ANNUAL REVIEWS

Annual Review of Entomology

Historical and Contemporary Control Options Against Bed Bugs, *Cimex* spp.

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Annu. Rev. Entomol. 2023. 68:169–90

First published as a Review in Advance on October 5, 2022

The *Annual Review of Entomology* is online at ento.annualreviews.org

https://doi.org/10.1146/annurev-ento-120220-015010

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Keywords

Cimex hemipterus, *Cimex lectularius*, management, chemical control, nonchemical control, global resurgence

Abstract

Bed bugs (Hemiptera: Cimicidae) are an important group of obligate hematophagous urban insect pests. The global resurgence of bed bugs, involving the common bed bug, *Cimex lectularius* L., and the tropical bed bug, *Cimex hemipterus* (F.), over the past two decades is believed to be primarily due to the development of insecticide resistance, along with global travel and poor pest management, which have contributed to their spread. This review examines and synthesizes the literature on bed bug origins and their global spread and the literature on historical and contemporary control options. This includes bed bug prevention, detection and monitoring, nonchemical and chemical control methodologies (and their limitations), and potential future control options. Future research needs are highlighted, especially the factors behind the modern resurgence, the necessity of identifying differences between the two bed bug species relevant to control, and the need to improve insecticide test protocols and management strategies.

1. INTRODUCTION

Over the past two decades, there has been a global resurgence of bed bugs involving *Cimex lectularius* L. (common bed bug) and *Cimex hemipterus* (F.) (tropical bed bug). The resurgence has been widespread, affecting virtually every sector of society, from homes, hotels, and other public accommodation to office buildings, healthcare facilities, libraries, transportation (airplanes, cruise ships, trains, buses), and poultry farms (45).

Bed bug bites can cause irritating dermatological lesions (117), mental (8) and other health impacts (41), social stigma, and severe economic impacts (46, 112). Although there is no evidence of field transmission of infectious agents (42), bed bugs in the field have been found to be naturally infected with a wide range of pathogens, and bed bugs in the laboratory have been shown to transmit the pathogen of Chagas disease (*Trypanosoma cruzi*) (115). Histamines produced by bed bugs in infested premises may trigger respiratory diseases (38).

Bed bug control is expensive, amounting to billions of dollars each year globally (46). Unfortunately, the socially disadvantaged are the most impacted by bed bugs. Therefore, many infestations may go unreported or untreated, and the poorer sectors of society have become the reservoir for bed bugs (79).

The leading cause for the resurgence has been the development of insecticide resistance in both bed bug species (31, 109). Due to the high resistance levels, chemical control options against these pests are limited (80). Exacerbating this is the flooding of the market with products and devices that are largely ineffectual in bed bug management (43). Several reviews on bed bug control options (42, 73, 80), detection and monitoring (25, 28, 135), integrated pest management (IPM) strategies (112), and insecticide resistance (31, 109) have been published.

This article reviews and contrasts historical and contemporary control options for the management of bed bugs. The successful decline in infestations post World War II is examined, along with the factors behind the current resurgence. The challenges of controlling modern insecticide-resistant bed bugs are discussed, along with potential future management strategies. Examining management strategies from the past may provide lessons on how to successfully combat this nuisance public health pest in modern society. The review also highlights future research directions and needs, focusing on those relevant to bed bug management.

2. *CIMEX LECTULARIUS* AND *CIMEX HEMIPTERUS*

Cimex lectularius is predominantly found in temperate and subtropical regions, while *C. hemipterus* mainly occurs in the warmer subtropics and tropics (45, 99, 134). Both species can coexist sympatrically in localities such as Africa, Australia, Florida, Hawaii, and Taiwan (31, 74). Recently, *C. hemipterus* has also been recorded in Europe (9, 15, 88). Even though the two species are closely related and may mate with one another in the field without producing viable offspring (97), molecular phylogenetic analysis has indicated that the clades encompassing both *Cimex* species diverged 47 million years ago (113). There are several morphological differences between the species. For example, *C. lectularius* has a wider pronotum compared with that of *C. hemipterus* (**Figure 1**); the hemelytral pads on the adult mesothorax of the *C. hemipterus* are broadly rounded, in contrast to those of *C. lectularius*, which are less oval (134); and *C. hemipterus* has significantly more tenent hairs on the fossula spongiosa (tibial pad) than *C. lectularius* (74).

3. BED BUG ORIGINS AND GLOBAL SPREAD

3.1. Historical Spread

The earliest record of bed bugs associated with humans was from an Egyptian archeological site dating to some 3,550 years ago (100). During the Roman era, bed bugs were common in the

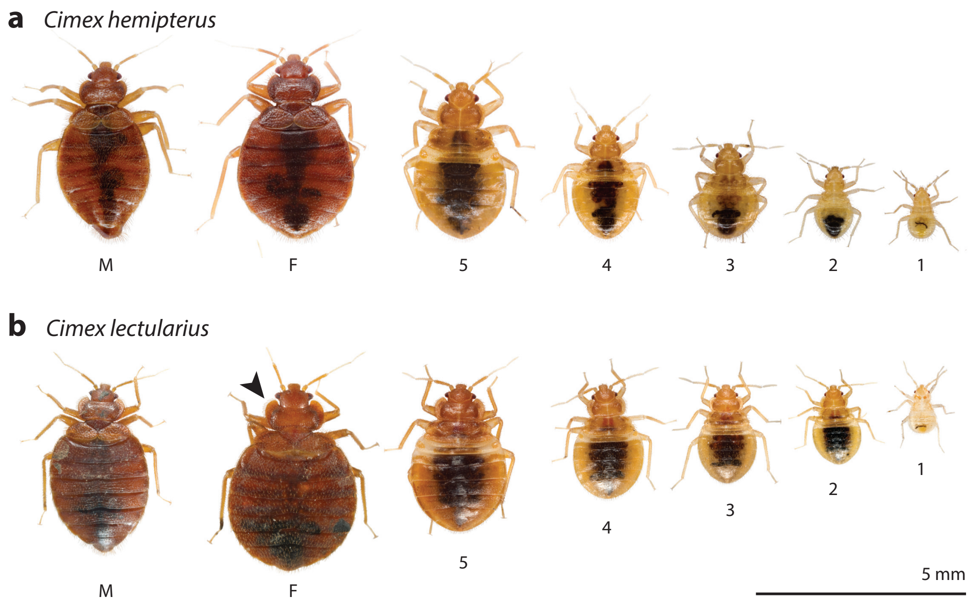

Figure 1

The various stages of (*a*) the tropical bed bug, *Cimex hemipterus*, and (*b*) the common bed bug, *Cimex lectularius*. The distinguishing feature of *C. lectularius* is the lateral flange on the pronotum (as indicated by the arrow), which is more than 2.5× as wide as long (134). The lateral flange is evident from the fourth instar onward. M and F indicate male and female, respectively, and the numbers 1–5 indicate the first–fifth instars.

Mediterranean (105), and the subsequent worldwide spread of bed bugs was the result of the shipping trade (127). By the early twentieth century, bed bugs had become extremely widespread. However, the introduction of dichlorodiphenyltrichloroethane (DDT) and other synthetic organic insecticides from the early 1940s onward helped reduce bed bug infestations. By the 1960s, infestations had become rare in developed countries (19, 45).

3.2. The Modern Resurgence (1998–Present)

The first report of a possible resurgence was from a 1998 article describing anecdotally an increasing number of bed bug bite incidents in Cambridge, United Kingdom, and the apparent ineffectiveness of insecticides (17). A later report originating from the United States in 2000 also anecdotally suggested a rise in bed bug numbers (71). In Venezuela, the first report of bed bugs for some 30 years occurred in 2001, in the city of Baruta (101).

The first hard evidence of the resurgence came from the United Kingdom. Boase (19) reported that a pest control company and a municipal council each reported a rise in bed bug infestations from less than 5 in 1997 to approximately 30 in 2000, i.e., a six-fold increase. In Australia, bed bug submissions to a pathology reference laboratory increased by 700% in the years 2001–2004 compared with the previous four years, 1997–2000 (44). A subsequent Australian pest management industry survey reported a rise in bed bug numbers of 4,500% for the period of 1999–2006, compared with pre-1999 levels (47). In the United States, one large multinational pest management company reported an increase in bed bug calls of over 500% between 2002 and 2003 (90). In Japan, bed bug enquiries to the Tokyo government rose from 20 in 2000 to almost 350 in 2012, while the number of bed bug treatments by two leading pest control companies rose from zero in 2004 to more than 220 in 2013 (78). A survey by the National Environment Agency of Singapore of pest management companies in the country in 2012 recorded a rise in bed bug jobs (treatments) from 200 in 2006 to 470 in 2011 (78). In Israel, a questionnaire of pest management professionals conducted in 2009 showed a 50–150% increase in bed bug infestations compared to the period 2001–2005 (94).

What quickly became apparent was that the global resurgence involved two bed bug species, *C. hemipterus* and *C. lectularius* (45), although very few of the above reports mentioned which species were involved. Since the above reports, a resurgence in bed bugs has now been reported in more than 50 nations, including all regions of the globe (31, 45). Maps showing the past and current global distribution of the two bed bug species have recently been published (128). Despite it being approximately 25 years since the start of the resurgence, relatively little data on the epidemiology of the bed bug resurgence exist (79). One of the great impacts of bed bugs has been the economic burden that they impose of those affected, and it has been estimated that these insects are costing the world economy billions of dollars annually (46).

The reasons behind the global bed bug resurgence are many and varied; however, it is now evident that the evolution of insecticide resistance in both species has played a significant role (45). Increased global travel facilitated the dispersal of these resistant strains worldwide (45). Compounding the resurgence was poor pest control, coupled with human-mediated spread that dispersed bed bugs from initially infested sites (especially apartments) to other sites (and apartments) within the same and/or surrounding buildings, which significantly enhanced the speed of the global resurgence (20, 47).

4. HISTORICAL AND CONTEMPORARY CONTROL OPTIONS AND CHALLENGES

A list of historical, contemporary, and novel control options against bed bugs and their limitations is presented in **Table 1**.

4.1. Prevention

Historically, there were limited options for bed bug control; thus, prevention was paramount. In the early eighteenth century, the belongings of new servants and second-hand furniture were thoroughly inspected before being allowed into the home in case they were infested with bed bugs (127). German and Swedish landlords demanded written testimonials from exterminators that apartments were bed bug–free when tenants vacated premises (105). Today, second-hand furniture is acknowledged as a bed bug risk, and many educational institutions in the United States require a tenant's items to be heat-treated before being brought onto the premises (45). Landlords in the United States now often prescreen tenants for past exposure to the insect (105).

In the early 1800s, French boarding houses had a persistent bed bug smell, and cheaper lodgings were often riddled with the insect. Infestations were so bad in many London lodges in the 1850s that lodgers were advised to become half-drunk to obtain some sleep (21). Even today, due to the modern resurgence, lower-cost accommodations with high guest turnover, such as backpacking lodges, are highly vulnerable to bed bugs (47).

Good hygiene and a reduction in the number of cracks and crevices to prevent potential harborages have long been recommended throughout history (105). Even today, sealants are recommended to fill potential harborages on furniture and around rooms (73). To minimize infestations and for ease of treatment, simplified furniture and beds with few gaps for bed bugs to harbor have been recommended (127). In 1766, the English surgeon Samuel Sharp noted that many Italian hospitals used iron beds to reduce crevices for the insects to hide in and suggested that English hospitals adopt this approach, leading to reduced bed bug problems (21). By the

Table 1 Historical, contemporary, and novel control options against bed bugs and their limitations

Type	Option	Method and/or agents	Usage status[a]	Known challenges and limitations	Selected reference(s)
Prevention	Simplified furniture	Metal beds or limitation of harborages	Past, present	Not 100% preventative	21, 40, 105, 127
	Harborage reduction	Sealing cracks and crevices, using hard surfaces	Past, present	Not 100% preventative	21, 40, 105, 127
	Isolation of beds and furniture	Preventing insects from reaching the bed	Past, present	Bed linen touching the floor gives access to bed bugs	40, 105
	Dish filled with oil or kerosene	Placed under bed legs to prevent access by bed bugs	Past	Flammable	105
	Clutter minimization	Reducing harborages	Past, present	Fewer personal belongings	40, 105
Detection and monitoring	Survey	Interview of residents	Past, present	Unreliable	27, 139
	Traps	Sticky traps	Present	Bed bugs are repelled	25
	Visual inspection	Visual inspection by pest management professional	Past, present	Moderate reliability	25, 40, 139
	Canine inspection	Dog	Present	Moderate to high accuracy	26, 102
	Active monitors	Monitor with lure (heat, CO_2, semiochemicals)	Present	More expensive, requires maintenance, efficacy unknown	6, 25, 28
	Passive monitors	Pitfall-style monitor	Present	Ineffective against *Cimex hemipterus*	25, 74, 136
	Swabbing	Fecal testing	Present	Expensive	28
		Lateral flow assay	Experimental	Expensive	75
		PCR	Present	Expensive, false positives	25
	Detection of nymph scraping	Infrared and sound detection	Experimental	Impractical, high cost	86
	Detection of compound(s) emitted by bed bug	Electronic nose	Experimental	Inefficient, high cost	77
	Sampling of indoor air	GC-MS	Experimental	Impractical, high cost	48

(*Continued*)

Table 1 (*Continued*)

Type	Option	Method and/or agents	Usage status[a]	Known challenges and limitations	Selected reference(s)
Chemical	Painted or brushed on	Mercury chloride, kerosene, gasoline, turpentine, benzene	Past	Fire hazard, highly toxic	105
	Liquid spray	Alcohol	Past, present	Fire hazard	105
		Chlorinated hydrocarbon	Past	Resistance	31, 80, 105
		Organophosphate	Past, present	Resistance	31, 80
		Carbamate	Past, present	Resistance	31, 80
		Pyrethrin, pyrethroid	Past, present	Resistance	31, 80
		Neonicotinoid	Present	Resistance	31, 80
		Pyrrole	Present	Slow action, variable efficacy	23, 80, 83, 143
		Insect growth regulators	Experimental	Slow action	58, 80, 92
		Botanical insecticides	Present	Slow action	80
		Pyrethroid–neonicotinoid mixture	Present	Resistance	23, 29, 56, 81, 107, 140, 141
	Pressurized aerosol	Pyrrole	Present	Slow action	23, 80, 110
		Pyrethroid	Present	Resistance	5, 80, 131
		Neonicotinoid	Present	Resistance	56, 80, 143
		Minerals and inorganic desiccant	Present	Slow action	4
		Juvenile hormone analog	Experimental	Slow action	92
	Total release fogger	Pyrethroid	Present	Resistance, poor penetration into harborages	69
	Dust	Arsenic	Past	Highly toxic	105
		Chlorinated hydrocarbon	Past	Resistance	129
		Pyrethrum	Past	Resistance	105
		Pyrethrin, pyrethroid	Present	Resistance	80
		Minerals and inorganic desiccant	Present	Slow action	2, 3, 4, 23, 125
		Botanical insecticides	Present	Poor residual efficacy	3

(*Continued*)

Table 1 (*Continued*)

Type	Option	Method and/or agents	Usage status[a]	Known challenges and limitations	Selected reference(s)
	Mattress liner	Pyrethroid (permethrin)	Present	Resistance	47, 69, 82
	Resin strip	Organophosphate (dichlorvos)	Present	Resistance	106
	Fumigant	Heavy naphtha	Past	Toxic	55
		Burning of candles dipped in sulfur	Past	Fumes damaged many household items	21, 105
		Hydrogen cyanide	Past	Highly toxic	18, 61
		Sulfuryl fluoride	Present	Logistically challenging, special fumigation license to operate	132
		Methyl bromide	Past	Depletes ozone layer	80
		Ozone	Experimental	Toxic	80
		Botanical insecticides	Present	Small scale only	50
		Dichlorvos	Past, present	Resistance	80, 106
	Repellent	DEET	Experimental	Short-term	138
		Picaridin	Experimental	Poor repellency	138
		Catnip	Experimental	Short-term	119
		Coconut oil	Experimental	Short-term	147
		Human skin triglycerides	Experimental	Unknown	51
		Terpenoids	Experimental	Unknown	62
		Ultrasonic frequencies	Experimental	Ineffective	43
	Laundry enhancer	Enzymes	Present	Unknown	Not available
	Oxygen depletion	Remove O_2 from contained atmosphere	Present	Slow	43
Biological	Liquid spray	*Beauveria bassiana*	Present	Inactivates at warm temperatures	1, 10, 11, 120, 121, 133
Physical	Heat	Fire Boiling water	Past Past	Dangerous Small scale only	105 105
		Steam	Past, present	Time-consuming, no residual action	63, 73, 144
		Drying	Present	Expensive, no residual action	73, 96

(*Continued*)

Table 1 (*Continued*)

Type	Option	Method and/or agents	Usage status[a]	Known challenges and limitations	Selected reference(s)
	Cold	Cryonite	Present	Can blow away bed bugs unharmed	73
		Freezers	Present	Time-consuming, requires multiple days	73
Mechanical	Trap	Trapping with a wicker trap and killing using boiling water	Past	Limited number trapped	21
		Bean leaves (*Phaseolus vulgaris*)	Past, experimental	Limited number trapped	22, 73, 108, 130
	Physical removal	Dislodging using a hatpin	Past	Time-consuming	73
		Vacuuming	Present	Does not remove bugs from deep harborages	40, 73
	Discarding infested items	Removes bed bugs in belongings	Past, Present	Loss of personal belongings	40, 105
	Barrier	Mattress encasement, plastic bags for belongings	Present	Does not prevent infestations	137, 142
	Proofing	Elastomer sealant	Present	Does not prevent infestations	73
Novel	RNAi	dsRNA against vitellogenesis and key ATPase enzymes	Experimental	Lack of feasible delivery system	12, 60, 93
	Bait	Fipronil, clothianidin, abamectin, boric acid, spinosad, fluralaner	Experimental	Lack of feasible delivery system	116, 122, 123
	Disruption of microbiome	Antibiotics	Experimental	Lack of feasible delivery system	64, 103
	Systemic insecticides	Ivermectin, moxidectin, ibuprofen, caffeine, afoxolaner	Experimental	Ethical concerns	16, 43, 95, 118, 146
	NF-kB signaling inhibitors	Entomopathogenic bacteria	Experimental	Unknown	104

[a]Past and present refer to methods used before and during the modern resurgence, respectively. Experimental refers to methods that are not available commercially and only discussed in the literature.

Abbreviations: DEET, diethyl-m-toluamide; dsRNA, double-stranded RNA; GC-MR, gas chromatography–mass spectrometry; PCR, polymerase chain reaction; RNAi, RNA interference.

mid-1800s, dismantlable metal beds were preferred over wooden beds for ease of treatment (21). Today, simply constructed metal beds and a reduction in potential bed bug harborages are promoted in bed bug industry standards (40).

In Balkan nations, there was a tradition of spreading bean leaves (*Phaseolus vulgaris* L.) on the bedroom floor to capture bed bugs, as the leaves would ensnare the insects (108). It was later found that hook-like trichomes on the bean leaves trapped the bed bugs (22, 130). This inspired the microfabrication of surfaces that mimicked the action of the trichomes, which could then be placed around the bed to capture newly introduced bed bugs (130). However, this product has yet to be commercialized.

Today, white mattress encasements are often installed on beds to make the inspection process for bed bugs much easier (40). If a mattress is infested, then an installed mattress encasement prevents bed bugs within the mattress from accessing the host (137, 142). The encasement also serves as a barrier against exposure to pesticides applied on the mattress (72, 73).

4.2. Detection and Monitoring

Early bed bug detection reduces the risk of an infestation spreading and lowers control costs (40). A mark–release–recapture study showed that up to 5% of *C. lectularius* spread to adjoining apartments within 14 days of release (27), demonstrating the rapid dispersal of an infestation. Historically, traps were used to reduce insect numbers, rather than for monitoring (21); today, in contrast, they are mainly used for monitoring. Some of the early traps were simply pieces of wood with drilled holes; however, the most widely used type was made of wicker (21). Bed bugs crawled into the trap during the night and were later killed with boiling water.

The modern resurgence of bed bugs has led to the development of numerous detection and monitoring methods. The various methods employed may include surveys, visual inspections, canine detection, and bed bug monitors and traps. Surveys involve interviewing residents to ask them if their premises are infested with bed bugs. Studies have suggested that this methodology is unreliable; for example, two studies found that 50% (139) and 62% (25), respectively, of elderly residents in community housing were not aware that bed bugs were on their premises. However, similar research has not been conducted with other age groups who might have differences in knowledge, risk perception, and awareness of infestations. Visual inspection is the most common procedure used by pest management professionals. However, the effectiveness of visual inspections relies on the experience and thoroughness of the inspector (25, 40). One study found that only 52% of apartments with bed bug activity ($n = 101$) were detected through extensive visual inspections by researchers experienced in bed bug recognition (139).

Canine inspections involve using trained dogs to recognize bed bug scents. The dogs' precision depends on the dog and the handler and can be up to 98% accurate in artificial environments (102). However, a field evaluation of 11 canine teams found that the mean detection rate was only 44%, with an average false-positive rate of 15% (26). Despite these limitations, canines are still considered useful for rapid and large-scale inspections (25).

Bed bug monitors can be passive, with no lure, or active, with a lure such as heat, CO_2, or various semiochemicals (25). The challenge with active monitors is that they require the regular replacement of consumables or use power, thereby increasing costs and making them less feasible for routine usage, especially in low-income housing (43). Traps supplemented with CO_2 capture significantly more bed bugs than other traps, and CO_2 appears to be the most effective attractant available (25). However, the ongoing supply of CO_2 poses a logistical and safety issue. Anderson and colleagues (6) tested a device that produced heat and released CO_2 and found that continued operation of the device resulted in a significant reduction of *C. lectularius* over time. A recently identified aggregation pheromone (59) is now being employed as a lure in a bed bug trap (28). Several electronic smart monitors have also been developed that send an alert to a device (phone or computer) when an insect enters the unit. However, their effectiveness has yet to be scientifically assessed.

Most bed bug monitors on the market are passive monitors, typically a simple harborage or a pitfall trap (25). Harborage monitors are primarily constructed out of corrugated cardboard, which the bed bugs can enter, and are intermittently inspected. Testing of harborage-style traps has been limited, but one study showed that they detected only 39% of *C. lectularius* infestations in apartments, compared to 79–89% for pitfall-style traps (137). Pitfall traps are typically dish-like plastic structures with a central well and an outer channel. The traps are low-cost and can be placed in various positions, especially under bed legs or near beds. Unlike visual or canine inspections, which only offer a snapshot in time, traps provide continuous monitoring. Pitfall traps are inexpensive, have been extensively tested in low-income housing, and are reliable for detecting low-level *C. lectularius* infestations (25). The placement of only two pitfall traps in low-income housing was sufficient to detect 79% of *C. lectularius* infestations of which the facility management was previously unaware (136).

4.3. Nonchemical Control

In many ways, nonchemical control options have not dramatically changed over the years. In the past, such methods were used because insecticides were not available. Today, nonchemical methods are employed because many insecticides are largely ineffective due to resistance issues. Nonchemical control options include extreme environmental conditions, exclusion, and physical removal.

Both dry heat and steam are practical and effective. An exposure to temperatures of 45–48°C for 1 h will kill all stages of both *C. lectularius* (14, 37, 67) and *C. hemipterus* (65), and insects are killed even more rapidly at temperatures >60°C (85, 96). Even at sublethal temperatures of 35–40°C, bed bug reproduction is impaired (114). The early use of heat involved using boiling water to kill the insects on beds and bed linen (105). Gunpowder was applied in cracks in furniture and ignited to destroy bed bugs in harborages, candles were used to burn bugs in bedsprings, and blowtorches were applied to bed frames (105). Steam was first used to treat bed bugs on a small scale using a kettle-like device in 1873 (105). Later, whole-room steaming at 71°C was undertaken by forcing steam from a boiler into a building (73). Rooms were steam-heated from a central heating plant in the 1920s to eliminate bed bugs in 210 rooms in a college dormitory (63). Slum dwellings were even burnt down before World War II to destroy chronically infested buildings (105).

Today, heat treatments are applied using handheld devices, heating chambers of varying sizes, or whole-room treatments. With handheld steamers, cheap units perform as effectively as expensive steamers for treating under fabric materials or in cracks (144). Infested furniture, mattresses, suitcases, boxes, and other household items can be placed and treated in a heat chamber, insulated tent, utility trailer, cube van, or shipping container, with the heat provided by electricity or propane gas. Infested linen and fabrics can be disinfected in laundry driers (96). Whole-room treatments, which require minimal preparation from the residents, involve heat-treating the living spaces, but some items (e.g., pressurized cans, musical instruments, medicines, indoor plants, etc.) can be damaged by heat and must be removed before the treatment is initiated (73). An advantage of employing heat is that bed bugs are less likely to develop heat resistance than to develop resistance to other treatment methods (7). Sublethal heat exposure has been found to reduce bed bug feeding (145) and lengthen the nymphal development period (7), although mating behavior and fecundity are not impacted (145). Low temperatures are also lethal to bed bugs, especially at temperatures <17°C for 2 h (96).

Historical physical forms of control included using hatpins to dislodge bed bugs from their harborages (73) and picking bed bugs off infested items (105). Vacuuming is widely employed today and rapidly removes free-living stages from an infested site (40, 73), as well as removing exuviae, which may harbor young nymphs (24, 35, 36). Vacuuming may also reduce insect allergens associated with an infestation. The technique is inexpensive and requires minimal training, but it does not kill the insects; thus, the vacuum bag must be adequately sealed before being disposed of.

Biological agents such as entomopathogenic fungi [*Beauveria bassiana* (Bals.-Criv.) and *Metarhizium anisopliae* (Metschn.)] have been tested against *C. lectularius* (1, 11, 135). *Metarhizium anisopliae* was only effective at very high humidities (133). In contrast, *B. bassiana* performed well at 50% relative humidity (11), leading to the commercialization of a *B. bassiana*–based liquid spray formulation. The fungal-based formulation was effective against both susceptible and pyrethroid-resistant *C. lectularius* (10) and when combined with other insecticides (120, 121). The use of this product in hotter climates has yet to be assessed, and its performance may be affected by warmer conditions (79).

4.4. Chemical Control

Advertisements for chemicals to treat bed bug infestations appeared as early as the 1730s. One was nonpareil liquor (127), which may have been derived from *Quassia* wood (105). Mercury mixed with egg white was recommended for bed bug control in 1735 (21), and later, other mercury compounds were used (105). By the mid-1800s, a product known as Keating's Powder (pyrethrum powder) was widely sold for bed bug control in Europe and the United States (105). Highly toxic compounds such as mercury chloride and arsenic dust were sold and used until the early 1900s and were implicated in several deaths (105).

Fumigants were commonly used in the early twentieth century. The burning of candles or sticks dipped in sulfur became the first fumigant treatment routinely used in bed bug control (21, 105) and was able to kill all bed bug stages. However, the sulfur fumes damaged many household items (105). Heavy naphtha, derived from coal tar distillation, was heated to form vapors and effectively killed bed bugs (55), although it never became widely used, presumably due to its flammable nature. Hydrogen cyanide, with its excellent penetrative ability, was first tested in 1912 (18) and became a widely used fumigant (61), as it was not flammable and did not affect household items; however, it was highly lethal to humans. By the time synthetic organic insecticides such as DDT, cyclodienes, and organophosphates were introduced and used successfully to control bed bugs from the 1940s onward, fumigation had fallen out of favor due to safety concerns.

During the modern resurgence of bed bugs, at least 12 classes of insecticides have been evaluated or used, including organophosphates, carbamates, pyrethroids, neonicotinoids, pyrroles, insect growth regulators (IGRs), inorganic silica and mineral compounds, and botanical insecticides (80). Despite widespread pyrethroid resistance (31), pyrethroids remain the most commonly used insecticide class against bed bugs (80). More recently, pyrethroid–neonicotinoid mixtures have been formulated for liquid residual sprays and aerosols; these include betacyfluthrin+imidacloprid (23, 29, 81, 83, 140, 141), lambdacyhalothrin+thiamethoxam (29, 81, 83, 141, 143), and bifenthrin+acetamiprid (107, 141, 143).

The pyrrole chlorfenapyr is available as both a liquid spray and a pressurized aerosol (23, 80, 83, 143), although variable efficacy even in the same formulation has been reported between different studies (80). IGRs, when tested against *C. lectularius* (58, 92), often required many times the label rate to be effective (58). To be impacted by the IGR, the immature stages must feed on their host before molting, meaning that these chemicals will not quickly reduce an infestation (42). Botanical insecticides are an increasingly popular option due to their perceived reduced risk to human health (3, 124), but they have a short residual life and pungent odor. Bed bugs avoided geraniol, eugenol, citronellic acid, and carvacrol (57).

Many insecticides are applied as liquid sprays against bed bugs, while some are in the form of pressurized aerosols or dust. Liquid spray formulations (e.g., capsule suspensions, emulsifiable concentrates, suspension concentrates, microemulsion, microencapsulations, water-dispersible granules, and wettable powders) are diluted in water and sprayed onto the insects or applied as a toxic residue onto surfaces and in cracks and crevices. These methods have been used since the introduction of DDT in the 1940s (80). Pressurized aerosols, in a self-contained system, are helpful for the treatment of cracks and crevices and other tight voids where bed bugs are harboring. The insecticide could be a pyrrole (23, 110), pyrethroid (5, 131), carbamate (40), neonicotinoid (56, 143), or inorganic desiccant (4). Interestingly, pressurized aerosols containing pyrethroids are effective against pyrethroid-resistant bed bugs when applied directly to the insect but provide poor residual control once dried on a surface (42). Pyrethroid-based total release foggers that produce aerosolized particles performed poorly against pyrethroid-resistant *C. lectularius*, as the insecticide failed to penetrate into harborages (69).

Almost universally across the globe, fumigation using poisonous gases requires a special license for treatment (80), in contrast to other options. Like heat treatments, fumigants cannot always be used on site. It is often necessary to remove items marked for fumigation and undertake the treatment elsewhere, which may impose logistical constraints and increase the cost of control. Nevertheless, fumigants such as sulfuryl fluoride effectively control bed bugs in personal belongings (132). On a smaller scale, fumigants derived from essential oils can be used for disinfesting smaller items such as electronic goods (50). Resin strips containing dichlorvos, a volatile organophosphate, killed all insects and eggs of *C. lectularius* in laboratory evaluations when used singly or in combination with heat (106); however, dichlorvos resistance has been reported (31), and its performance may vary between strains of bed bugs.

Permethrin-impregnated mattresses and liners have been found to be ineffective against most modern strains of *C. lectularius* (47, 70, 82) and *C. hemipterus* (82). Even after continuous exposure for a week or more, many field strains of bed bug tested failed to show any mortality (82). Inorganic and mineral compounds including diatomaceous earth (3, 4, 125) and silica dioxide (23, 125) are commonly referred to as desiccant dusts due to their desiccant mode of action. These are available in dust or aerosol formulations, with silica dioxide producing the most rapid kill (125). Field studies using CO_2 (to stimulate bed bug movement) combined with a desiccant dust demonstrated better efficacy than desiccant dust alone (2).

Lastly, repellents such as diethyl-m-toluamide and picaridin (138), diethyl phenyl-acetamide and dimethylphthalate (76), or catnip oils (119) were found to provide variable repellency. More recently, human skin triglycerides prevented the arrestment behavior of bed bugs in harborages (51). However, it is premature to speculate on the potential of this finding in bed bug management.

4.5. Bed Bug Management Protocols

In 1730, John Southall produced the world's first bed bug control manual, *A Treatise of Buggs* (127), which reviewed their life cycle, prevention, inspection, and control methods. A later document, "The bedbug" (87), developed by the US Department of Agriculture, provided an overview of the pest and control methods, including sulfur fumigation and heat treatment. With the growth of bed bugs in slums during the early twentieth century, the UK Ministry of Health in 1934 produced a comprehensive report on the bed bug, focusing on its control and education for all stakeholders (91). Subsequently, the UK Medical Research Council provided a comprehensive document covering biology, prevention, nonchemical and insecticidal control, and the limitations of the various control technologies (89). Because of the unprecedented effectiveness of DDT when first used in the 1940s against the pest, the need for bed bug educational programs soon declined.

With the realization that failed treatments were responsible for the degree of the modern resurgence, it became imperative to educate all stakeholders in managing insecticide-resistant bed bugs. The first comprehensive attempt to provide education on modern bed bug management was initiated by the Australian Environmental Pest Managers Association (AEPMA) in 2005. In that year, AEPMA developed and published the first industry standard for the control of the modern bed bug to enhance stakeholder knowledge, define best practices in bed bug management, and protect all stakeholders against poor management and ineffectual bed bug products (39). The document also promoted IPM, especially with nonchemical control options, and reviewed the limitations of all management choices. Subsequently, the European Code of Practice for Bed Bug Management (13) and the National Pest Management Association's Best Management Practices for Bed Bugs (98) were developed and published, both in 2010. During the late 2000s, many groups independently released management guidelines specific to certain environments, such as low-income housing or group living accommodation (54).

Bed bug management protocols are largely nonexistent in developing nations, and the World Health Organization has yet to produce any standards. In many African nations, malaria cases are on the rise, thought partially due to bed bugs (34, 66). Long-lasting insecticidal nets are widely used throughout malaria regions of Africa to prevent mosquito–human contact. Unfortunately, insecticide-resistant bed bugs are utilizing the nets as harborages, resulting in lower compliance in the use of the nets (34, 66). There is an urgent need to adapt the bed bug management protocols listed above in nations with limited resources.

4.6. Insecticide Resistance

Since the first report of DDT resistance in *C. lectularius* was recognized in 1947 (68), both bed bug species have become resistant to most of the major classes of insecticides used in their control, including the pyrethroids, organophosphates, carbamates, chlorinated hydrocarbons, and neonicotinoids (31), and reduced susceptibility to desiccant dust has been reported (84). Resistance mechanisms documented include penetration resistance, metabolic resistance [namely to cytochrome P450 monooxygenases (P450s), esterase, and ATP-binding cassette transporters], and target site insensitivity (*kdr*) (31, 109). Recently, it was found that insecticide susceptibility in *C. hemipterus* is influenced by the presence of bacterial symbionts (126). Currently, there is no ongoing global monitoring for resistance in bed bugs. However, wherever bed bugs have been tested during the years of the modern resurgence, they have demonstrated resistance to some class of insecticide (33, 101). It is safe to assume that insecticide-resistant bed bugs occur worldwide.

5. FUTURE MANAGEMENT

Bed bugs can be challenging to detect when their numbers are low. Various technologies to aid detection have come onto the market since the start of the modern resurgence. Swabs from rooms can be subjected to a lateral flow assay, with bed bug antigens detected by corresponding antibodies (75). Other, less practical technologies include the detection of early instars by measuring infrared signal durations, sound impulse-burst durations, and sound pressure levels (energy) of impulses (86); electronic noses to detect specific compound(s) emitted by insects (77), such as aldehyde blends of bed bugs (35, 36); and sampling and analyzing indoor air of an infested room using gas chromatography–mass spectrometry to detect bed bug aldehydes (48). None of these techniques have come to be in routine use.

Given the limited effectiveness of insecticides due to resistance and the fact that few new chemistries are coming onto the market, chemical control options for bed bugs are presently limited. This has necessitated research into formulations and alternative chemical strategies. A recent discovery demonstrated that some plant essential oils enhance deltamethrin efficacy by inhibiting P450 activity in pyrethroid-resistant bed bugs (52, 53). Field studies could test the potential of an essential oil–deltamethrin mixture against pyrethroid-resistant bed bug populations.

Systemic approaches have also been investigated to control bed bugs. The antiparasitic drugs ivermectin and moxidectin killed *C. lectularius* when fed systemically at human therapeutic doses and caused sublethal effects including reduced fecundity, nymphal molting inhibition, and reduced movements at lower doses (118, 146). Although these drugs are administered for antiparasitic treatments, the approval for their systemic usage in humans against bed bugs could prove ethically challenging. Toxicants including fipronil, clothianidin, abamectin, boric acid (122, 123), spinosad, and fluralaner (116), added to the blood and delivered via an artificial membrane feeding system, were lethal to *C. lectularius*. RNA interference (RNAi) can downregulate gene expression, and experiments using RNAi on *C. lectularius* led to reduced adult female fecundity (60, 95) and impaired egg production and viability (12). Bed bug symbionts provide essential nutrients to the insect, such as vitamin B. When bed bugs are fed antibiotics, these symbionts can be eliminated, resulting in slower bed bug development and reduced fecundity (64).

The biggest challenge with these systemic control methods is developing a feasible oral delivery system. Even with the addition of phagostimulants such as ATP (111), the challenge will be to cause the bed bugs to preferentially feed on the baits rather than the sleeping humans. Furthermore, as bed bugs primarily affect the poor, for any new control technology to be commercially viable, it must be low cost, low maintenance, simple to apply, and effective.

6. FUTURE RESEARCH DIRECTIONS

6.1. Differences Between *Cimex lectularius* and *Cimex hemipterus*

With technological advances, changes in building design, and climate control systems, the indoor environment is becoming progressively more uniform throughout the developed world. In such regions, there will inevitably be an increase in the number of localities where both species will be found. In less-developed nations with limited climate control, global warming may lead to a spread of *C. hemipterus* to traditionally cooler climes.

Most bed bug control products were developed for *C. lectularius*, with the assumption that they would also work on *C. hemipterus*. However, biological differences between the species are being discovered that have implications for the management of the latter species. A recent study demonstrated that *C. hemipterus* readily escapes from pitfall traps that contain *C. lectularius*, as the former species has more tenent hairs on its fossula spongiosa, giving it more grip and enabling it to climb smooth surfaces (74). Are there other physiological and biological differences in *C. hemipterus* that could have implications for the products or devices used in management programs against this species? Similarly, it is not known if *C. hemipterus* produces different health impacts, perhaps due to the existence of different antigenic compounds in the saliva. More research comparing the two species is required.

6.2. Improvement in Insecticide Test Procedures

There is an urgent need to streamline bed bug product testing protocols. Many field control failures arise from inadequate testing during the product development period. With the exception of the United States Environmental Protection Agency's OCSPP 810.3900: *Laboratory Product*

Performance Testing Methods for Bed Bug Pesticide Products (49), which requires the assessment of susceptible and multiple field-collected strains (79), other test protocols have employed susceptible strains or field-collected strains that have been reared in the laboratory for many years, which may have lost much of their resistance. Thus, a product that appears promising in the laboratory may not produce the desired result in the field. Different exposure surfaces (36), exposure times, and assessment intervals (83) also impact test results. In contrast to *C. lectularius*, which has several standard susceptible strains (e.g., Harlan, Monheim), no insecticide-susceptible strain of *C. hemipterus* exists (30, 32, 34, 81, 83). Without such a strain, studies of insecticide resistance in *C. hemipterus* will continue to rely on a *C. lectularius* susceptible strain for comparison.

6.3. Resistance Mechanisms and Management Strategies

Widespread insecticide resistance has rendered many chemical control options ineffective. This means that a deeper understanding of the resistance mechanisms of both bed bug species, especially the less studied *C. hemipterus*, is warranted. Mechanisms such as behavioral resistance, insensitive GABA receptors that confer dieldrin and fipronil resistance, and altered nicotinic acetylcholine receptor that confer resistance to neonicotinoids have not been detected to date (31). Investigation into the evolution of resistance mechanisms in field bed bug populations in areas with resistance management strategies such as rotation and mixtures may shed light on the feasibility of chemical control strategies in the long term. Ongoing resistance monitoring is also required to determine if bed bugs are becoming resistant to other classes of insecticides.

6.4. The Degree and the True Costs of the Global Resurgence

As noted above, there is a dearth of detailed epidemiological information on the bed bug resurgence, as most published reports are anecdotal, and there is no information on the differences in infestation rates between *C. hemipterus* and *C. lectularius* (79). Similarly, an accurate economic quantification of the resurgence has yet to be determined, although it is believed that bed bugs are costing the world economy billions of dollars annually (46). These factors are limiting justifications for research funding, and thus there is an urgent need for data on both fronts. This means that the global bed bug problem is largely being addressed through the education of stakeholders and via industry standards that promote best practices in bed bug management (79). Without research on more effective control options, bed bugs will likely continue to plague humanity for years to come.

SUMMARY POINTS

1. The modern resurgence of bed bugs involves *Cimex lectularius* (common bed bug) and *Cimex hemipterus* (tropical bed bug), both of which show widespread insecticide resistance.
2. Early bed bug control options were limited, consisting mainly of prevention (inspections, furniture with minimal harborages); nonchemical control (heat treatments); and chemical control with highly toxic compounds, including fumigants.
3. Modern bed bug detection and monitoring involve interviews, visual inspections, canines, and bed bug monitors (active and passive traps).
4. Nonchemical control options include vacuuming, temperature extremes (freezing, dry heat, and steam), exclusion, and entomopathogenic fungi.

5. At least 12 insecticide classes have been used or tested against bed bugs in various formulations, including liquid sprays, pressurized aerosols, impregnated mattress liners, desiccant dusts, fumigants (including resin strips), and repellents.
6. Insecticide resistance in both *C. lectularius* and *C. hemipterus* is due to at least three known resistance mechanisms: penetration resistance, metabolic resistance (cytochrome P450s, esterase, and ATP-binding cassette transporters), and target site insensitivity (*kdr* and altered acetylcholinesterases). Symbiont-mediated reduced insecticide susceptibility has been reported in *C. hemipterus*.
7. Novel control approaches such as RNA interference, toxicant baits, and systemic toxicants show future potential but presently lack feasible, low-cost, and effective delivery systems.
8. Important future research directions include the factor(s) behind the modern bed bug resurgence, the economic impacts of the resurgence, the biological differences between *C. lectularius* and *C. hemipterus*, improvements in insecticide test procedures, resistance mechanisms, and resistance management strategies.

DISCLOSURE STATEMENT

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

ACKNOWLEDGMENTS

We apologize to authors whose work could not be presented in this review due to space limitations. We thank Kai Dang for comments on the draft manuscript.

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