the house flies densities by parasitoids and predators.

Augmentative biological control (periodic release of parasitoids during winter and spring, and following manure removal) using insectary-reared parasitoids has been quite successful in some dairies, feedlots and poultry house situations. The species most often released for biological suppression in North America are *Muscidifurax raptor*, *Muscidifurax raptorellus*, *Sphalangia endius*, and *Sphalangia nigroaenea*. These different species function better under different conditions, some performing better under cooler or warmer conditions, others parasitizing flies near the surface or deeper in the pupation medium. In North Carolina, tests showed that when house fly populations occur near the surface on the drier periphery of the manure, the conditions favor parasitism by *Muscidifurax raptor*. When the flies pupate at greater depths the conditions favor *Sphalangia cameroni*. In North Florida, releases conducted with *Sphalangia endius* showed that they could successfully parasitize pupae, both above and below the soil surface. The larva of the black dump fly, *Hydrotaea* (= *Ophyra*) *aenescens*, is also regaining popularity as a biological control agent for controlling house flies on poultry farms without the use of pesticides. The adult black dump fly is similar in appearance to the adult house fly (Hogsette and Jacobs 2003).

Integrated fly control. Integrated fly control programs for caged-poultry houses are based on the following strategy:

- selective applications of insecticides against the adult,
- start insecticide control measures early in the spring before flies appear and repeat as frequently as needed through the warm months, and
- the manure is left undisturbed throughout the warm months when fly breeding may occur. The manure should be removed once very early in the spring before any flies appear.

Chemical control. When the house fly is a major pest in commercial egg production facilities, the control of this insect is by the application of adulticides or larvicides to directly or indirectly suppress adult densities. Residual wall sprays can be applied where the flies congregate. It is important to manage potential insecticide resistance by rotating formulations with different modes of action.

Outdoors, the control of flies includes the use of boric acid in the bottom of dumpsters, treatment of vertical walls adjacent to dumpsters and other breeding sites with microencapsulated or wettable powder formulation, and the use of fly baits near adult feeding sources.

Manure can also be treated with an insecticide, though this method is highly discouraged as it interferes with biological control of flies, often resulting in a rebound of the fly population. More commonly, insecticides (especially insect growth regulators) can be fed to livestock, and residual insecticide in the manure inhibits fly breeding. In animal facilities, insecticides are often applied to the favored resting places of adults, or bait stations established to poison adults with either solid or liquid formulations. Continuous exposure of flies to insecticides has led to development of insecticide resistance to many insecticides.

Indoors, the control of flies includes automatic misters, fly paper, electrocuting and baited traps that can be used in milk rooms and other areas of low fly numbers.

Review Article

Human louse-transmitted infectious diseases

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Abstract

Several of the infectious diseases associated with human lice are life-threatening, including epidemic typhus, relapsing fever, and trench fever, which are caused by *Rickettsia prowazekii*, *Borrelia recurrentis*, and *Bartonella quintana*, respectively. Although these diseases have been known for several centuries, they remain a major public health concern in populations living in poor-hygiene conditions because of war, social disruption, severe poverty, or gaps in public health management. Poor-hygiene conditions favour a higher prevalence of body lice, which are the main vectors for these diseases. Trench fever has been reported in both developing and developed countries in populations living in poor conditions, such as homeless individuals. In contrast, outbreaks of epidemic typhus and epidemic relapsing fever have occurred in jails and refugee camps in developing countries. However, reports of a significantly high seroprevalence for epidemic typhus and epidemic relapsing fever in the homeless populations of developed countries suggest that these populations remain at high risk for outbreaks of these diseases. Additionally, experimental laboratory studies have demonstrated that the body louse can transmit other emerging or re-emerging pathogens, such as *Acinetobacter baumannii* and *Yersinia pestis*. Therefore, a strict survey of louse-borne diseases and the implementation of efficient delousing strategies in these populations should be public health priorities.

Keywords: *Bartonella quintana*, body louse, *Borrelia recurrentis*, epidemic typhus, homelessness, lice, refugees, relapsing fever, *Rickettsia prowazekii*, trench fever

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Introduction

There are more than 3000 species of lice. Among these, humans constitute the preferred host for only two species: *Pediculus humanus* and *Phthirus pubis* (pubic lice). *P. humanus* includes two morphotypes, *P. humanus* morphotype capitis (head lice) and *P. humanus* morphotype corporis (body lice). Head, body and pubic lice live on the head, in clothing, and in the pubic area, respectively. It has been suggested that the head louse is the ancestor of *P. humanus*, and that the body louse originated from the head louse when humans began to wear clothes [2]. In addition, it has been recently proposed that humans with both poor hygiene and head louse infestations provide an opportunity for head louse variants to ingest a greater amount of blood, colonize clothing,

and differentiate into body lice [3]. Louse infestations have been prevalent among humans for thousands of years [4], and they still affect hundreds of millions of people worldwide each year [5]. In this article, we review the transmissible infectious diseases associated with human louse infestation.

Epidemiology of Human Lice

The louse life cycle begins when a female louse lays eggs, called nits, on hair follicles, folds of clothing, or on the base of the pubic hair shaft, according to the species of louse. A female louse lays approximately eight eggs a day, and can lay up to 300 eggs during her lifetime. In a favourable environment with a constant temperature, eggs will hatch after

6–10 days into nymphs. Lice mature into adults after 10 days, and live for approximately 1–3 months. Lice are obligate host-specific blood-sucking insects that typically feed five times a day. When head and body lice are separated from their host, they die in less than 24 h and 48 h, respectively. Humidity and temperature are also critical for louse survival. For example, body lice prefer humidity ranging from 70% to 90%, and temperatures between 29LC and 32LC; they cannot survive when humidity drops below 40% or when the temperature is greater than 50LC [6,7].

Clinical Characteristics of Louse Infestations

Louse infestation, called pediculosis, is very contagious and easily transmitted by close body-to-body contact or contact with infested linen, brushes, or clothes, according to the species of louse. Pediculosis capitis, caused by head lice, is the most common louse infestation; it particularly affects school-children 3–11 years of age [5]. It has been demonstrated that pediculosis capitis is associated with low socio-economic status of the parents (unemployed or manual workers), family size (four or more children), and clustering of children in classes and schools [8]. Its clinical hallmark is scalp pruritus. Diagnosis is established by the identification of viable adult lice, nymphs or, more easily, of nits glued to the hair on the scalp (Fig. 1) [5]. Pediculosis corporis, caused by body lice, represents a major public health concern. It is strongly associated with close body-to-body contact, and occurs only when clothes are not changed or washed regularly. These conditions are more prevalent in individuals living in crowded and unhygienic environments, such as refugee camps or shelters for the homeless [5–7]. During the civil wars in Burundi,



FIG. 1. Nits glued to the hair on the scalp. The immature lice are seen through the nit membrane. Inverted light microscope.

Rwanda and Zaire in the 1990s, the prevalence of louse infestations reached 90–100% [9]. In sheltered homeless populations in developed countries, the reported prevalence of body louse infestation ranged from 11% to 22% [10,11], with rates up to 80% being observed in the poorest-hygiene conditions. Clinical manifestations include generalized pruritus associated with scratching; lesions are typically localized to the neck, thorax, waist, and ankles [5]. Diagnosis is based on a finding of adult lice and, more importantly, eggs in clothing seams (Fig. 2). Simultaneous infestation with both head and body lice has been recently reported in 4.3% of homeless individuals seen in emergency settings in San Francisco, CA [12], and in 59% of street children in Nepal [13]. Pubic lice are typically transmitted sexually, and transmission cannot be prevented by condom use. Pubic infestation predominantly results in pubic itching [5].

Louse-borne Infectious Diseases

Of the three types of louse that affect humans, only body lice act as vectors for human pathogens. Body lice are known to transmit epidemic typhus, relapsing fever, and trench fever, diseases caused by *Rickettsia prowazekii*, *Borrelia recurrentis*, and *Bartonella quintana*, respectively [6,7]. These three pathogens have been recovered experimentally in body louse faeces [6,14,15], suggesting that the transmission of these organisms occurs through the contamination of bite sites, conjunctivae, and mucous membranes, either by faeces from infected body lice or by crushed infected louse bodies. Louse-borne diseases are associated with a high prevalence of body louse infestation, and have recently re-emerged in jails and refugee camps in central and eastern Africa [9], in



FIG. 2. Body lice and eggs in clothing seams.

rural communities in the Peruvian Andes [16], in rural louse-infested populations in Russia [17], and in homeless populations living in poor-hygiene conditions in developed countries [10,11,18–20]. Head and pubic lice have been found to be competent vectors in laboratory settings [6,21]. *B. quintana* DNA has been detected in head lice from Nepalese slum children [22], Ethiopian street beggars [23], and homeless adults in San Francisco [12]. It has also been detected in head louse nits from a homeless man in Marseilles (France)

[26]. However, *B. quintana* DNA was not detected in head lice collected from schoolchildren in France and seven other countries [25,26]. Factors contributing to the presence of

B. quintana in head lice are debated [25], and could include genotype C head lice and high altitude (>2121 m) [23,27]. Currently, head and pubic lice are not considered to be vectors for human pathogens.

Epidemic typhus

Epidemic typhus is caused by *R. prowazekii*, an obligate intra-cellular bacterium. The mortality rate of epidemic typhus varies from 0.7% to 60% for untreated cases. Lice become infected with *R. prowazekii* when they feed on bacteraemic individuals; however, lice die within 1 week after becoming infected. Humans with self-limiting infections that fail to clear the bacteria and exhibit bacterial persistence in adipose tissue endothelial cells constitute the main reservoir of *R. prowazekii* [6,28]. Under stress, infection recrudescence can occur years after the primary infection, resulting in a relatively mild bacteraemic illness called Brill–Zinsser disease. Infection recrudescence can initiate the re-emergence of a focused epidemic if body louse infestations are prevalent [6,28]. In the USA, *R. prowazekii* has also been isolated in flying squirrels, *Glaucomys volans volans*, indicating the existence of another reservoir [29]. However, the mechanism by which *R. prowazekii* is transmitted from flying squirrels to humans remains unknown. Inhalation of aerosolized infected faeces from lice of flying squirrels has been suggested [28,29]. Outbreaks of epidemic typhus have generally been associated with war, famine, refugee camps, cold weather, and gaps in public health management. Recent outbreaks of epidemic typhus were reported in the 1990s in Burundi and Russia [9,17]. No outbreaks of epidemic typhus have been recently identified in wealthy developed countries. However, a case of Brill–Zinsser disease [30], a sporadic case of imported typhus from Algeria [31], significantly high anti-*R. prowazekii* antibody titres within a homeless population and an autochthonous case of epidemic typhus in a homeless individual [32] have been reported in Marseilles, France. Anti-*R. prowazekii* antibodies were also detected in the sera of two of 176 homeless individuals assessed in

Houston, Texas [33]. These reports suggest that the disease is likely to re-emerge at any time in homeless populations.

Epidemic typhus is a life-threatening, acute exanthematic febrile illness with a broad range of clinical manifestations [9,28]. Any severe outbreak of an unexplained fever in unhygienic environments, such as jails, chronically poor countries, and cold countries, or during civil wars, social collapses, and natural disasters, may indicate epidemic typhus. After an incubation period of 10–14 days, patients usually experience 1–3 days of malaise associated with fever and multiple painful symptoms, which are then followed by the development of rashes (20–40% of patients), neurological manifestations (80%), respiratory manifestations (38–70%), and shock (7%). Relevant laboratory findings include thrombocytopenia (40%), elevated transaminase levels (63%), and renal dysfunction. In the pre-antibiotic era, the mortality rates were estimated to reach up to 60%; currently, the mortality rate is approximately 4% in correctly treated patients. In the most extreme situations of malnutrition, mortality rates higher than 50% may occur [28]. Patients with Brill–Zinsser disease exhibit milder clinical manifestations and a shorter disease duration. However, death can occur in some cases [6,28].

Epidemic typhus is microbiologically diagnosed with a serology-based microimmunofluorescence test for the detection of rickettsial antibodies, and western blot analysis combined with cross-adsorption tests for the distinction between *R. prowazekii* and *Rickettsia typhi*. Patients with Brill–Zinsser disease have increased IgG antibodies to *R. prowazekii* but have no specific IgM antibodies. Other diagnostic methods include culture with a shell-vial assay that can be used to isolate *R. prowazekii* from clinical specimens (blood or skin biopsy) and quantitative real-time PCR assays that target the *R. prowazekii*-specific *gltA* gene. This PCR technique can be utilized to assess samples from various sources [28].

Treatment of epidemic typhus is based on the administration of tetracycline and chloramphenicol. Treatment for 5 days (or for 2–4 days after defervescence) has been recommended [28] for each antibiotic. In outbreak situations, a single 200-mg oral dose of doxycycline can be effective [9].

Epidemic relapsing fever

Epidemic relapsing fever is a louse-borne infection caused by the spirochete *Borrelia recurrentis* that affected several million people worldwide during the first half of the 20th century, particularly during the world wars [6]. Although it has disappeared in many regions around the world, it is still a major public health concern in northern and eastern Africa [6,34]. It is the seventh most common cause (up to 27%) of hospital admission and the fifth most frequent cause of death in the highlands of Ethiopia [35]. Antibodies against *Borrelia recurrentis*

have also been detected in a rural Andean community in Peru [16]. Additionally, we observed a significant increase in the prevalence of anti-*Borrelia recurrentis* antibodies in home-less populations in Marseille in 2002, suggesting that a small, unnoticed outbreak occurred in this population [18]. As with epidemic typhus, relapsing fever predominantly affects populations living in poor-hygiene conditions where body louse infestations are prevalent [6,18].

Humans constitute the only known reservoir and host of *Borrelia recurrentis*. After becoming infected by ingesting an infected blood meal, a louse remains infected throughout its lifetime; however, it cannot transmit *Borrelia* to its progeny. Modes of *Borrelia recurrentis* transmission are similar to those for *R. prowazekii*. However, *Borrelia recurrentis* is able to penetrate and infect intact mucosa and skin surfaces [6].

The illness begins abruptly with a high-grade fever, pain, anorexia, dry cough, and fatigue. Complications can occur, including skin and mucosal haemorrhaging; neurological, liver and renal involvement; and splenic rupture. Jaundice is a diagnostic clue that suggests relapsing fever among louse-borne diseases [6]. Following a primary potentially fatal episode, the disease is predominantly characterized by a series of relapses that are less severe and shorter in duration, and occur at intervals of 7 or 10 days. Common diagnostic methods include the detection of *Borrelia* in Giemsa-stained blood films and PCR assays. The death rate varies from 10% to 40% in untreated patients, and from 2% to 4% in patients treated with antibiotics such as doxycycline or erythromycin. However, in up to 75% of patients, treatment can result in the Jarish–Herxheimer reaction; this reaction is particularly prevalent in patients over 14 years of age [7].

Trench fever

Trench fever, which is caused by the facultative intracellular Gram-negative bacterium *B. quintana*, is a old disease. *B. quintana* DNA was detected in the dental pulp of a 4000-year-old man [36]. Recent identification of *B. quintana* DNA in lice found in a mass grave of Napoleon's soldiers in Lithuania suggests that many of the soldiers were affected by trench fever

[33]. The name 'trench fever' was chosen because the disease was first described in both Allied and German troops crowded into trenches during World War I [6]. It has been estimated that trench fever affected several million people worldwide during the two world wars, especially in Russia and on the Eastern, Central and Western European fronts [6,7]. The incidence of trench fever dramatically decreased after World War II; however, in the early 1990s, it was recognized as a major re-emerging infectious disease in urban homeless populations of developed countries who have poor living conditions char-

acterized by extreme poverty, lack of hygiene, and exposure to extremely low temperatures [9,18–20].

B. quintana is predominantly transmitted to humans by the body louse via transmission routes similar to those of *R. prowazekii* and *Borrelia recurrentis* [6]. Humans constitute the natural reservoir of the bacterium, which persists in erythrocytes and erythroblasts [38]. Nevertheless, *B. quintana* has been recently detected in cat fleas, cat dental pulp, and in a patient who owned a cat and sought treatment for chronic adenopathy [39–41]; these findings suggest that other possible vectors and transmission modes similar to those of *Borrelia henselae*, the aetiological agent of cat scratch disease, may exist. *B. quintana* was also detected by PCR in *Ixodes pacificus* adult ticks collected in California [42]. The endothelial cell tropism of *B. quintana* frequently results in the development of angioproliferative lesions [6,43].

Trench fever results from a primary infection with *B. quintana* [6,43]. The incubation period typically varies from 15 to 25 days, but can be reduced to 6 days in experimental infections. The most frequent presentation is the acute onset of a high-grade fever, headache, dizziness, and characteristic shin pain. The first fever episode can last for between 2 and 4 days. Occasionally, the primary episode is followed by a relapse every 4–5 days, giving it the name of 'quintan fever'. Although trench fever often results in prolonged disability, no deaths have been reported [6,43].

Other clinical presentations have been reported, including chronic bacteraemia. We found chronic *B. quintana* bacteraemia in 5.4% of 930 sheltered homeless individuals in Marseille. In our experience, chronic bacteraemia can last for up to 78 weeks [17,43]. A link between chronic bacteraemia and endocarditis has not yet been established. However, *B. quintana* endocarditis was first reported in three homeless men in France [44]. It is most often observed in chronic alcoholic homeless individuals who have been exposed to body lice and do not have a previously described valvulopathy. Because the disease is typically indolent and blood culture results are usually negative when stopped on day 8, diagnosis is often delayed, resulting in a higher mortality rate than for infectious endocarditis caused by other pathogens [43]. Bacillary angiomatosis is a vascular proliferative disease that most often involves the skin; however, it can also involve other organs, such as the spleen or liver. The disease was first described in human immunodeficiency virus-infected patients and organ transplant recipients, but in rare circumstances it can also affect immunocompetent patients. Bacillary angiomatosis is caused by both *B. quintana* and *Borrelia henselae* [6,43]. *B. quintana*-induced lymphadenopathy has also been reported on the basis of isolation of *B. quintana* from blood cultures and bone marrow biopsies [41].

The microbiological diagnosis of *B. quintana* infections can be achieved through the use of serology-based indirect immunofluorescence assays, molecular biological assays (PCR), and immunohistochemical tests; for these serological tests, western blot analysis and cross-adsorption are performed to avoid cross-reactions with other *Bartonella* species, *Coxiella burnetii*, and *Chlamydia pneumoniae*. When *B. quintana* infection is suspected, serological testing (IgG titres of >1/50 indicate *Bartonella* infection) and a blood culture should be performed. The most efficient culture method for *B. quintana* isolation is subculturing of blood culture broth onto agar medium. Subcultures are usually positive by 14 days, but it can take as long as 45 days to obtain a result [45]. When endocarditis is suspected (IgG titres of >1/800), culture on shell vials, immunohistochemical tests and PCR analysis should be performed on cardiac valve samples. These tests should be performed on skin biopsy specimens when bacillary angiomatosis is suspected [43,45].

Antibiotic therapy for treatment of *B. quintana* in humans is a challenge. The recommended regimen for patients with chronic bacteraemia is a combination of gentamicin (3 mg/kg intravenously once daily for 14 days) and doxycycline (200 mg orally once daily) for 28 days; for patients with endocarditis, this regimen is extended to 42 days [46].

Other Louse-associated Diseases

The role of body lice in the transmission of other bacterial human pathogens is still under debate. *Acinetobacter baumannii* DNA was detected in 21% of 622 lice collected worldwide [45], and in 33% of head lice collected from 245 children in 44 schools in Paris (France) [25], demonstrating that this bacterium is commonly found in human body lice. However, to date, no *A. baumannii* infections transmitted by a body louse have been reported. Since *Yersinia pestis*, the aetiological agent of plague, was recovered from a body louse collected from a septicemic patient during a familial plague outbreak in southern Morocco in the 1940s [48], the role of lice in plague transmission has been strongly suspected. Although louse-mediated plague transmission has been experimentally demonstrated in our laboratory [49], direct louse-bite transmission has yet to be demonstrated in humans; this mode of transmission for plague needs to be further studied [7].

Delousing

The best way to control louse-borne diseases is delousing. Efficient delousing methods include: regularly changing the

clothing, including underwear; boiling infested clothes and linens; and the use of insecticides and ivermectin for infected persons. However, all of these methods were found to be inefficient when applied to socio-economically deprived individuals living in homeless shelters, where delousing still remains a challenge [7].

Conclusion

To date, there are three known louse-borne diseases: epidemic typhus, epidemic relapsing fever, and trench fever. These infections particularly affect populations living in poor-hygiene conditions where body louse infestations are prevalent. Whereas epidemic typhus and epidemic relapsing fever are particularly prevalent in vulnerable populations in developing countries, trench fever is common worldwide, especially in homeless individuals. Regular surveys of these populations and the implementation of efficient delousing strategies are necessary to prevent major epidemics of known louse-borne diseases or other potentially emerging louse-borne pathogens, such as *A. baumannii* and *Y. pestis*. Efficient delousing methods include regularly changing the clothing, boiling infested clothes and linens, and the use of insecticides and ivermectin for infected persons. In addition, in an epidemic typhus outbreak, a single 200-mg oral dose of doxycycline should be used.

Author Contributions

S. Badiaga and P. Brouqui conceived and designed the review. S. Badiaga conducted the literature search and wrote the drafts of the review. P. Brouqui critically revised all of the draft.

Transparency Declaration

We declare no conflicts of interest.

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CHAPTER -5

Cockroaches

Unhygienic scavengers in human settlements

Cockroaches are among the most common pests in many homes and other buildings. At night they search for food in kitchens, food storage places, rubbish bins, drains and sewers. They are pests because of their filthy habits and bad smell. Some people may become allergic to cockroaches after frequent exposure. Cock-roaches can sometimes play a role as carriers of intestinal diseases, such as diarrhoea, dysentery, typhoid fever and cholera.

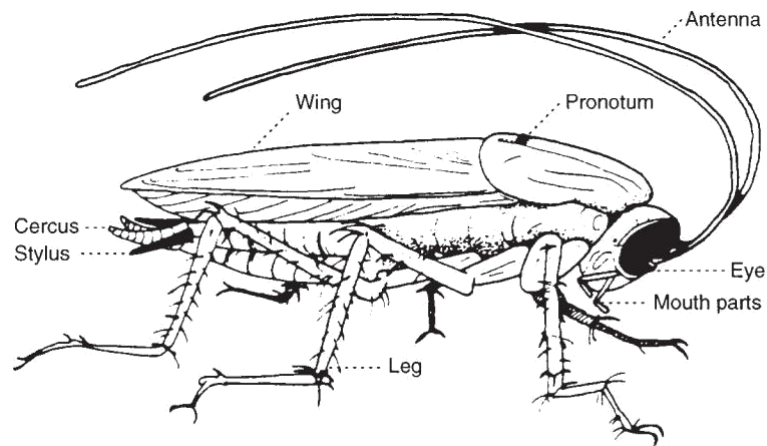
Biology

Cockroaches are insects, flattened from top to bottom, usually with two pairs of wings folded flat over the back (Fig. 5.1). Most species rarely fly but they walk very fast. The colour usually varies from light brown to black. The species vary from 2–3 mm to over 80 mm in length. Of over 3500 identified species only a few are of importance to people because they have adapted to living in buildings. The most common species are:

1. *Periplaneta americana*, the American cockroach, which occurs around the world. It is 35–40 mm in length and is a shiny reddish to chocolate brown colour (Fig. 5.2a). The egg case measures 8–10 mm and contains 16 eggs.
2. *Periplaneta australasiae*, the Australian cockroach, which occurs mainly in tropical and subtropical areas. It is similar to the American cockroach, but smaller (31–37 mm long) and darker (Fig. 5.2b). It has a pale yellow stripe on each forewing extending for about one-third its length. The egg case contains about 22–24 eggs.
3. *Blatta orientalis*, the Oriental cockroach, found mainly in cool temperate regions. It is blackish and 20–27 mm long (Fig. 5.2c). The egg case is 10–12 mm long and contains 16–18 eggs.
4. *Supella longipalpa*, the brown-banded cockroach, which occurs around the world. It is 10–14 mm long and has yellow and brown bands (Fig. 5.2d). The egg case is 4–5 mm in length and contains about 16 eggs.
5. *Blattella germanica*, the German cockroach, found in most parts of the world. It is light yellowish brown and 10–15 mm in length, making it one of the smallest domestic cockroaches (Fig. 5.2e). The female usually carries the egg case until shortly before the young come out. The egg case is light in colour, about 7–9 mm long and contains about 40 eggs.

Life cycle

Cockroaches are relatively primitive, having only three stages in their life cycle: egg, nymph and adult (Fig. 5.3). The female deposits its eggs in groups surrounded by a leathery, bean-shaped egg case or capsule called an ootheca. Some



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Fig. 5.1
Side view of a cockroach (*Blattella germanica*) (© WHO).

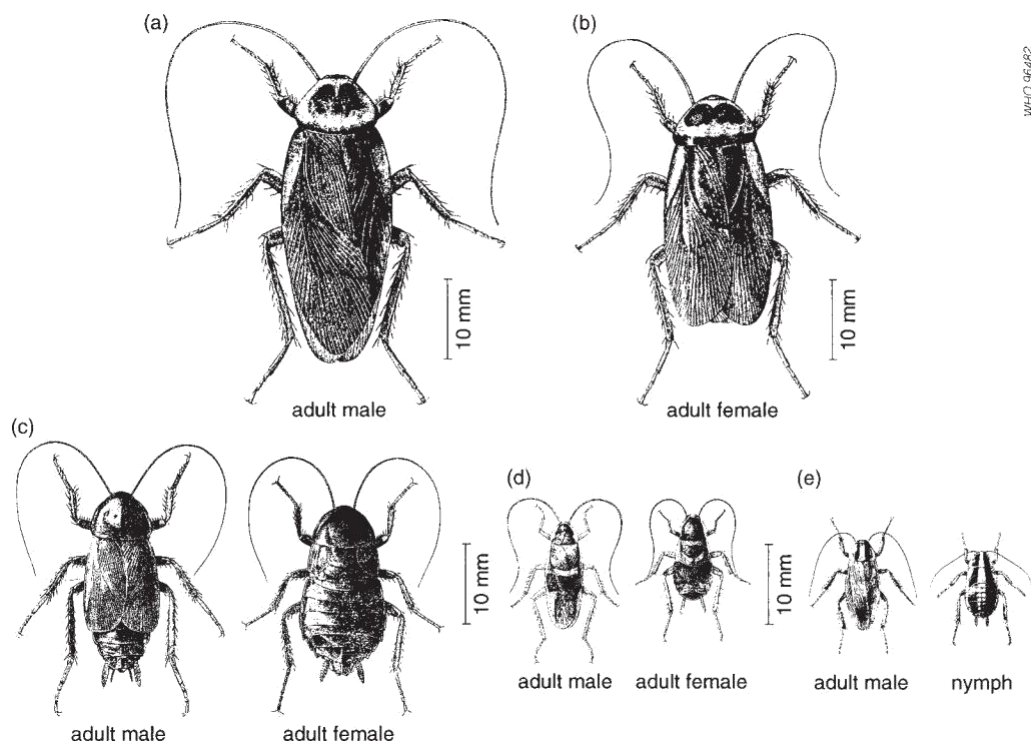
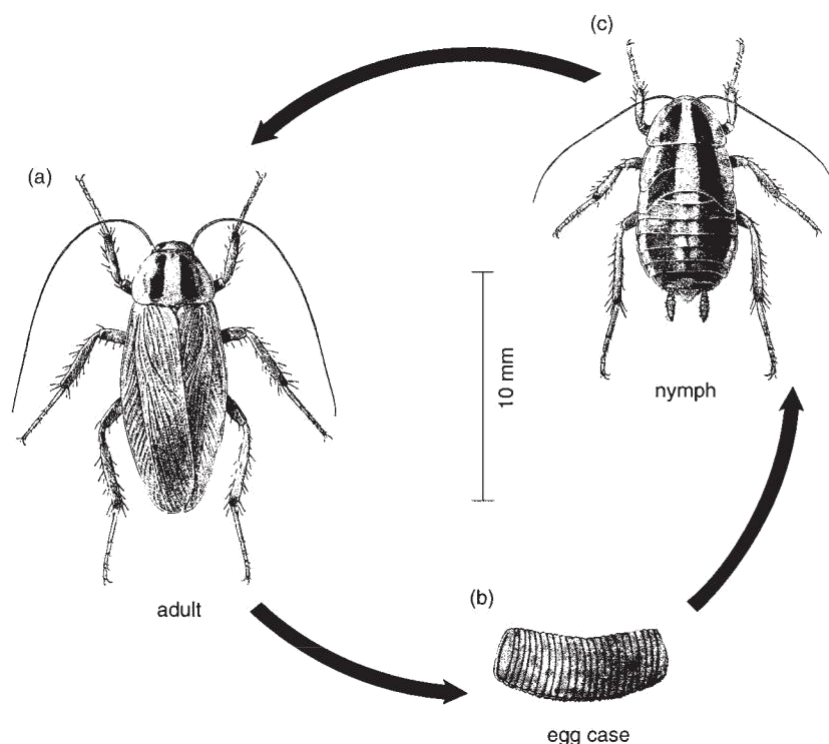


Fig. 5.2
The most common cockroach species: (a) American cockroach, *Periplaneta americana*; (b) Australian cockroach, *Periplaneta australasiae*; (c) Oriental cockroach, *Blatta orientalis*; (d) brown-banded cockroach, *Supella longipalpa*; (e) German cockroach, *Blattella germanica* (by courtesy of the Natural History Museum, London).

**Fig. 5.3**

Life cycle of the German cockroach (by courtesy of the Natural History Museum, London).

species, such as the German cockroach, carry the ootheca for several weeks attached to the back end of the body. Most others deposit the ootheca after one or two days. Oothecae are very distinctive and can frequently be used to determine the species present. Depending on the species, temperature and humidity, the eggs hatch after 1–3 months.

The young cockroaches, or nymphs, are wingless, and usually only a few millimetres long; they are white on hatching but darken within a few hours. They grow in stages by repeatedly shedding the cuticle or skin. They are fully grown after several months to more than a year, depending on the species. The adults may or may not possess wings, consisting of one outer leathery pair beneath which is folded a membranous pair.

Behaviour

Pest cockroaches live in close association with people (1, 2). They are tropical in origin but in the temperate zones most species live in parts of houses and other buildings where warmth, moisture and food are adequate. Cockroaches usually live in groups. They are mostly active at night; in the daytime they hide in cracks and crevices in walls, door frames and furniture, and in secure places in bathrooms, cupboards, steam tunnels, animal houses, basements, televisions, radios and other

electric devices, drains and sewer systems. If the lights are turned on in an infested kitchen at night the cockroaches will run from dishes, utensils, working surfaces and the floor towards shelter.

**Fig. 5.4**

Uncovered garbage bins offer an excellent environment for cockroaches to develop (© WHO).

Cockroaches eat a great variety of food, including all food used for human consumption (Fig. 5.4). They prefer starchy and sugary materials. They sip milk and nibble at cheese, meats, pastry, grain products, sugar and sweet chocolate. They also feed on cardboard, book bindings, ceiling boards containing starch, the sized inner lining of shoe soles, their own cast-off skins, dead and crippled cockroaches, fresh and dried blood, excrement, sputum, and the fingernails and toenails of babies and sleeping or sick persons.

Dispersal

Mass migrations have been reported for some species, apparently resulting from overcrowding. The migrants move into new areas by crawling or flying. They commonly enter houses in boxes of bottled drinks and bags of potatoes, onions or other foodstuffs that have become infested in poorly maintained foodstores. Long-distance transportation of the pests can occur on aircraft, ships or other vehicles.

Public health importance

Nuisance

Cockroaches are important pests because they spread filth and ruin food, fabrics and book-bindings. They disgorge portions of their partially digested food at intervals and drop faeces. They also discharge a nauseous secretion both from their mouths and from glands opening on the body which give a long-lasting, offensive cockroach smell to areas or food visited by them.

Diseases

Cockroaches move freely from building to building or from drains, gardens, sewers and latrines to human habitations. Because they feed on human faeces as well as human food they can spread germs that cause disease (Fig. 5.5) (2, 3). Cock-roaches are not usually the most important cause of a disease, but like houseflies



Fig. 5.5

Cockroaches can spread disease by contaminating human food with germs they pick up in latrines, garbage dumps, etc.

they may play a supplementary role in the spread of some diseases. They are proven or suspected carriers of the organisms causing:

- diarrhoea
- dysentery
- cholera
- leprosy
- plague
- typhoid fever
- viral diseases such as poliomyelitis.

In addition they carry the eggs of parasitic worms and may cause allergic reactions, including dermatitis, itching, swelling of the eyelids and more serious respiratory conditions (4).

Control measures

Effective control is easier in temperate climates (where cockroach populations cannot survive outdoors in winter) than in humid and warm areas. The key to control is cleanliness, which may be difficult in houses where there are children and domestic animals. In isolated homes, control is easier to achieve than in apartments where cockroaches may have easy access from adjacent quarters. Reinfestation occurs from outdoors in warm areas, or along heating ducts and water pipes in apartments, or from groceries or luggage brought from cockroach-infested areas. Cockroaches may even sometimes be found in very clean houses, but are unlikely to establish colonies.

The presence of several sizes of nymphs and oothecae is an indication of a well-established colony. Infestations can be detected by searching behind skirting-boards, boxes, furniture and other common hiding places. At night, cockroaches are easily detected using light.

Heavy infestations of cockroaches can be dealt with by chemical control measures, followed by environmental management to deprive the insects of food and shelter. Low numbers can be effectively controlled by baits or traps.

Environmental management

Cleanliness and hygiene

Food should be stored in tightly covered containers in screened cabinets or refrigerators (Fig. 5.6). All areas have to be kept clean so that no fragments of food or organic matter remain. Rubbish bins should be securely covered and emptied frequently, preferably daily.

Basements and areas underneath buildings should be kept dry and free of accessible food and water.

Reduction of accessibility

Groceries, laundry, dirty clothing, egg crates and furniture should be checked before being taken into a building.

In some instances, accessibility to buildings can be reduced by closing gaps in floors and door frames. Openings for drain water and sewer pipes, drinking-water and electricity cables should also be closed (Fig. 5.7).

Chemical control

Cockroaches are difficult to control with insecticides for several reasons, one of which is that they may become resistant to commonly used compounds. More-over, many insecticides are repellent to them and are therefore avoided (5). Chemical control gives only temporary relief and, wherever possible, it should be accompanied by environmental sanitation and house improvement (6).

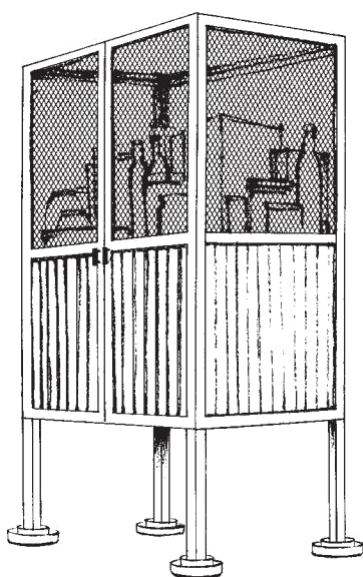


Fig. 5.6
Food can be protected in a cockroach-, fly- and ant-proof cabinet.

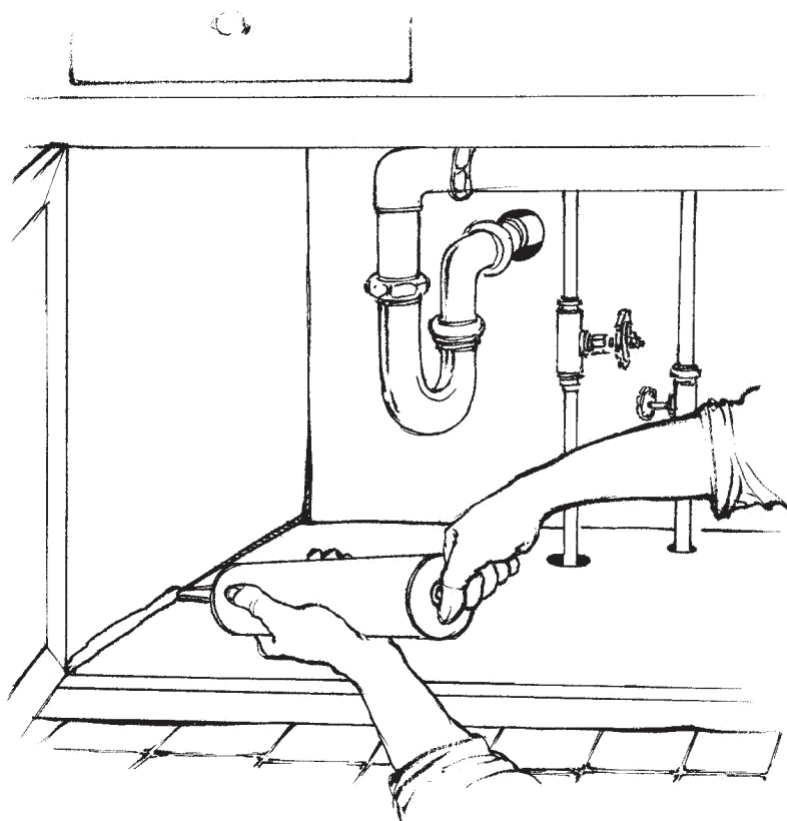


Fig. 5.7
Reduce accessibility to cockroaches by sealing openings, cracks and crevices.

Insecticides are applied to the resting and hiding places as residual sprays and insecticidal dusts. Such applications are effective for periods ranging from several days to months, depending on the insecticide and the substrate on which it is deposited. Insecticides can also be combined with attractants as toxic baits.

Resistance

The German cockroach is resistant to several organochlorine, organophosphorus, carbamate and pyrethroid insecticides (7). The Oriental cockroach, the American cockroach and the large brown cockroach (*Periplaneta brunnae*) have developed little resistance, mainly to DDT and chlordane. Recently, the American cockroach has been found to be resistant to trichlorfon in China and the large brown cockroach to diazinon in the USA.

Application

Areas to be treated

Areas to be treated include kitchens, galleys, behind and along skirting-boards, in and around sinks, in or under cupboards, under chairs and tables, in utility cabinets, near refrigerators and ice boxes, under loose floor coverings, food prepa-

ration areas, ducts, pipes, sewers and manholes. Food storage areas in restaurants, warehouses and other commercial establishments should be treated.

Frequency of treatment

How long the deposits of insecticide remain effective depends on a number of factors, such as the thoroughness of application, the speed of re-infestation, the chemical used, the dosage and formulation applied, the type of surface to which it is applied, the temperature and humidity, and the amount of wearing or rubbing off that occurs. Insecticides generally last longer on painted than on unpainted surfaces and longer on wood than on brick or block surfaces.

Frequent washing of a treated surface or coatings of dust or grease can render an insecticide useless. A single treatment rarely results in eradication. For most species, additional treatments may be necessary at monthly intervals to kill newly hatched nymphs or to prevent reinfestation.

Safety and precautions

Care should be taken to avoid food contamination. Avoid treating areas where children may come into contact with the residue. In special situations, such as the treatment of zoos or pet shops, residual sprays or dusts cannot be used. In such cases it may be possible to apply a limited quantity of chemical with a brush. Alternatively, a chemical with low toxicity to mammals and birds, such as boric acid powder or silica aerogel, may be used.

Some formulations may stain fabrics, wallpaper, floor tiles or other household materials. Information should be obtained on this subject before treatment is carried out.

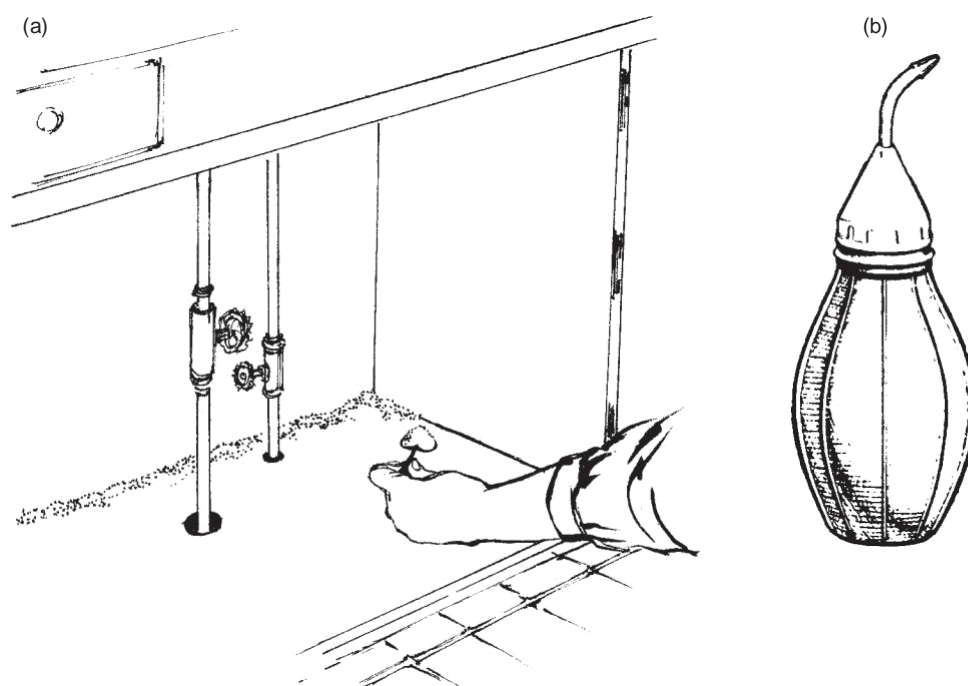
Residual sprays

Residual sprays are usually applied with household plunger-type sprayers or hand-compression air sprayers. The sprayers are equipped with pinstream nozzles to spray the insecticide into cracks and areas that are hard to reach. A broader fan spray is useful for areas that are more accessible. The spray should moisten the surface thoroughly but not to the point of water running off or dripping.

A volume of four litres of diluted insecticide per 100 m² sprayed in swaths 30–50 cm wide is often appropriate. The insecticide can be applied with a paint brush when other equipment is not available. Thorough treatment of runways and harbourage areas is essential for effective control. Usually, a heavy initial treatment is followed by periodic follow-up treatments. Sewer shafts sprayed once with chlorpyrifos or diazinon may remain cockroach-free for nine months or more (8).

Insecticides

Because of the development of resistance, and for environmental reasons, the chlorinated hydrocarbons have been replaced by the biodegradable organophosphorus and carbamate insecticides, the synthetic pyrethroids and, most recently, by insect growth regulators. Insect growth regulators are compounds that are highly toxic to insect larvae or pupae, interfering with their development into

**Fig. 5.8**

Insecticidal dusts can be applied with (a) a spoon (© L. Robertson) or (b) a puff-duster (© WHO).

adults (see also Chapter 1, p. 134). They have a very low toxicity to non-target organisms. Their use is limited by their high cost and limited availability, but they may be of considerable value where cockroaches have developed resistance to other commonly used insecticides. Table 5.1 lists a number of these insecticides and the recommended dosages. For more information on spraying and the safe use of insecticides, see Chapters 9 and 10.

Dusts

Dry powder formulations are made by mixing insecticide powder with talcum or another inert carrier powder. They are most useful for the treatment of hollow walls, false ceilings and other cockroach hiding places that cannot easily be reached. The powders can be blown into spaces with a hand-operated puff-duster or a plunger-type duster, or even applied with a spoon (Fig. 5.8). Long, slender extension tubes can be attached to some types of duster to put the dust deep into hiding places. The dust disperses well and may penetrate deep into cracks and crevices. Heavy dust deposits may repel or drive away cockroaches and cause them to move to untreated areas or less accessible places. Dusts should not be applied to wet surfaces as this reduces their effectiveness. When used together with residual sprays, dusts should be applied only once the sprayed surfaces are dry.

Aerosols

Insecticidal aerosols are fine sprays of very small (0.1–50 μm) droplets of insecticide. Aerosols are not suitable for residual treatment but they can be used for space

Table 5.1

Insecticides commonly employed in the control of cockroaches

Insecticide	Chemical type ^a	Formulation	Concentration		Safety classification by WHO ^b
			g/l or g/kg	%	
Alphacypermethrin	PY	spray	0.15	0.015	MH
Bendiocarb	C	spray	2.4–4.8	0.24–0.48	MH
		dust	10	1.0	
		aerosol	7.5	0.75	
Betacyfluthrin	PY	spray	—	12.5	MH
Chlorpyrifos	OP	spray	5	0.5	MH
Cyfluthrin	PY	spray	—	5–10	MH
Cyphenothrin	PY	spray	1.25–2.5	0.125–0.25	SH
		aerosol	1–3	0.1–0.3	
Deltamethrin	PY	spray	0.025	0.0025	MH
		dust	0.5	0.05	
		aerosol	0.2	0.02	
Diazinon	OP	spray	5	0.5	MH
		dust	20	2.0	
Dichlorvos	OP	spray	5	0.5	HH
		bait	19	1.9	
Dioxacarb	C	spray	5–10	0.5–1.0	MH
Fenitrothion	OP	bait	250	25	MH
		spray	5–10	0.5–1.0	
		aerosol	7.5	0.75	
Flufenoxuron	IGR	bait	0.01	0.001	SH
Hydramethylnon	ETI	bait	—	1–2	SH
Jodfenphos	OP	spray	10	1.0	UH
Malathion	OP	spray	30	3.0	SH
		dust	50	5.0	
Permethrin	PY	spray	1.25–2.5	0.125–0.25	MH
		dust	5	0.5	
Pirimiphos methyl	OP	spray	25	2.5	SH
		dust	20	2.0	
Propetamphos ^c	OP	spray	5–10	0.5–1.0	HH
		dust	20	2.0	
		aerosol	20	2.0	
Propoxur	C	spray	10	1.0	MH
		bait	20	2.0	

^a C = carbamate; OP = organophosphorus compound; PY = synthetic pyrethroid; IGR = insect growth regulator; ETI = electron transport inhibitor.

^b [27]. Classes: HH = highly hazardous; MH = moderately hazardous; SH = slightly hazardous; UH = unlikely to present acute hazard in normal use. ^c If applied by non-commercial operators, it should be supplied, for safety reasons, in a diluted form not exceeding 50 g of active ingredient per litre.

**Fig. 5.9**

An aerosol spray being used to apply residual insecticide to cockroach hiding places under a kitchen sink.

spraying because the droplets remain in the air for some time, killing insects by contact. Aerosol spray cans containing a residual insecticide with a knock-down insecticide (e.g. propoxur and a pyrethroid) are suitable for cockroach control and are widely available. Aerosols can penetrate into small crevices and other enclosed, inaccessible cockroach hiding places (Fig. 5.9). They usually contain pyrethrins, pyrethroids or another irritant to drive cockroaches out of their hiding places so as to shorten the time of kill. Aerosol application can cause a quick reduction in cockroach numbers but, to obtain longer-lasting control, follow-up treatment with a residual spray may be necessary (see p. 295).

Cities sometimes control cockroaches on a large scale with fogs produced by thermo-fogging machines.

Smokes

Smokes are clouds of insecticide particles produced by heat. The particle size (0.001–0.1 μm) is smaller than in aerosols. Smokes penetrate deep into hiding places and are particularly useful in basements of buildings and sewer and drainage systems.

Baits and traps

Baits have been used for many years in cockroach control and are still employed in certain situations, such as offices and laboratories, particularly if there is resistance to some of the insecticides in use.

Many commercially available products work on the principle of attracting cockroaches to a specific point and then trapping or killing them there. Some substances used as attractants are various food items, pheromones and other attractive chemicals. The trapping element may be a mechanical trap or a sticky material. A simple jar trap can be constructed from an empty jar, petroleum jelly and some food: the cockroaches are attracted to the jar by bread, raisins or other food placed at the bottom, and a thin layer of petroleum jelly on the inside rim prevents the insects from escaping (Fig. 5.10).

Toxic baits are used without a trapping device. They consist of a mixture of attractive food material and an insecticide. Several types of bait are commercially available as pellets or pastes. Pellets are usually dispensed in small containers or scattered in concealed areas. Pastes can also be dispensed in small containers. Some of the newer formulations are self-drying and can be applied directly to

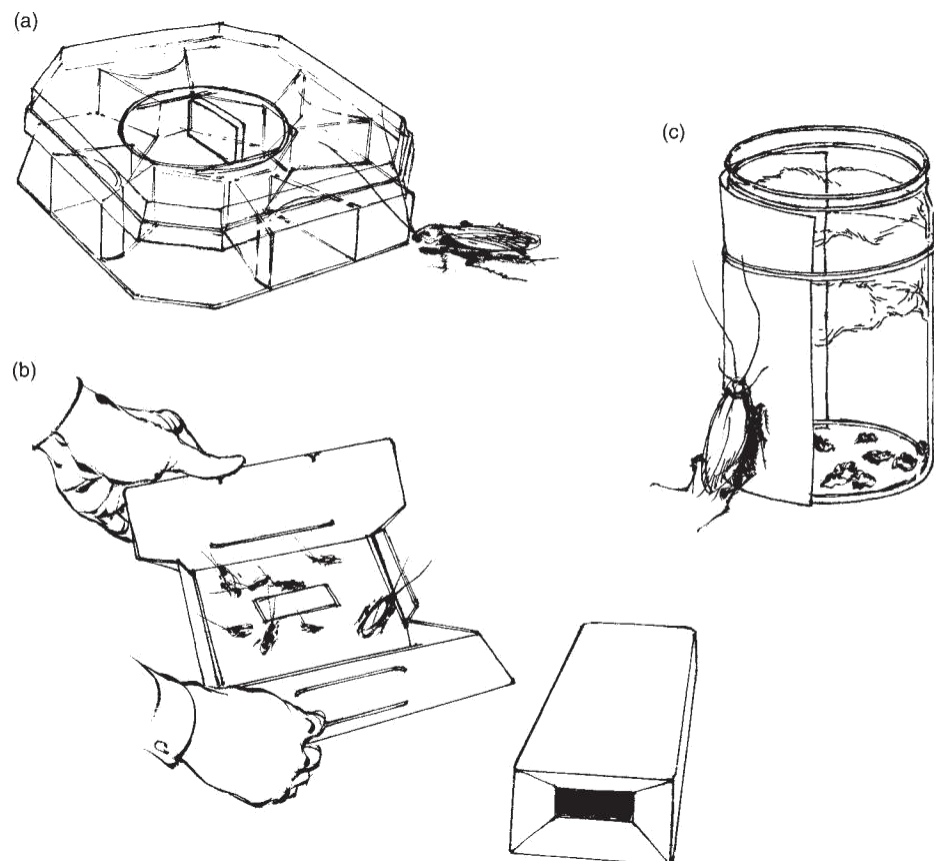


Fig. 5.10

Some types of trap. (a) A sophisticated mechanical trap, containing attractant food. (b) Sticky paper with trapped cockroaches: the trap contains a chemical attractant. (c) A simple jar trap baited with raisins: a sheet of paper enables cockroaches to enter, and a thin coating of jelly prevents escape.

surfaces. In some countries, dry baits are available in sealed traps which are safe to use where children or pets are present. Some food materials which may be used in baits are peanut meal, dog food and maltose.

Application

Baits and traps are easy to use and should be placed at sites frequented by cockroaches. They are most effective in situations where there is little or no food to compete with the bait, as is the case in offices. The maintenance of environmental hygiene is especially important when baits are used alone. In heavily infested areas, baits need to be replaced frequently.

Repellents

There is growing interest in the use of repellents in the control of cockroaches. They may be of special interest for application to hiding places in shipping containers, and in cases and boxes containing drinks, food and other materials. Keeping cockroaches away from such places prevents the distribution or movement of the insects from one locality to another. Repellents can also be used in kitchen cupboards, food and beverage vending machines, and so on.

Several essential oils, such as mint oil, spearmint oil and eucalyptus oil are known to repel cockroaches, but the best results are obtained with synthetic products that are easier to standardize. For example, packing materials or interior surfaces of storerooms can be treated with appropriate dilutions of deet (*N,N*-diethyl-3-toluamide) or DMP (dimethyl phthalate). A deposit of 0.5mg of deet per cm² repels more than 90% of *Blattella germanica* and more than 80% of *Periplaneta americana* from cardboard boxes for about a week, depending on temperature and humidity. More promising synthetic compounds, such as DEPA (*N,N*-diethylphenylacetamide) and DECA (diethylcyclohexylacetamide), currently being studied in India (9), may be commercially available in the near future.

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Dung beetles and their role in the nature

Adam Byk, Jacek Piętko

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Summary:

Scarabaeoid beetles (*Scarabaeoidea*) inhabit all zoogeographical regions of the world. However, coprophagy as the type of nutritional specialization dominates among the scarabaeoid beetles. The number of dung beetles (coprophagous *Scarabaeoidea*) is estimated at about 7,000 species. There are about 460 of dung beetles species in Europe, and about 90 of dung beetles species in Poland. Dung beetles can be endocoprids (dwellers), paracoprids (tunnelers) or telecoprids (rollers). Endocoprid species lay eggs directly into the dung, paracoprid species dig earth tunnels of various lengths ending with brooding chambers beneath the dung, and telecoprid species separate a portion of dung and roll it into round balls which are then transported, sometimes far from the original source of the dung, to a place where the beetles dig tunnels ending with brooding chambers. Such a variety of methods of using faeces by dung beetles cause an accelerated circulation of nutrients, increased soil aeration, plant spreading, and a reduction in the number of parasites (flies and nematodes). Among dung beetles presently encountered in Poland there are endocoprid and paracoprid species.

Key words: *Scarabaeoidea*, *Scarabaeidae*, *Geotrupidae*, dung beetles, scarab dung beetles, earth-boring dung beetles, animal faeces

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Whatever it is that dung beetle buries and abandons the next day, is by no means lost. Nothing is lost in the balance of life, the whole of the inventory remains constant. A small pellet of manure buried by an insect will make the neighboring patch of grass turn delightfully green. The ram will come over and pluck the whole patch, and thus the better the roast a man expects of him will be. Thanks to the dung beetle industry, we get a perfect bite of meat.

Jean Henri Fabre

Introduction

Insects are the most numerous group of animal species on Earth with their quantity estimated at around 1.5 million species. The largest group of the insects (over 400,000 species) belong to the order of beetles (*Coleoptera*). *Scarabaeoidea* is one of the superfamilies of the beetles, which inhabit all zoogeographical parts of the world. Most of them inhabit the tropical zone, and their number tends to rapidly decrease northwards (Tesař, 1957).

The *Scarabaeoidea* superfamily is dominated by a group of species that feed on animal dung (coprophages). The recently found dung fossils indicate the existence of dung beetles (coprophagous *Scarabaeoidea*) in the age of the dinosaurs, even before the evolution of mammals (Chin and Gill, 1996). Currently, the number of dung beetles is estimated at 7,000 species (Hanski and Cambefort, 1991).

In Europe, the dung beetles include primarily the representatives of two families: earth-boring dung beetles – *Geotrupidae* (approximately 60 coprophagous species) and scarab dung beetles – *Scarabaeidae* (approximately 400 coprophagous species).

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In Poland, the dung beetles fauna – formerly re-ferred to by Hildt (1896) as “*Domestic dung beetles*” – represents approximately 90 species. However, the prevalence of several of these species is yet to be confirmed by new finds.

The systematic arrangement and nomenclature of the species have been adapted from the “*Catalogue of Palearctic Coleoptera*” (Löbl and Löbl, 2016).

Farther and deeper

The dung beetles (coprophagous *Scarabaeoidea*) are the Endocoprid (dwellers), Paracoprid (tunnelers) or Telecoprid (rollers) insects (Bornemissza, 1976). The Endocoprid species lay their eggs directly in dung or in

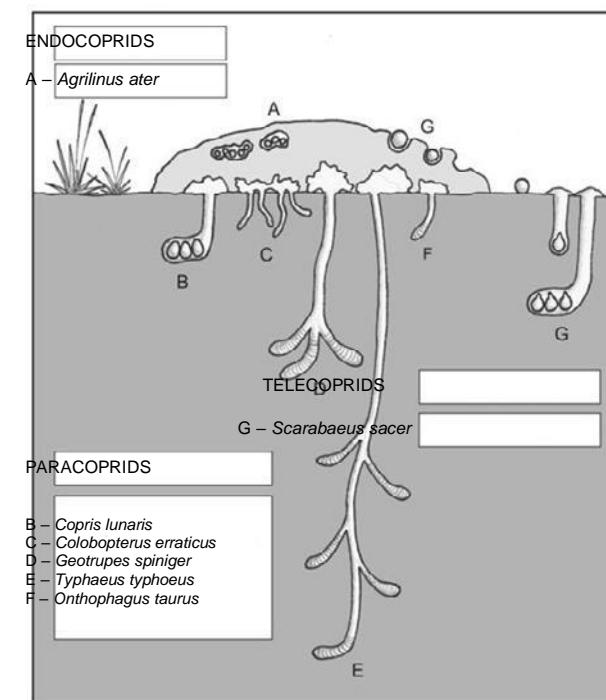


Fig. 1. Diagrams of dung beetles nests (drawn by J. Piętko).

the top layer of the soil, directly underneath the dung. The Paracoprids dig tunnels of various lengths in the ground, underneath the faeces. The tunnels are terminated with hatching chambers. As regards the Telecoprids, upon earlier separation and formation of a piece of dung, they roll it away and dig their tunnels, terminated with hatching chambers, at considerable distances from the dung. The chambers are used for storing the transported portions of the dung (Fig. 1).

The dung beetles commonly found in Poland include the Endocoprid and Paracoprid species (Byk, 2011; Byk, 2012; Kamiński, Byk and Tykarski, 2015).

The Endocoprid grouping is represented by aphodiine dung beetles (Fig. 2). They are the dominant coprophagous beetles in northern Europe and play a significant role in disposing of dung, and thus in circulating the natural organic substances and providing nutrients to the flora (Fry and Lonsdale, 1991).

Agrilinus ater (De Geer, 1774) (Fig. 2A) feed on fresh dung inside which females lay eggs. The eggs are laid as early as on the second day after the exposure of the dung, but most frequently within a period of 4 to 10 days after the exposure. The larvae prey in the vicinity of where the eggs are hatched (Hirschberger, 1998).

In the 19th and 20th centuries, a very beautifully colored dung beetle, *Acrossus bimaculatus*, (Laxmann, 1770) (Fig. 2B), was observed in the area of Warsaw. Here is what Hildt (1896) wrote about this particular species: “One can tell that it is the prettiest specimen of the Aphodiidae group. Glittering, as if it was covered in porcelain topping [...]. An insect rarely seen in our region and nowhere to be found in some other years. [...] I found one specimen in *Saska Kępa* in 1863. [...] Another time, I found it in 1865 [...] and on April 19, 1868, I found as many as forty of them in cow dung [...]. The last one, I found in 1888 [...] and haven't found a single one ever since”. In Poland, this particular species has not been

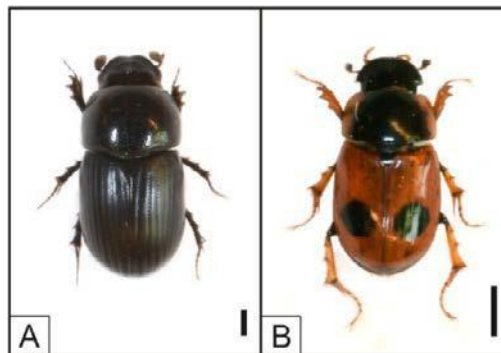


Fig. 2. Endocoprid aphodiine dung beetles: A – *Agrilinus ater*, B – *Acrossus bimaculatus* (photo by J. Piętko).

stumbled upon for nearly 100 years. In 1995, a site of the species was discovered near the village of Rudeńsk located close to Minsk in Belarus. Imagines and larvae were found directly in horse dung (Frolov and Akhmetova, 2006).

The aphodiine dung beetles grouping observable in Poland also includes species applying a slightly different method of using dung (Fig. 3).

Orodaliscus rotundangulus (Reitter, 1900) (Fig. 3A) lives in the burrows of speckled ground squirrel – *Spermophilus suslicus* (Güldenstaedt, 1770), bobak marmot – *Marmota bobak* (Müller, 1776) (Byk and Bidas, 2011), which is not present in our country, and little ground squirrel – *Spermophilus pygmaeus* (Pallas, 1778) (Martynov, 2007). In Poland, this beetle is observed on extremely rare occasions, in the form of a single specimen, and is known to exist only on 5 sites located in the Lublin Upland. Strong populations of this species are found in the “Popówka” and “Suśle Wzgórza” reserves. The swarming of this species takes place during the last days of April or in the first half of May. The beetles leave the squirrels' burrows during the afternoon or evening hours. From a nest chamber located

at a depth of 60-150 cm and a tunnel (latrine) extending from it, the beetles leave the site via a short and slanted corridor (elbow) and then, they climb up the side-walls of the vertical corridors (wells). It is both, males and females that leave the burrows, and after that, they bury themselves underneath a moist soil, at a close distance to the exit holes (Byk and Bidas, 2011). The presence of this beetle species in traps filled with cattle dung bait indicates their coprophagous genus (Piasecki, 2013).

Contrary to the Endocoprids, the *Colobopterus erraticus* (Linnaeus, 1758) (Fig. 3B), which is quite popular in our country, has a different way of behaving. A female of this species digs 4-10 curved tunnels in the soil, directly underneath the dung, at a depth of 3-5 cm (10-11 cm on rare occasions). She always lays eggs one-by-one in a small-size cavity in the soil, most frequently in the lower part of the tunnel. It takes the beetle a few hours to fill the tunnel (or rather its lower part referred to as larder) and to create a sausage-like breeding lump (brood mass). The mass weighs between 0.6 and 4 grams. It is about 7 mm in diameter and from 1.5 to 3.5 cm in length. It takes approximately 10 days for the female to build a nest with 8 tunnels filled with nourishment for the offspring. The larvae feed on the dung collected by the female and, should their supplies run out, they move close to the dung located right above them. The metamorphose takes place in the soil, at a depth of 12-13 centimeters (Rojewski, 1983).

The aforementioned is similar to how the largest and sporadically observed in our fauna *Coprismorphus scrutator* (Herbst, 1789) (Ryc. 3C) behaves. Over the recent years, this species has been observed in Skowronno near Pińczów (Bidas, 2004), Tylawa near Dukla, Huta Polańska near Krempna, Wojkowa near Krynica Zdrój (Bidas and Cieślak, 2006), Żubracze near Cisna, and in Przełęcz Wyżna near Wetlina (Zięba and Dworakowski, 2008). It inhabits cow dung on the mountain pastures.

These beetles copulate on dung and then each female digs directly underneath the dung 7-8 shallow and vertical tunnels. At the bottom of these tunnels, food is collected for the upcoming offspring and this is also where eggs are laid – always in the lower part of the breeding lump and in compliance with the “one tunnel-one egg” principle. At the initial stage, the larvae feed on food collected in the tunnels and switch to using the dung located above them at a later stage. Prior to the metamorphose stage, the larvae penetrate into the soil and build pupation chamber (Barbero and Palestini, 1995). The last two dung beetles belong to the Paracoprid group of the species.

Typical Paracoprids (Fig. 4) are domestic species of the following genus: *Anoplotrupes* Jekel, *Geotrupes* Latreille and *Trypocopris* Motschulsky.

Dor beetle – *Anoplotrupes stercorosus* (Scriba, 1791) (Fig. 4A), is the most common and widespread member of the earth-boring dung beetles (*Geotrupidae*) that inhabits the forests of Poland. It digs 15-35 cm thick tunnels in the soil which are terminated with breeding lumps. Borowski (1960) made a comprehensive investigation into the nourishment spectrum of the dor beetle and presented it to the public. His analysis of the breeding lumps showed that they consist of fragments of leaves, including needles, pieces of bark, and rotting moss. They include no fragments of mushroom fruit-bodies or rotten wood. The total amount of the mold buried by beetles of this species is about 1,400 kg per hectare. The most attractive food for the imago dor beetle is dung of large animals as well as decomposed mushroom fruitbodies. Plewińska (2007) points out to the high level of attractiveness of rodent dung for the dor beetle, which is even higher than that of cow and horse dung. She also draws attention to a significant contribution of this dung to the beetle's diet. Therefore, one may come to a conclusion that the dor beetle fancies

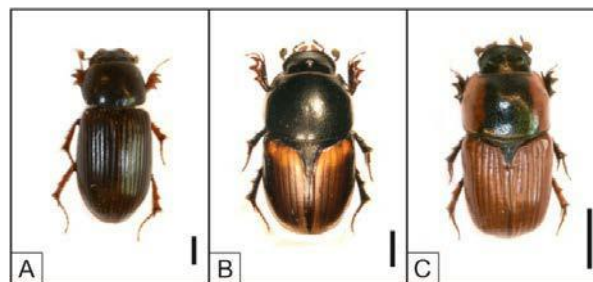


Fig. 3. Aphodiine dung beetles: A – *Orodaliscus rotundangulus* (photo by J. Piętko), B – *Colobopteris erraticus* (photo by T. Gazurek), C – *Coprimorphus scrutator* (photo by J. Piętko).

forests rich in rotten plants, animal faeces, and fungi. According to Teichert (1959), 7 pairs of the *Geotrupes spiniger* species (Marsham, 1802) (Fig. 4B) can bury over 12.6 kg of fresh manure during nesting. The mass of the dung buried by a single specimen exceeds by 560 times the mass of the beetle itself (Rojewski, 1980).

Another representative of the minotaur beetle – *Typhaeus typhoeus* (Linnaeus, 1758) (Fig. 4C) digs in the ground tunnels that are up to 100-150 cm deep (Brus-saard, 1983). The nest of this species was once described by Fabre (1948), “This time, it is no longer the chamber of the scarab, homed dung beetle, or other, which is easy to dug out with the help of a pocket hoe, but a shaft the bottom of which can only be reached by digging for a few hours with a solid shovel. For this work, with the sun still beating down, the hands and legs become numb. Oh, my poor, old bones! Sensing such an interesting riddle under the ground and yet not being able to dig!” The minotaur beetle inhabits moorlands and pine forests on sandy soils where they feed on the excrements of rabbits, deer, roe, and sheep, more seldom of cows and horses (Bura-kowski, Mroczkowski and Stefańska, 1983). The beetles of this species are sometimes found under the carrion of large mammals (Byk, 2011). Nests are usually built

directly under the dung or in their direct vicinity. Males and females work together while digging nests and transporting faeces. The females dig a tunnel and the males remove the excavated load of earth. The males put the faeces into the burrows where they initially grind it. In a sausage-like shaped hatching chamber, the females transform the faeces into a breeding lump about the size of a finger. An egg is laid in the soil under the breeding lump (Fabre, 1948). In laboratory conditions, the males first picked up the faeces located within a radius of 45 cm of the burrow entrance and then the faeces located at a greater distance. In the latter case, however, they often decided to dig a new entrance to the nest, and when the distance exceeded one meter, they usually left the nest and built new ones located closer to the faeces (Brus-saard, 1983; Brussard and Visser, 1987).

Copris lunaris (Linnaeus, 1758) (Fig. 4D), which belongs to the scarab dung beetles, is a widespread species in our country. It likes to inhabit cattle and horse dung on sunlit pastures, sandy and loamy soils (Stebnicka, 1976a). The females dig in the ground, directly under the dung, a few centimeter-long tunnels that end with hatching chambers, where – together with the males – they store food for their offspring (Myrcha, 1973). According to Rommel (1967), the males of this species transport the dung to the entrance of the tunnel, and the females take it into the hatching chamber. At the next stage, the females use the dung (previously collected in the chamber) to sculpt it into 4-8 pear-shaped breeding lumps and lay single eggs in their upper section. The females, and sometimes also the males, remain in the hatching chambers to take care of their offspring. They protect the breeding lumps filled with larvae and pupae and leave the nests with adult offspring (Myrcha, 1973; Mašan and Halliday, 2009). In Poland, a large group of the Paracoprid species is represented by *Onthophagus* genus. Quite a number of

these species are known for their sexual dimorphism. Males tend to have horn-like projections or even antlers. According to Fabre (1948), “No bull specimen typical for Swiss pastures has horns so exquisite and so beautifully curved” as the bull-headed dung beetle – *Onthophagus taurus* (Schreber, 1759) (Fig. 4A). It inhabits open sandy and limestone lands of xerothermic nature and the sunlit edges of forests (Burakowski, Mroczkowski and Stefańska, 1983). In our country, it is widespread in the pastures of the Bug River area. This beetle usually digs in the ground vertical sidewalks at the bottom of which a hatching chamber is built. Then, the side walls of the tunnel and the chamber are reinforced with the dung brought in from the outside. The egg is laid on one of the hatching chamber side walls, and then the chamber

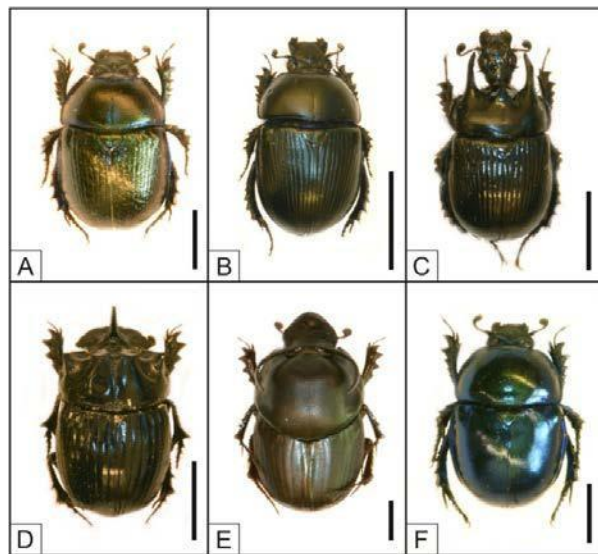


Fig. 4. Paracoprid dung beetles: A – *Anoplotrupes stercorosus* (dor beetle), B – *Geotrupes spiniger*, C – *Typhaeus typhoeus* (minotaur beetle), D – *Copris lunaris*, [3]. – *Onthophagus taurus* (bull-headed dung beetle), F – *Trypocopris vernalis* (spring dor beetle) (photo by J. Piętko)

is filled with dung (Fabre, 1948; Halffter and Edmonds, 1982).

Sometimes, the minotaur beetle (*Typhaeus typhoeus*), and sporadically the spring dor beetle – *Trypocopris vernalis* (Linnaeus, 1758) (Fig. 4F), are able to roll the dung at short distances. However, the Telecoprids group (Fig. 5) has no representatives in our domestic fauna.

A typical telecoprid species, *Gymnopleurus geoffroyi* (Fuessly, 1775) (Fig. 5A), was first observed more than a century ago in the vicinity of Ustroń in the Cieszyn Silesia (Stebnicka, 1976a). According to Hildt (1896) this particular species, “[...] inhabits every type of dung. They form balls about the size of a bean and then lay eggs in them. If they find the ground unsuitable, they roll the ball to a more appropriate location, where they bury it and themselves deep in the ground. Although, these beetles live in groups, each pair manufactures its own ball. [...] They are totally absent in the Warsaw area. They appear only in the Radom Governorate and, more often, in the Hrubieszów district.”

Sisyphus schaefferi (Linnaeus, 1758) (Fig. 5B), the second species of the Telecoprid group, was found over a century ago in Puławy and Janowiec of the Lublin Upland. It inhabits steppe areas, dry pastures, and mild

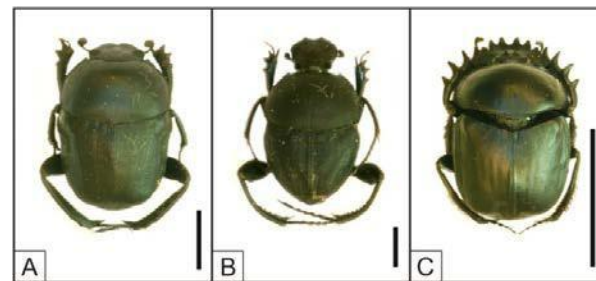


Fig. 5. Telecoprid true scarab dung beetles: A – *Gymnopleurus geoffroyi*, B – *Sisyphus schaefferi*, C – *Scarabaeus sacer* (sacred scarab beetle) (photo by J. Piętko)

sunlit slopes. Adults feed on cattle dung, particularly that of the sheep. The food is collected in the form of pear-shaped balls stored in underground chambers which is where these beetles lay their eggs. However, they fail to care for their offspring (Burakowski, Mroczkowski and Stefańska, 1983). According to Hildt (1896), “It stays in fat manure and quite willingly in human excrements. It lives in pairs. Each pair forms little balls of the dung, buries them in the ground and lays eggs in them. They move in a clumsy, goat-like manner and with difficulty on even ground. [...] In our country, they are observed mostly in the southern part of the Lublin Gov-ernorate; they are pretty popular in the Galicia. [...] It is absent in the Warsaw area”.

Sacred scarab beetle – *Scarabaeus sacer* (Linnaeus, 1758) (Fig. 5C), is the third species of the Telecoprid group reported in our country several years ago. J. A. Wolf's collection included a scarab specimen from the Cracow area. We know this from Karol Herman de Perthées' notes archived in the Institute of Systematics and Evolution of Animals of the Polish Academy of Sciences (PAN). However, the specimen itself was destroyed during a fire at the University of Kiev (Śliwa, 2003). At present day, the closest sites of the scarabs are located in Hungary (*Scarabaeus typhon* (Fischer von Waldheim, 1823) and *S. pius* (Illiger, 1803) and Ukraine (*S. sacer* and *S. typhon*). In the 18th, 19th and early 20th centuries, the scarabs were also found within the areas of the present-day Austria, the Czech Republic, and Slovakia. In 1961, the *S. typhon* scarab was found in Kováčov on the Danube in the southern part of Slovakia. According to Hildt (1896), “Insects of this genus are not at all present in our region [...]. They are sometimes

observed in the Podolia and Kherson Governorates [...] two specimens [...]. I found near the Rozdzielna railroad station”. The city of Rozdzielna is currently located within the territory of Ukraine, approximately 60 km from

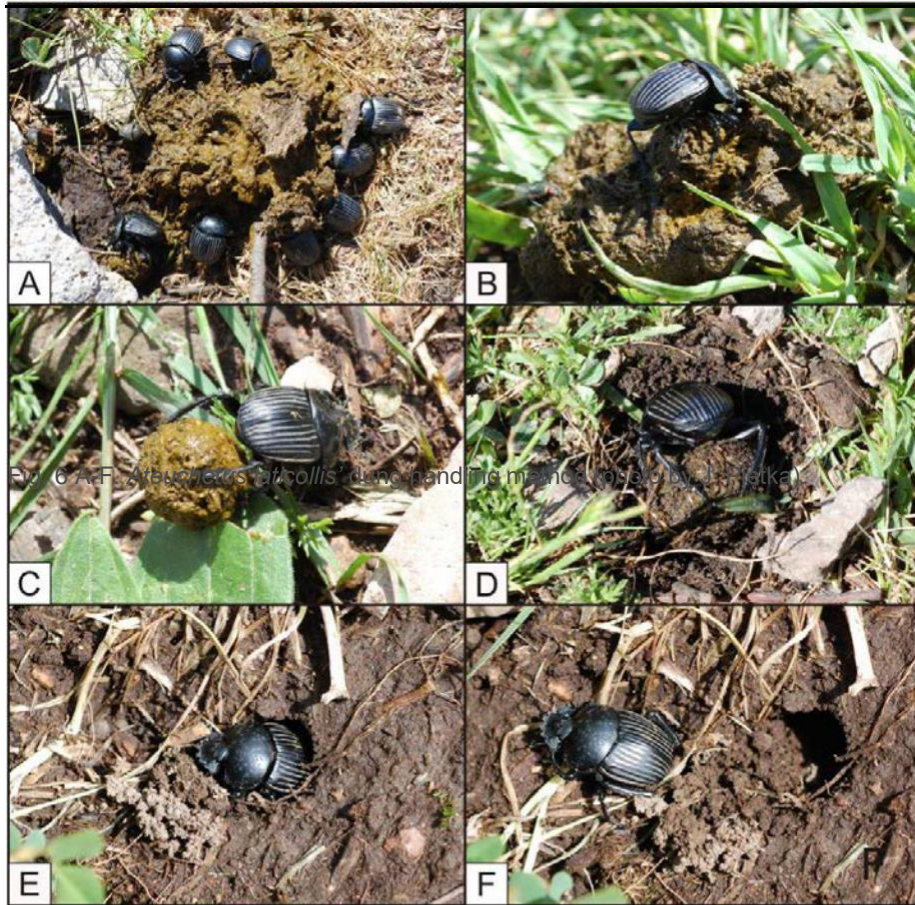


Fig. 6 A-F. *Ateuchetus laticollis* dung handling method (modified by J. Piętka).

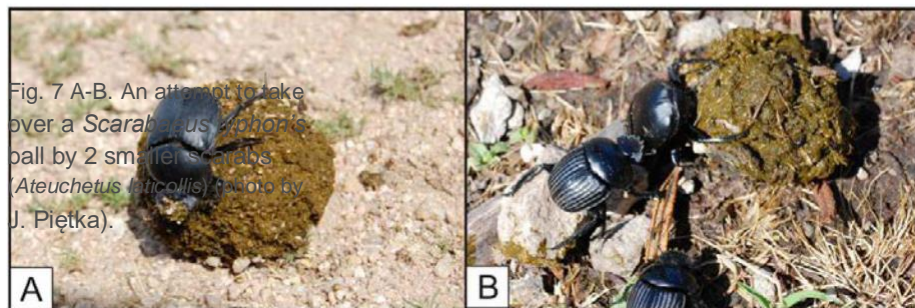


Fig. 7 A-B. An attempt to take over a *Scarabaeus aphodii* ball by 2 smaller scarabs (*Ateuchetus laticollis*) (modified by J. Piętka).

Odessa. The scarabs' natural habitat is fresh dung lying on the routes of the livestock (sheep, cows, and horses). The adult scarabs use their front section of the head and the legs (with distinctive tooth-like projections on the outer edges) to cut down portions of the dung.

On midsize pastures located near Cuglieri in Sardinia, the authors observed a swarm of *Ateuchetus laticollis* (Linnaeus, 1767) (Fig. 6) and the method the scarabs used to handle the dung. In the afternoon of a sunny May day, hundreds of specimens could be admired in the air and on the ground. One of the observed scarabs of this species cut the dung off and tentatively modeled a ball in 4 minutes. This beetle was vigorously moving his head and legs while turning around his own axis. After making suitably deep cuts, the pre-formed ball was separated from the rest of the dung under the weight of the beetle sitting on it. Next, the scarab embraced the ball with his hind legs and, standing still in vertical position with his head down, began to push his forelegs away from the ground, setting the ball in motion. Rolling a portion of fresh dung cut by the beetle caused its shape to become more spherical with its diameter reaching approximately 2 cm. Larger scarabs (3-5 cm in diameter) are able to roll balls much larger in size (3-5 cm) and the largest specimens are skilled enough to manufacture a ball as large as 6 cm. Quite frequently, the size of a ball exceeds that of the beetle itself (Byk and Piętka, 2011), and it is 10 to 20 times heavier (Doubé and Dalton, 2003). The modeled ball of manure can be rolled by a scarab, or a pair of scarabs, even at a distance of several dozens of meters.

It is not uncommon that scarabs of the same species fight for the modeled ball. It happens that an individual who has put a lot of effort into modeling the ball is chased away by a stronger opponent. Sometimes, the specimens of two species, differing largely in size, compete for the ball. In Sardinia, the authors observed an

unsuccessful attempt to take over a ball of a giant *S. typhon* scarab by 2 individuals of the smaller *A. laticollis* (Byk and Piętko, 2011) species (Fig. 7).

Fabre (1948) described this behavior in the following way, “*I lack the more meaningful data to investigate the original causes of these dispossession sanctified by tradition, of the abuse of power to gain a tiny bit of manure; I can only state that theft is a common practice amongst the scarabs. These dung-ball turners rob each other with unparalleled impudence.*” The scarabs dig 10-30 cm deep tunnels in the ground. The tunnels are terminated with

[3]. large-size chamber where the scarab places the ball which he has rolled to the site. It is this chamber where copulation takes place. Afterwards, the male leaves the nest and the female stays inside to form 1-3 breeding lumps from the ball. She lays eggs in the narrower sections of it and then leaves and covers the burrow afterward. In her life cycle, a single female can make dozens of nests. The hatching period takes from 5 to 12 days, the larva period from 30 to 35 days, and the pupa period – approximately 14 days. After the transformation period, depending on atmospheric conditions, the young beetles remain in the breeding lumps until late autumn or spring. Once the indoor growing period has come to an end, the majority of the manure, which has been digested by the beetles, is left in the nest and is used to enrich the soil with organic substances (Byk and Piętko, 2011).

The colder it gets, the lower the number of species

As we advance towards the south of Europe, the number of individuals of coprophagous species belonging to the *Scarabaeidae* family increases amongst the representatives of the *Scarabaeoidea* superfamily, both in open and forested areas. They are dominated by species

of the following genus: *Onthophagus*, *Gymnopleurus*, *Sisyphus* and *Scarabaeus* (Balthasar, 1964). Concurrently, the number of individuals of the *Geotrupidae* species tends to be reduced (Byk, 2012). According to Hortal et al. (2011), no low-temperature adaptation mechanisms were developed amongst the representatives of the *Onitini* and *Scarabaeini* tribes that would allow new areas to be colonized or the species to survive in northern Europe. Located in northeastern Italy, the La Mandria Park – a patchwork of the open and forested areas – as much as 94% of the coprophagous *Scarabaeoidea* were the *Scarabaeidae* (including 32.5% of the *Aphodiinae* specimens) and the *Geotrupidae* specimens constituted as little as 6% of the group (Barbero et al., 1999).

Across the pastures of Poland, the core of the coprophagous *Scarabaeoidea* groupings consist of the *Scarabaeidae*, but the *Aphodiinae* subfamily, i.e. the *Acrossus rufipes* (Linnaeus, 1758), *Agrilinus ater*, *Aphodius pedellus* (De Geer, 1774), *Bodilopsis rufa* (Moll, 1782), *Chilothorax distinctus* (Müller, 1776), *Colobopter-us erraticus*, *Esymus pusillus* (Herbst, 1789), *Eupleurus subterraneus* (Linnaeus, 1758), *Melinopterus prodromus* (Brahm, 1790), *M. sphacelatus* (Panzer, 1798), and *Othophorus haemorrhoidalis* (Linnaeus, 1758) (Breymeyer, 1974; Stebnicka, 1976b; Bunalski, 1996a, b; Żuk, 2005; Górz, 2007). The core of the coprophagous *Scarabaeoidea* groupings in the forests of Poland are made by two species of the *Geotrupidae* – the dor beetle (*Anoplotrupes stercorosus*) and the spring dor beetle (*Trypocopris vernalis*). The core is sometimes supplemented by the *Acrossus depressus* (Kugelann, 1792), *A. rufipes*, *Aphodius pedellus*, *Chilothorax distinctus*, *Euorodolus coenosus* (Panzer, 1798), and *Planolinus fasciatus* (Olivier, 1789) (Szyzsko, 1983; Szwałko, 1995; Byk, 2011, 2012; Byk and Węgrzynowicz, 2015; Kamiński, Byk and Tykarski, 2015). The dor beetle plays a particularly important role in our domestic forests. It is a frequent

inhabitant of the pine forests growing on the wooded areas and is observed in much larger numbers in the forests growing on the former farmlands. By inhabiting the forest stands growing on the former farmlands, by digging tunnels and burying wild animal dung and rotten leaves, it changes the properties of the post-agricultural soil hollowing and speeds up the forest-type land forming process (Byk, 2004; Byk and Semkiw, 2010). The above considerations show that open areas (meadows, pastures, fallows) as well as wooded areas are inhabited by groups of dung beetles of different structure (composition and quantity of the species).

First come, first served

A large quantity of dung beetles forces individual species to compete for food of an ephemeral nature. It appears suddenly and disappears within a short time or is unsuitable to inhabit. The result of this competition includes, without limitation, the previously presented different strategies the Endocoprids, Paracoprids, and Telecoprids apply to deal with dung. It is also extremely important to have the time necessary to reach the dung. The “first come, first served” strategy has been adopted by a large group of Telecoprids. Quite often, the Telecoprids find dung within a few minutes after its appearance as only the fresh dung is suitable for modeling a ball. To do this, the scarabs sometimes follow directly a herd of sheep. Their rush was described by Fabre (1948), “*Who is that stepping so hastily, as if afraid of being late? Long legs are moving quickly and awkwardly as if set in motion by an invisible mechanism hidden in the insect’s stomach; little red horns distributed in a fan-like manner – a sign of restless lust. Here it comes – it’s already arrived running over a few fellow revelers. It is Scarabaeus sacer, the sacred scarab beetle.*” The Paracoprids and Endocoprids usually come to

dung within the first several days following the dung's appearance. The *Melinopterus* Mulsant or *Chilothorax* Motschulsky beetles of the *Aphodiinae* subfamily are usually there within the first few hours and the *Aphodius* Illiger and *Teuchestes* Mulsant – within the first few days. A similar way of conduct is attributable to the beetles of the *Geotrupes* and *Onthophagus* genera and the *Ammoecius* Mulsant genus is keen on inhabiting old dung, e.g. the one that appears in the spring once the snow has thawed. An unusual “sit and wait” strategy has been adopted by some of the tropical species of the *Canthon* Hoffmannsegg genus. The amount of dung in neotropical forests is limited due to small quantities of large vertebrates, and for this reason finding the location of dung is an important element of the survival strategy. Beetles which first come to dung have an advantage over those arriving at a later time. The coprophagous tumblebugs (*Canthon sp.*) dwells in areas located close to the anus of arboreal monkeys – the brown-haired *Callicebus brunneus* (Wagner, 1842) titi and *Pithecia irrorata* (Gray, 1842) saki monkeys. The imagines of this beetle inhabit ape dung already during defecation and fall from the trees down on the ground together with the dung (Jacobs et al., 2008). A similar way of conduct is attributable to species of the *Uroxys* Westwood and *Pedariidum* Harold genera. They inhabit the sloth's fur and leave it with their hosts' dung in which they continue to feed and lay their eggs (Halffter and Mathews, 1966; Ratcliffe, 1980; Howden and Young, 1981; Waage and Best, 1985). In Australia, 6 species of the *Onthophagus* genus dwell on marsupials. They cling on the marsupial's fur thanks to a specific structure of their claws (Matthews, 1972b). They also fall to the ground together with the marsupials' dung where they continue to develop.

What's in it for us?

The dung beetles (coprophagous *Scarabaeoidea*) play an extremely significant role in natural ecosystems, especially in the circulation of elements and secondary dispersal of seeds (Nichols et al. 2008). According to Rojewski (1980), Bunalski (1995) and Górz (1999), the role of the coprophages in meadow ecosystems consists in:

- [28]. Preventing the occurrence of the “dung pollution” phenomenon by reducing the mass of animal dung;
- [29]. Stimulating the dung mineralization process by burying and grinding it;
- [30]. Aerating and improving the structure of the soil by digging tunnels at various depths;
- [31]. Improving the amount of humus in the soil by burying the dung;
- [32]. Reducing the number of coprobiontic dipterans (including the bloodsucking species);
- [33]. Reducing the quantity of parasitic nematodes by crushing their eggs.

According to Rembalska (1980), the role of the pasture and forest species of the dung beetles is similar and consists in grinding and mixing of the soil with faeces of different species of mammals. A slightly different role is played by the dor beetle, which enriches the deeper, mineral layers of the soil with organic matter by burying the forest litter in the form of breeding lumps. This is of special importance for meager forest habitats where saprophagous macrofauna, e.g. earthworms, is rarely observed. The commonness and the role of the dung beetles are best evidenced by numbers:

- [29]. 10 specimens of the minotaur beetle (*Typhaeus typhoeus*) species can bury around 400 balls of rabbit dung in 25 days (Spaney, 1910);
- [30]. On a pasture located near Berlin, there were 825 specimens of the aphodiine dung beetles, 38 spe-

cimens of the earth-boring dung beetles and 70 specimens of the *Onthophagus* genus dwelling in a portion of sheep dung, and 92 specimens of the *Geotrupes stercorarius* (Linnaeus, 1758) (Burmeister, 1936) species were found in a portion of horse dung;

- [34]. European species of the earth-boring dung beetles during the nest building period bury approximately from 0.2 to 0.7 kg of dung (Teichert, 1959);
- [35]. In Algeria, some 450 specimens of the *Gymnopleurus* genus and 190 other dung beetles in a single, Ø35 cm portion of cow dung, and 31 scarabs in another portion of dung (Balthasar, 1963) were observed;
- [36]. In Algeria, 80 beetles of the *Thorectes* Mulsant genus and *Stereopyge* A. Costa subgenus were observed on each square meter of a cornfield with freshly dispersed manure; each of these beetles buried 20 grams of dung; therefore, 800,000 specimens buried almost 16 tons of dung per hectare (Balthasar, 1963);
- [37]. In the Johannesburg area, there were usually 400 specimens of the *Aphodiinae* subfamily, 50 specimens of the *Onthophagus* genus, 50 specimens of the *Oniticellus* genus, 40 specimens of the *Onitis* genus, 2 specimens of the *Copris* genus, and 5 specimens of the *Sisyphus* genus (Gillard, 1967);
- [38]. Parasitic flies of the *Haematobia irritans* (Linnaeus, 1758) species cause approximately \$730 million in losses to cattle farming (Drummond et al., 1981), while the dung beetles can reduce the number of these flies by as much as 95% (Bornemissza, 1970, 1976);
- [39]. Under laboratory conditions, a pair of specimens of the *Onitis* genus can bury 0.7 kg of dung within 10 days' time (Doube and Dalton, 2003);

[46]. It is estimated that the dung beetles allow the US farmers to save \$380 million a year (Losey and Vaughan, 2006). The key evidence of the tremendous importance of the dung beetles for nature is the role they played in Australia. In 1778, the Europeans settled in Australia and brought with them many species of crops and livestock. As cattle farming developed across the entire country, along came unprecedented pollution of pastures with dung (the so-called dung pollution) as well as the mass emergence of flies developing in the dung. Unfortunately, it also included the parasitic and bloodsucking species. Due to dung pollution, the area of pastures available to animals was rapidly decreasing. Under the country's climatic conditions, the dung quickly dried up and turned into "crust" that remained in place for several years. For this reason, the further development of sheep, cows, and horses has been questioned. The main reason for this was the lack of native coprophages that could grow in the cattle dung. Therefore, further development of sheep, cow and horse farming became pretty questionable. The main reason of this situation was the lack of domestic coprophages that could develop in animal dung. Domestic dung beetles have evolved together with the marsupials and failed to adopt the process of inhabiting cattle dung (Tyndale-Biscoe, 1971; Mathews, 1972b). Dung beetles in Africa, Asia, and Europe have evolved together with large ruminants and learned to use their faeces (Waterhouse, 1974; Bornemissza, 1976). It was, therefore, accepted that they could accelerate the dung decaying process on Australian pastures, so they were put to work. Between the years of 1970 and 1980, over 50 species of African and European dung beetles were sent from South Africa to Australia as part of the "Dung Beetle Project". 43 species of the dung beetles successfully passed the incubation and quarantine process and were then released to the pastures. As a result,

a number of pastures polluted with dung drastically decreased. The key "heroes" included: gazella scarab – *Onthophagus gazella* (Fabricius, 1787), northern sandy dung beetle – *Euoniticellus intermedius* (Reiche, 1850), alexis dung beetle – *Onitis alexis* (Klug, 1835), hump-backed dung beetle – *Onthophagus binodis* (Thunberg, 1818), and bull-headed dung beetle (*Onthophagus taurus*) (Edwards, 2007).

From among the insects that defend us against dangerous waste, shamelessly decaying in the rays of sunshine, dung beetles deserve most of the attention (Fabre, 1948).

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Blister beetle:

Introduction

Blister beetle families (Fig. 36-16) include Meloidae and Staphylinidae beetles. Meloidae beetles are distributed worldwide and account for most cases of blister beetle dermatosis. Oedemeridae beetles, or “false” blister beetles, can also produce blistering. Cantharidin may protect the beetle from being eaten. Cantharidin is transferred from male to female during mating, and the strategy has been referred to as a “mate or die” strategy.



Basic Information

Definition

Blister beetles (*Epicauta* spp.) are insects that contain the toxin cantharidin, a potent vesicating agent that is readily absorbed from the gastrointestinal (GI) tract and skin. Cantharidin is a direct irritant that can cause shock and death within 4 hours after a massive dose or affect various organ systems, depending on the dose.

Synonym(S)

- Cantharidin toxicosis
- Cantharidiasis

Cantharidin:

Blister beetles prefer [alfalfa](#) fields where large [swarms](#) tend to congregate. When these fields are harvested, the blister beetles are crushed and incorporated into the bales of hay. They contain a poisonous substance known as [cantharidin](#). It is an inhibitor of the serine–threonine [protein phosphatase](#). Cantharidin blocks the adenosine A₁ receptors, regulates myocardial oxygen consumption, yielding [antiadrenergic](#) effects in ventricular cardiac [myocytes](#) (Narayan et al., 2000). Cantharidin can exert a positive inotropic effect in [cardiac muscle](#) by increasing calcium influx (Neumann et al., 1995).

In [equids](#), the LD₅₀ of cantharidin is reported to be 1 mg/kg b.w. (Guglick et al., 1996). A dose of 4 g of dried beetles is lethal to a horse and 1–1.5 mg/kg b.w. for cats and dogs. The cardiac symptoms of cantharidin poisoning include increased heart rate and myocardial dysfunction. There is no [antidote](#) for cantharidin, but symptomatic treatment is recommended with administration of fluids and maintenance of serum [electrolytes](#).

Epidemiology

Occurrence

Blister beetles feed on flowering foliage, primarily alfalfa, and are incorporated into hay when it is harvested. Cantharidin is stable in the environment and persists for extended time periods. Toxicosis was originally confined to the Southern states, but outbreaks now occur elsewhere because of the widespread shipment of alfalfa hay, and occasionally weedy meadow hay, infested with the beetles.

Risk Factors

The greatest risk factor for horses is the ingestion of blister beetle–contaminated hay. The beetles contain cantharidin, and administration of 1 g of ground beetles by nasogastric tube is fatal to a pony. The ingested lethal amount in adult horses is 0.5 to 1 mg/kg or about 4 to 6 g of dried beetles.^{2,3} The cantharidin content of the beetles varies widely (0.77%–3.31% dry weight) between species, and male beetles contain more toxin than females.

Transmission

Whole or crushed blister beetles can be incorporated into hay and fed to horses and other livestock. It is possible that cantharidin released from crushed beetles may contaminate hay without any evidence of their presence.

Other Forms of Injury

Blister beetles (insect order Coleoptera) may cause blistering on human skin when touched or handled. The beetles contain the blistering agent cantharidin in their body fluids, which is released when they sense danger. Many species of blister beetles exist in the United States, most in the family Meloidae, although a few beetles in the Staphylinidae family cause blisters. Blisters resulting from blister beetle exposure are usually not serious, with reabsorption occurring in a few days if the blisters are unruptured.³¹ The skin may flake if the blisters have ruptured, leaving an area of mild erythema for a week or so. Affected areas should be washed with soap and water and bandaged until the blisters reabsorb. Antibiotic ointments or creams may help prevent secondary infection.

Antiparasitic Properties of Cantharidin and the Blister Beetle *Berberomeloe*

majalis (Coleoptera: Meloidae)

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Abstract: Cantharidin (CTD) is a toxic monoterpene produced by blister beetles (Fam. Meloidae) as a chemical defense against predators. Although CTD is highly poisonous to many predator species, some have evolved the ability to feed on poisonous Meloidae, or otherwise beneficially use blister beetles. Great Bustards, *Otis tarda*, eat CTD-containing *Berberomeloe majalis* blister beetles, and it has been hypothesized that beetle consumption by these birds reduces parasite load (a case of self-medication). We examined this hypothesis by testing diverse organisms against CTD and extracts of *B. majalis* hemolymph and bodies. Our results show that all three preparations (CTD and extracts of *B. majalis*) were toxic to a protozoan (*Trichomonas vaginalis*), a nematode (*Meloidogyne javanica*), two insects (*Myzus persicae* and *Rhopalosiphum padi*) and a tick (*Hyalomma lusitanicum*). This not only supports the anti-parasitic hypothesis for beetle consumption, but suggests potential new roles for CTD, under certain conditions.

Keywords: cantharidin; blister beetle; *Berberomeloe majalis*; nematicide; ixodicide; antifeedant

Key Contribution: cantharidin is active against a diverse range of organisms including protozoa; nematodes; ticks; and insects; supporting the hypothesis that Great Bustards might reduce parasite loads via ingestion of blister beetles.

1. Introduction

Cantharidin (CTD) is a toxic tricyclic monoterpene with the chemical formula: 3,6-epoxy-1,2-dimethylcyclohexane-1,2-dicarboxylic anhydride (Figure 1). Found in blister beetles, CTD was one of the first pharmacoactive natural products used by humans [1–3], and was long considered a sexual stimulant [4–8]. In the late Middle Ages, *Lytta vesicatoria* blister beetles were collected and sold throughout Europe as an aphrodisiac, known as “Spanish Fly” (Figure 2) [9–13]. Today, CTD is used on humans to treat both common and molluscum warts, to remove tattoos, and as a counterirritant, and, until recently, was used as a sexual stimulant in livestock breeding [4,14]. Against vertebrates, CTD is a powerful vesicant and highly toxic. However, in low doses it “stimulates” or irritates vertebrate mucus membranes [10,15,16]. Human ingestion can result in vomiting, diarrhea, bleeding from the gastrointestinal tract, nephritis, hematuria, proteinuria, liver, kidney and other organ edema

and failure, and death [4,16–21]. The consumption of beetles in fresh forage or hay, or drinking beetle-contaminated water, can seriously harm pets, poultry, or livestock [16,18,22,23].

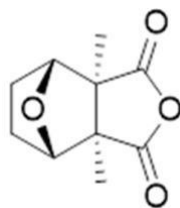


Figure 1. Cantharidin.

Biochemically, CTD acts at multiple levels [16]. It is a potent and specific inhibitor of protein phosphatases 1 (PP1) and 2A (PP2A) [24,25]. It causes the release of serine proteases, which break the peptide bonds in proteins, destroying the adhesion between cells, releasing fluids and causing blistering and bleeding [4]. It disrupts mitosis [16].

CTD was first discovered in blister beetles (Order: Coleoptera; Family: Meloidae), a group of ~3000 species found in temperate and tropical regions world-wide [16,26]. Most meloids are chemically protected from predators by the presence of CTD, which also plays a role in mating [27]. CTD is transferred from males to females during mating in CTD producing insects [28]. Furthermore, CTD synthesis takes place in the male body and is finally deposited in the testes—hemolymph transport is not involved. In females, CTD enters the genitalia from the male as a nuptial gift [28].



Figure 2. Spanish fly (*Lytta vesicatoria*) (from Stefanie Hamm), an example of commercial cantharadin preparation, and collecting blister beetles in Spain in the 17th Century.

A few insect predators have evolved partial immunity to CTD and, in some cases, actually use this poisonous substance for their own benefit. Some insects [27], frogs, toads [29], birds [30], and mammals [31] consume them in the wild. Other uses described include the protection of white breasted nuthatches nestholes by sweeping the bark with a meloid insect [32] or traditional pharmacological use by humans [33].

For example, great bustards, *Otis tarda*, a vulnerable and protected bird species in Europe, consume red-striped oil beetles, *Berberomeloe majalis*, a common CTD-containing blister beetle in the Mediterranean area, even though the beetle is highly toxic [17,34,35]. Bravo et al. (2014) [36] suggest that beetle consumption by bustards (particularly males) represents CTD self-medication to reduce parasites and diarrhea that impair the appearance of the cloaca of the birds (a central element of courtship), thus increasing their chances of reproduction.

Bravo et al.'s hypothesis is reasonable, considering that CTD is bactericidal [36], and that birds are greatly harmed by a diverse range of pathogens and parasites, including numerous bacteria, protozoa, helminths and arthropods. The protozoans *Eimeria* spp., *Cryptosporidium* spp., *Giardia* spp., *Trichomonas* spp., *Histomonas* spp. and *Hexamita* spp. commonly infect bird digestive tracts [37]. Two protozoa cause oropharyngeal diseases in bustards: *Trichomonas gallinae* and *Entamoeba anatis* [38]. Cestodes (*Hispaniolepis* sp., *Raillietina cesticillus*, *Schistometra* (*Otiditaenia*) *conoidea*, and *Idiogenes otidis*), nematodes (*Capillaria* sp., *Syngamus trachea*, *Cyathostoma* sp., *Heterakis gallinae*, *H. isolench*, *Aprocta*

orbitalis, *Oxyspirura hispanica*, and *Trichostrongylus* sp), insects (including mallophaga such as *Otilipeurus turmalis*, and fly maggots such as *Lucilia sericata*) and ticks (*Rhipicephalus sanguineus*, and *Hyalomma* sp.) also infest bustards [37,39,40].

In this paper, we examine Bravo et al.'s (2014) hypothesis [36], by testing the antiparasitic efficacy of both pure CTD and extracts of *B. majalis* beetles against protozoa (*Trichomonas vaginalis*), a nematode (*Meloidogyne javanica*), and a tick (*Hyalomma lusitanicum*). Additionally, several phytophagous insects (*Myzus persicae*, *Rhopalosiphum padi*, *Spodoptera littoralis*) have been tested to include target species other than meloid predators or bird parasites. Our results show strong anti-parasite activity, supporting Bravo et al.'s hypothesis, and suggesting new roles for CTD.