

Bedbugs and Infectious Diseases

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Bedbugs are brown and flat hematophagous insects. The 2 cosmopolite species, *Cimex lectularius* and *Cimex hemipterus*, feed on humans and/or domestic animals, and recent outbreaks have been reported in occidental countries. Site assessment for bedbug eradication is complex but can be assured, despite emerging insecticide resistance, by hiring a pest-control manager. The common dermatological presentation of bites is an itchy maculopapular wheal. Urticarial reactions and anaphylaxis can also occur. Bedbugs are suspected of transmitting infectious agents, but no report has yet demonstrated that they are infectious disease vectors. We describe 45 candidate pathogens potentially transmitted by bedbugs, according to their vectorial capacity, in the wild, and vectorial competence, in the laboratory. Because of increasing demands for information about effective control tactics and public health risks of bedbugs, continued research is needed to identify new pathogens in wild *Cimex* species (spp) and insecticide resistance.

Bedbugs are hematophagous arthropods. The discovery of specimens in tombs at Tell al-Armana, Egypt, suggests that these insects have been pestering humans for at least 3550 years [1]. After World War II, bedbugs became uncommon in developed countries due to social and economic progress and insecticide development [2], while infestation in poor countries never decreased [3, 4]. Recently reported outbreaks have indicated bedbug resurgence in many occidental countries [5]. Medical interest in bedbugs (especially *Cimex lectularius* in temperate zones or *Cimex hemipterus* in tropical areas and sometimes temperate zones) has increased (Figure 1). Numerous authors have postulated that these

species could transmit pathogens to humans. Consensus on their medical impact remains limited to dermatological reactions to their bites [6, 7]. We undertook a literature review, describing their entomological characteristics, epidemiology, and medical impact and focusing on the vectorial behaviors of this insect.

ENTOMOLOGY

Bedbugs are Hemiptera order insects of the Cimicidae family. Medicine is well acquainted with 2 Hemiptera: Reduviidae, as vectors of Chagas disease (*Trypanosoma cruzi*), and Cimicidae, as pests [1]. *C. lectularius*, *C. hemipterus*, *C. columbarius*, *C. pipistrelli*, *C. dissimilis*, and *Oeciacus hirundinis* are the main species involved in humans, whereas birds or bats are the primary hosts for *C. columbarius*, *C. pipistrelli*, *O. hirundinis*, *C. lectularius*, and *C. hemipterus*. This review focuses on these last 2 species.

Adult *C. lectularius* and *C. hemipterus* are reddish-brown, flat, wingless ovals (4–7 mm) resembling confetti (Figures 2A and 2B). The 2 species are distinguishable only by specialists. Both sexes are hematophagous and can live for 12 months without feeding and even 1.5–2 years in colder environments.

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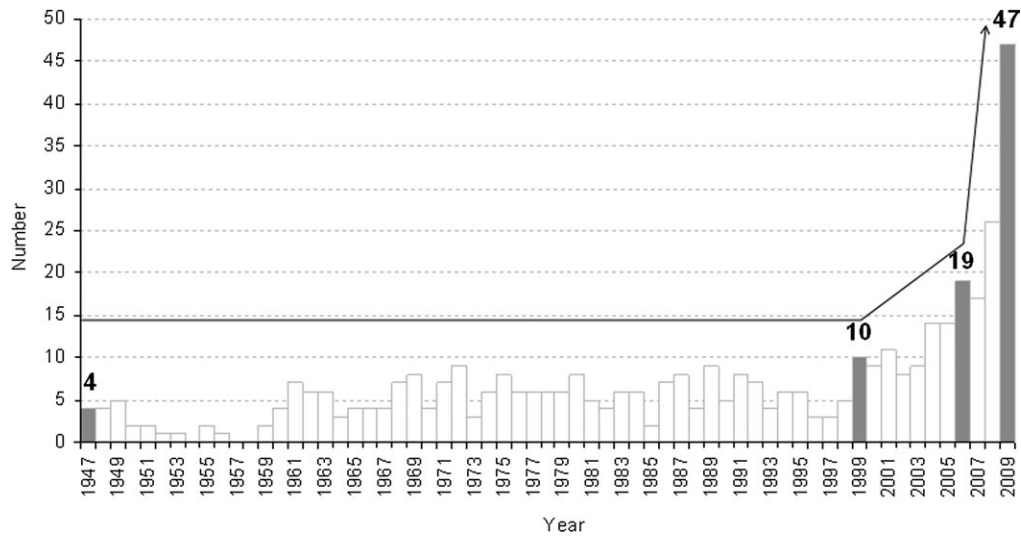


Figure 1. Increase in the number of PubMed citations for the search words *Cimicidae*, *Cimex*, *Afrocimex*, or *Oeciacus* over the past 10 years. The medical community's interest in bedbugs (*Cimex lectularius* or *Cimex hemipterus*) has increased dramatically.

During each Cimicidae mating, sperm are deposited by traumatic insemination, which bypasses the female genital tract. The male's intromittent organ pierces the cuticle via a surface groove, called the ectospermaleg (which purportedly evolved to guide the organ and reduce trauma but is a frequently missed target and hence the cuticle is punctured elsewhere) and injects sperm into the mesospermaleg, a specific female organ through which the sperm migrate. Males preferentially direct their sexual interest to recently fed females, which undergo ~5 traumatic inseminations per feeding [8]. High female mortality results from these numerous traumas, but other explanations have also been proposed (eg, microbe introduction by traumatic insemination). As for most female insects, sperm are stored in specific structures called seminal conceptacles. The female reproductive tract is used only for laying

fertilized eggs. Each adult female produces 200–500 eggs in her lifetime.

Under a constant temperature of 14–27°C, eggs hatch 4–10 days after mating, yielding the nymphs, which are 1–3 mm long, visible to the naked eye, translucent, and lighter in color [8]. Each molt requires a blood meal, which can last 10–20 min, to grow to the next stage every 3–7 days if a host is available. These developmental stages of the bedbug (Figure 3) explain how a previously unknown bedbug presence in a newly infested site achieves exponential multiplication by the end of the first month.

Bedbugs fear light and are generally active in the dark. They hide in any small dark place, such as bedclothes, mattresses, springs, bed frames, cracks, crevices, and wallpaper. They emit an easily recognized, offensive odor caused by an oily secretion produced by special glands [8, 9].

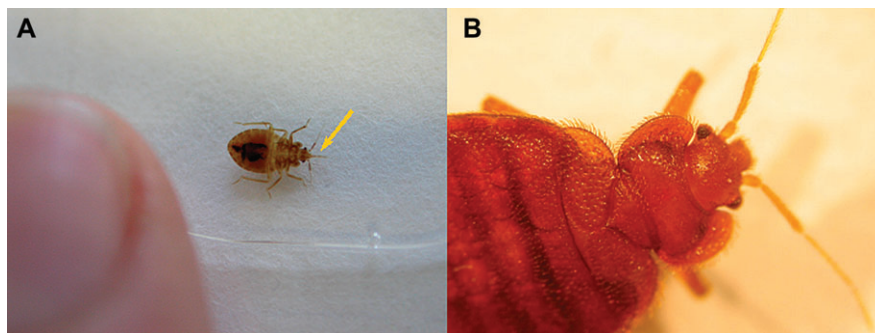


Figure 2. Physical appearance of bedbugs (*Cimex lectularius*). Bedbugs are hematophagous arthropods that resemble small, brownish, flat, and oval confetti. *A*, Bedbug nymph; note the bite unit in front of the head (*arrow*), which is usually folded under the head as for the adult. *B*, Adult bedbug.

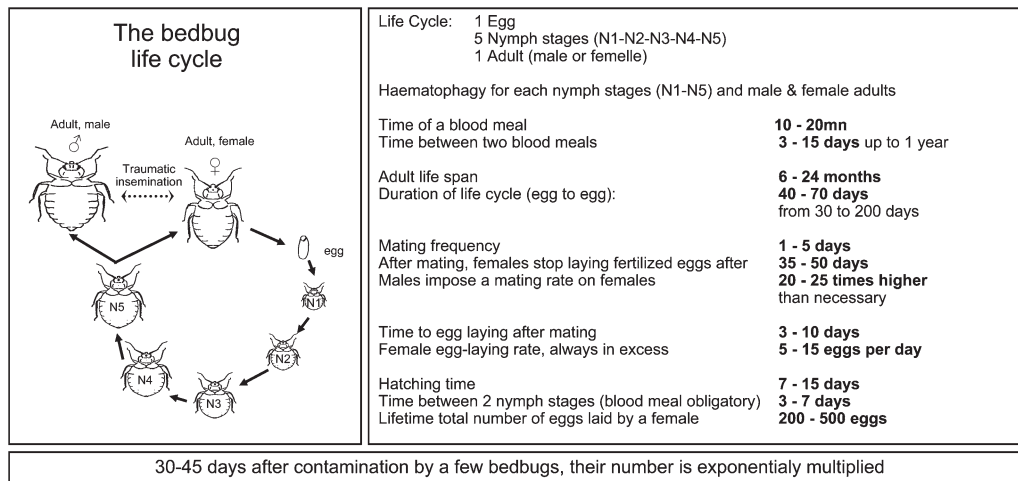


Figure 3. Life cycle of the bedbug (*Cimex lectularius* or *Cimex hemipterus*). These evolutionary stages and the reproduction biology of the bedbug explain how, over 1 month, an unknown introduction of several bedbugs into a new site leads to their exponential multiplication and sudden infestation.

EPIDEMIOLOGY

Beds bugs are cosmopolite insects. Isolated cases, clusters, or epidemics of bedbugs have been reported in most big cities on all continents [2, 10, 11]. Bedbugs have the ability to spread near and far. Local spreading, called “active dispersal,” occurs by walking short distances, such as when they try to reach hosts from their dark resting places. Active dispersal is the main means of room-to-room spreading in communities through ventilation ducts. Bedbugs can also travel longer distances by being transported by humans in clothing, luggage, or furniture; this is called “passive dispersal.” Hence, the rapid turnover of residents in certain locations is a risk factor for bedbug infestation. Furthermore, overcrowding and deprived conditions are factors that facilitate the bedbug burden. Finally, the infestation risk reflects rapid turnover and high human density but not specific geographic areas or climatic conditions [12–14].

Bedbug eradication from an infested site is a challenge: Insecticide resistance has been demonstrated experimentally and is an increasing problem [15]. Successful bedbug elimination relies mainly on good cooperation between the owner of the pest-infested site and the pest manager for site assessment, thorough inspection, identification, and eradication. An “efficient search-and-destroy” operation, as Doggett explained [16], must be imposed, starting by removing all bed linens and washing at a temperature $>60^{\circ}\text{C}$, then by checking and dismantling all furniture to access all bedbug hiding places, to identify and destroy eggs,

nymphs, and adults (Figures 4A–4F) [16]. Alternatively, a dog specifically trained to detect bedbugs’ characteristic odor can do the search [17]. Attractive traps can also be used in highly infested locations [18]. It is always best to vacuum first to reduce the overall bedbug population, but complete success is unlikely without remnant insecticides for residual protection against bedbug survivors. Fumigants, which are too frequently used by nonprofessionals, do not penetrate deeply into bedbug hiding places, fail to provide any residual protection, and can pose an immediate health risk to the user. Aerosolized insecticides against cockroaches, for example, are quick killing agents that can be accurately applied meticulously to specific areas (eg, mattress or cracks and crevices in furniture). The best option is a remnant insecticide, which is spread by a professional in all hiding areas identified during the inspection process. Sometimes, it may be advisable to treat adjoining rooms, even when no bedbugs were found during the inspection [12, 16]. Some methods can minimize the risk of infestation or expansion: regular inspections, hygiene procedures, and general education of the population. Complementary measures include modifying room temperature, destroying nearby bat or bird habitats, eliminating peeling paint and plaster, and caulking cracks and crevices in walls and furniture [16, 19].

MEDICAL IMPACT

After identification of bedbug bites, skin and infectious transmissible diseases are the 2 main medical concerns of human contact with the bedbugs [20, 21].

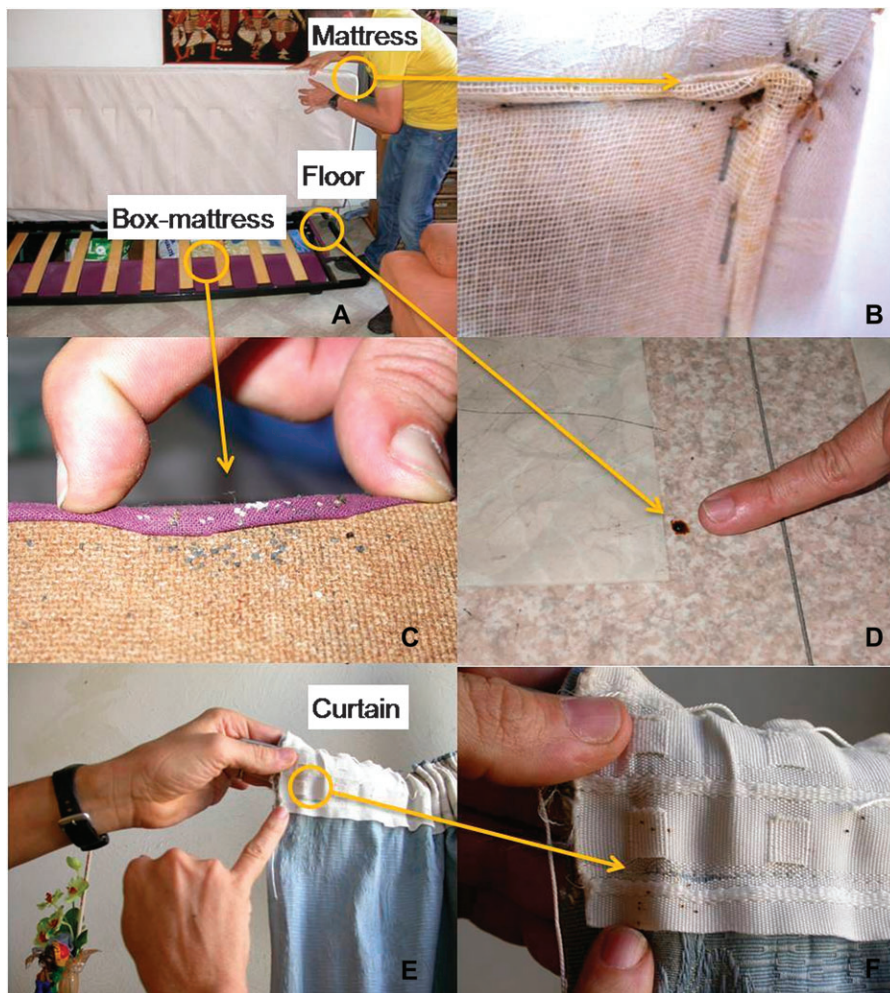


Figure 4. Hiding places of bedbugs (*Cimex lecturarius* or *Cimex hemipterus*). An efficient search-and-destroy operation against bedbugs (A) must start by removing the mattress (B) and box springs (C), then by exploring the floor close to the bed (D) and curtains (E, F) to identify and destroy eggs, nymphs, and adults.

Hosts are usually bitten at night. Because bedbug saliva contains anesthetic compounds, bites are painless and usually not felt until several hours later. Other compounds are also injected: anticoagulant factors (eg, factor-X inhibitor), vasodilatory compounds (such as nitric oxide), and proteolytic enzymes (eg, apyrase), which are all substances that participate in the ensuing local hypersensitivity reactions [6].

The typical skin lesion is a pruritic erythematous maculopapule, 5 mm to 2 cm in diameter, with a central hemorrhagic crust or vesicle at the bite site, similar to arthropod bites. Atypical forms vary from asymptomatic or pauci-symptomatic to purpuric, vesicular, and bullous lesions. The bedbug-bite distribution frequently follows a line or curve (Figure 5A and 5B). Lesion numbers range from several to many, depending on habitat-infestation intensity, and are

preferentially located in unclothed zones (Figure 5C). Sometimes, the eruption mimics urticaria (Figure 5D). Exceptional anemia [21] or anaphylactic reactions have been reported. Lesions resolve spontaneously within 2–6 weeks, but permanent postinflammatory hyperpigmentation may ensue [22–25].

Bedbugs have been suspected of transmitting infectious agents; over 40 microorganisms have frequently been considered strong candidates [6, 7]. In contrast to that for mosquitoes or ticks, the literature evidence level for disease transmission by bedbugs is very heterogeneous and sometimes incomplete.

Several steps are mandatory to demonstrate the causal relationship between a vector and a disease. The first is vector competence—that is, an attempt must be made to demonstrate by laboratory experiments an arthropod's ability to acquire an infectious agent from another



Figure 5. Presentation of bedbug (*Cimex lectularius* or *Cimex hemipterus*) bites: forms vary from asymptomatic or pauci-symptomatic to purpuric, vesicular, and bullous lesions. The typical skin lesion is a pruritic erythematous maculopapule that is 5 mm to 2 cm in diameter with a central hemorrhagic crust or vesicle at the bite site, similar to other arthropod bites (A). A series of bites in a line is characteristic of bedbug bites (B). Lesion numbers range from a few to numerous, depending on habitat-infestation intensity, and are preferentially located in unclothed zones (C). In some cases, the eruption mimics urticaria (D).

animal or infected blood, to maintain or amplify it, and then to transmit it to another animal [26]. Only successful demonstration of all of these abilities permits consideration of the vector as competent, but this remains insufficient to designate an arthropod as an effective vector for a defined infectious agent. Vector competence is invariable for a defined arthropod–pathogen couple. Location, climate, and entomological, ethological, and/or epidemiological parameters that may interfere in effective transmission must also be considered. This type of study, which is conducted in the wild, enables assessment of the potential vectorial capacity with a mathematical algorithm that includes the number of infected arthropods and the number of bites per night and per person [26]. Vectorial capacity varies for a defined arthropod–microbe couple.

In considering bedbugs as vectors of infectious diseases, older studies in scientific literature mainly consist

of logical but not evidence-based postulates [7]. Epidemiological links between human-disease prevalence in a population and bedbug presence, or infectious agent detection in wild bedbugs, without data concerning acquisition, multiplication, or transmission, led some authors to examine bedbug vectorial capacity [7, 27]. On the basis of some laboratory studies, we found relevant experimental evidence that ≥ 1 vectorial competence steps have been completed for bedbugs [6], but we found no published evidence for completion of all the necessary steps leading to the conclusion that bedbugs transmit a pathogen.

Table 1 lists 45 pathogens reportedly found in bedbugs (without considering study quality) and classifies bedbug–pathogen couples according to their vectorial competence (eg, acquisition, maintenance, and transmission) and vectorial capacity (eg, reasoning and detection in the wild) criteria, with a summary of each

Table 1. Classification of Studies on Pathogens Carried by *Cimex lectularius* or *Cimex hemipterus* According to Their Vectorial Competence or Vectorial Capacity

No.	Pathogen	Laboratory investigation: vectorial competence					Studies in the wild: vectorial capacity		
		Acquisition	Maintenance			Transmission to another animal	Inference, deductive reasoning, or conjecture	Found in wild bedbugs	
			Replication†	Detection					
	Detection ^a		Saliva	Feces	Transovarian				
Bacteria									
1	<i>Bacillus anthracis</i>	No [7]							Yes and no [7]
2	<i>Bartonella quintana</i>	No [7]		No [7]					
3	<i>Borrelia recurrentis</i>	Yes [7]							Yes [7]
4	<i>Borrelia duttoni</i>	No [7]							
5	<i>Bruceella melitensis</i>	Yes [7]			Yes [7]				Yes [7]
6	<i>Candidatus Midichloria mitochondrii</i>								Yes [36]
7	<i>Coxiella burnetii</i> (Q fever)	Yes [7, 28, 29]	Yes [28, 29]		Yes [28, 29]	Yes [28, 29]	Yes, suspected [28, 29]	Yes [28, 29]	Yes [28, 29]
8	<i>Francisella tularensis</i>	Yes [7]			Yes [7]		Yes, via feces [7]		
9	<i>Leptospira</i> spp	No [7]							
10	<i>Mycobacterium leprae</i>	Yes [7]	No [7]	Yes [7]		No [7]		Yes [7]	
11	<i>Mycobacterium tuberculosis</i>							Yes [6, 7]	
12	<i>Rickettsia africae</i>		No [7]						
13	<i>Rickettsia conorii</i>	Yes [7], injection	No [7]	No, meal; yes, injection [7]					
14	<i>Rickettsia prowazekii</i>		No [7]					Yes [7]	
15	<i>Rickettsia rickettsii</i>	Yes [7], injection	Yes and no [7]	Yes and no, meal; yes, injection [7]		Yes [7]	No, via feces or meal [7]		Yes [7]
16	<i>Rickettsia typhi</i>	Yes [7], injection							
17	<i>Salmonella typhi</i>	Yes [7]			Yes [7]		Yes [7]	Yes [7]	
18	<i>Staphylococcus aureus</i>	Yes [7]		Yes [7]					
19	<i>Streptococcus pneumoniae</i>		No dead bedbugs [7]			Yes [33]			
20	<i>Wolbachia</i> spp	Yes [7]							Yes [32, 33]
21	<i>Yersinia pestis</i>							Yes [7]	
Fungi									
22	<i>Aspergillus flavus</i>								Yes, carried [6, 37]

Table 1. (Continued)

No.	Pathogen	Laboratory investigation: vectorial competence						Studies in the wild: vectorial capacity	
		Acquisition	Maintenance			Transmission to another animal	Inference, deductive reasoning, or conjecture	Found in wild bedbugs	
			Replication†	Detection					
	Detection ^a		Saliva	Feces	Transovarian				
23	<i>Penicillium</i> spp							Yes, carried [37]	
24	<i>Scopulariopsis</i> spp							Yes, carried [37]	
Parasites (filariasis)									
25	<i>Brugia malayi</i>	Yes [7]	No [7]					Yes [7]	
26	<i>Wuchereria bancrofti</i>	Yes [7]	No [7]					Yes [7]	
27	<i>Mansonella ozzardi</i>	Yes [7]	No [7]						
28	<i>Onchocerca volvulus</i>	No [7]	No [7]						
29	<i>Leishmania braziliensis</i>	Yes [7]		Yes [7]					
30	<i>Leishmania donovani</i>	Yes [7]	No [7]	Yes and no, stomach [7]	Yes [7]	No [7]		No [7]	
31	<i>Leishmania tropica</i>	Yes and no [7]		Yes [7]			Yes [7]		
32	<i>Plasmodium</i> spp						Yes [7]		
33	<i>Trypanosoma cruzi</i>	Yes [6, 7, 39, 40]	Yes [7, 39, 40]	Yes [7, 39, 40]		Yes and no, via feces [7, 39, 40]		Yes [7, 39, 40]	
34	<i>Trypanosoma gambiense</i>						Yes [7]		
Viruses									
35	Hepatitis B	Yes [6]	Yes and no [6]	Yes [6]	No [6]	No [6]	Yes [6]	Yes [6]	
36	Hepatitis C	No [6]						Yes [6]	
37	Hepatitis E							Yes [6]	
38	Human immunodeficiency	Yes [6]	No [6]	No [6]		No [6]			
39	Influenza						Yes [7]		
40	O'nyong-nyong							No [46]	
41	Polio	Yes and no [7]							
42	Rabies	No [47]							
43	Reovirus							Yes [48]	
44	Variola (smallpox)	Yes [7]	Yes [7]	Yes [7]	Yes [7]				
45	Yellow fever	Yes and no [7]		Yes [7]					

NOTE. Classification of 45 microbes (bacteria, fungi, parasites, and viruses) in alphabetical order. For each pathogen, studies are classified according to vectorial competence (acquisition, maintenance, and transmission) and vectorial capacity (reasoning and detection in the wild). We intentionally listed a maximum of investigations without considering their quality to compare the process of studies. For each cell, no means negative results or failure, yes means positive results or success, and a blank cell means no published study was found.

^a After a blood meal (meal) or intragut injection (injection).

study's results. Below, we focus on the best studied pathogens and/or the best candidates for transmission by bedbugs, such as *Coxiella burnetii* and *Wolbachia* spp among bacteria, *Aspergillus* spp among fungi, *T. cruzi* among parasites, and hepatitis B virus (HBV) and human immunodeficiency virus (HIV).

Coxiella burnetii. Q fever is a cosmopolitan disease transmitted by aerosolization of *C. burnetii* spores contained in goat, sheep, or cattle bedding or by consumption of unpasteurized milk products [28]. In the 1960s, bedbugs were successfully infected by feeding on infected guinea pigs [29]. *C. burnetii* has been isolated at all bedbug stages, which demonstrates transstadial transmission. *C. burnetii* reportedly persisted in the bedbugs for up to 250 days without loss of pathogenicity, multiplied therein, and were excreted in bedbug feces. In an epidemiological study conducted by the same author at the same period [30] around Leningrad (Russia), *C. burnetii* was detected in field-collected bedbugs, with the Q fever prevalence there estimated at 29.2% of the population. The results of the first study suggested that the insect was able to acquire, replicate, transmit to progeny, and excrete *C. burnetii* via feces. Thus, hypothetical vectorial competence of possible pathogen transmission to another animal has to be considered. An apparent relationship between high Q fever prevalence in the Leningrad population and bedbug infestation could be an epidemiological argument supporting vectorial capacity, but it remains questionable, because many confounding factors may intervene; for example, it is known that ticks are also a potential Q fever vector [31]. Finally, the potential ability of bedbugs to transmit *C. burnetii* to humans requires further investigation.

***Wolbachia* spp.** *Wolbachia* spp (among Anaplasmataceae bacteria) are obligate intracellular bacterial symbionts that change the reproductive capacities of many arthropod and filarial nematode hosts. This effect has enhanced medical and scientific interest in view of new therapeutic options. *Wolbachia* spp have been detected in most tested *C. lectularius*, are specifically located in the bacteriomes (specialized organs found mainly in some insects that host endosymbiotic bacteria), and appear to be obligate nutritional mutualists. Transovarial transmission to future generations has been established. Thus, arguments supporting bedbug vectorial competence and capacity to spread this ubiquitous microorganism exist, but its human pathogenicity remains unknown. More knowledge is needed before *Wolbachia* spp can be used as a weapon to control bedbugs (eg, through sterilization, which is required for symbiosis) [32–36].

***Aspergillus* spp.** *Aspergillus* spp, along with various other molds (eg, *Penicillium* spp and *Scopulariopsis* spp) and bacteria (eg, *Enterobacter* spp and *Staphylococcus* spp), have been found on bedbugs. Like any biting or walking insect (such as cockroaches), bedbugs can be very good transporters and thus can participate in spreading molds [37]. Phoresy is the passive transportation of some pathogens by a carrier. To our knowledge, only such passive carriage could be a route of fungus transmission by bedbugs, but a real epidemiological impact remains to be proven. Furthermore, 9 bacterial and fungal species have been identified in male intromittent organs and bedbugs' hiding places [8].

Trypanosoma cruzi. *T. cruzi*, which causes Chagas disease, is transmitted by kissing bugs. Bedbugs and kissing bugs have many similarities: both have reflexive feces excretion after a blood meal, which is an important behavioral feature responsible for transcutaneous *T. cruzi* transmission from kissing bugs [38]. Indeed, scratching pruritic bites facilitates mechanical entry of parasites contained in bedbug feces into bite sites. Moreover, Latin American biotopes of the 2 bugs live in proximity in the wild and around or in houses, and contacts between the 2 insects are frequent, mostly in rural areas or poor districts, where *T. cruzi* transmission is frequent. Pertinently, *T. cruzi* has been detected in wild bedbugs. Moreover, in experimental laboratory studies, after eating an infectious meal, the bedbug had acquired the parasite, which replicated and was detected in feces [39]. Transstadial transmission has also been proven, and Azevedo et al [39] studied bedbug salivary glands to precisely describe their ultrastructure, as *T. cruzi* stored therein might be transmitted during a blood meal. Thus, arguments supporting vectorial competence and capacity exist in the literature, and bedbug transmission to humans would not be unlikely. To date, *T. cruzi* is among the most studied candidates for transmission via feces or saliva, and ongoing experimental and epidemiological studies are trying to determine whether transmission is fact or fiction [6, 7, 39, 40].

Hepatitis B virus. According to the literature, HBV is the best candidate for transmission by bedbugs. HBV has frequently been detected in wild bedbugs [6, 41–43]. In the laboratory, it has been detected up to 2 months after an infectious meal or after direct injection into the bedbug, it has been found in feces, and transstadial transmission has been demonstrated. However, the majority of studies were unable to demonstrate virus multiplication and transmission to chimpanzees. Moreover, in a Gambian study, insecticide spraying of

children's rooms was highly effective at reducing bedbug exposure but had no effect on HBV infection incidence, refuting the suspected relationship between children's HBV infections and bedbug presence [6]. Another study conducted in India obtained similar findings [6]. Finally, to date, no proof of effective transmission exists.

Human immunodeficiency virus. HIV has never been found in wild bedbugs. HIV survived for 8 days after experimental feeding, with no replication in bedbugs, and has never been observed in bedbug feces. Transmission assays from bedbugs to laboratory animals failed, despite very high virus concentrations. Thus, even though acquisition and persistence attest to partial vectorial competence, no evidence supports that such transmission may occur or has ever occurred. Therefore, to date, HIV is no longer a valid candidate pathogen for bedbug-borne transmission [6].

DISCUSSION AND CONCLUSION

Because common bedbugs have a worldwide distribution, are hematophagous insects, and have been suspected of transmitting infectious diseases to humans, the medical community's interest has increased dramatically over the past 10 years. Although regional centralization of information about bedbug epidemics or infested clusters is lacking in many countries, the United Kingdom, Canada, Australia, and the United States are leaders in collecting pest cases. As for head lice in schools, the insect's presence is known, but the majority of public health centers are unable to provide precise case numbers. Bedbugs have to be tracked, at least in public and crowded places (eg, hotels, trains, and dormitories). Furthermore, because of increasing travel and climate change, the scientific community has to monitor the differential identifications of *C. lectularius* (temperate climates) and *C. hemipterus* (tropical and temperate climates). Just as macroscopic identification of parasites is being confirmed more frequently by molecular biology analyses, the same holds true for the identification of these 2 bedbug species [44]. In each cluster, as is done in Australia, the United States, Canada, and the United Kingdom, other countries must work together to devise local eradication strategies and raise bedbug colonies to develop insecticide-susceptibility testing. Without the expansion of these different aspects of bedbug management, further escalation of this public health pest is expected, and the demand for information about effective control tactics will rise.

For general practitioners, identification of bedbug bites is difficult because of patients' widely varying

immunological responses. A serological test should be developed [45].

Concerning the possible transmission of pathogens, we know that bedbugs can be carriers of >40 microorganisms in their stomach, feces, teguments, and/or saliva. Those pathogens were isolated from bedbugs captured in the wild and in human habitats, or after feeding on natural or artificial infected laboratory animals or after direct injection into bedbugs. But the majority of reports failed to demonstrate that *C. lectularius* and *C. hemipterus* are infectious disease vectors. However, those studies were generally old and did not benefit from modern tools to identify microorganisms. Furthermore, emerging bacteria (eg, *C. burnetii* or *Wolbachia* spp) have not been evaluated using these new biological approaches. The pathogens carried by wild bedbugs have to be investigated and updated with modern tools and parallel studies in bedbug and human samples, with blinded clinical assessment to detect the same pathogens independently.

The discordance between microbe levels in bedbugs and low numbers of suspected germs transmitted remains a major enigma. We hypothesize that this insect's novel reproductive biology could affect this discordance. Among hematophagous arthropods feeding on humans, bedbugs are the only ones to mate by traumatic insemination. Bedbug immunity and infectious agent carriage could be related: frequent traumatic inseminations of a female are definitely a source of repeated pathogen introduction and thus a source of repeated immune stimulation. Because traumatic insemination has been shown to shorten the female lifespan, Reinhardt et al [34] presumed it to be a factor in the selection of high immunity bedbugs. These different factors and their various effects or interactions influence the female immune system, transmission intensity, and/or pathogen virulence. Some bacterial agents are likely to be obligate endosymbionts necessary for bedbug survival and evolution (eg, *Wolbachia* spp and other proteobacteria), whereas others are likely to be transstadially transmitted, such as HBV. Hence, the bedbug might only play the role of vector in pathogen transmission and, consequently, may be involved in human disease in special circumstances not yet discovered. Future investigations are needed to improve our knowledge on the medical importance of bedbugs.

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