

The Potential Effect of Global Warming on the Geographic and Seasonal Distribution of *Phlebotomus papatasi* in Southwest Asia

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The distribution of *Phlebotomus papatasi* in Southwest Asia is thought to be highly dependent on temperature and relative humidity. A discriminant analysis model based on weather data and reported vector surveys was developed to predict the seasonal and geographic distribution of *P. papatasi* in this region. To simulate global warming, temperature values for 115 weather stations were increased by 1°C, 3°C, and 5°C, and the outcome variable coded as unknown in the model. Probability of occurrence values were then predicted for each location with a weather station. Stations with positive probability of occurrence values for May, June, July, and August were considered locations where two or more life cycles of *P. papatasi* could occur and which could support endemic transmission of leishmaniasis and sandfly fever. Among 115 weather stations, 71 (62%) would be considered endemic with current temperature conditions; 14 (12%) additional stations could become endemic with an increase of 1°C; 17 (15%) more with a 3°C increase; and 12 (10%) more (all but one station) with a 5°C increase. In addition to increased geographic distribution, seasonality of disease transmission could be extended throughout 12 months of the year in 7 (6%) locations with at least a 3°C rise in temperature and in 29 (25%) locations with a 5°C rise. **Key words:** global warming, leishmaniasis, *Phlebotomus papatasi*, sandfly, sandfly fever, Southwest Asia. *Environ Health Perspect* 104:724-727 (1996)

Much of the impact of global warming on human activities has focused on physical consequences, such as more frequent violent storms and rising sea levels flooding low-lying areas. However, there are growing indications that the potential effects of global warming on human health are no less serious (1). For example, geographic and seasonal distribution of infectious diseases, particularly vectorborne diseases, could be markedly altered (2,3).

Vectorborne diseases are usually limited in their distribution, either by the range of the vector or by the range of a reservoir vertebrate host. The vector and host range are affected, directly or indirectly, by temperature and precipitation. According to Shope (4), global warming in North America could extend the distribution of the mosquito vectors *Aedes aegypti* and *A. albopictus*.

In addition to extending the geographic range of these vectors, the development of the mosquito larvae is faster in warmer climates, resulting in the mosquitoes becoming adults sooner. Also, the extrinsic incubation periods of yellow fever and dengue viruses in the mosquito vectors are dependent on temperature (4). With warmer temperatures, the incubation time required from when the mosquito first encounters an infected host until the mosquito is able to transmit an infectious virus may be shortened.

As a result of these factors, the mosquito vectors may be more widely distributed and metamorphose faster with global warming, and the extrinsic incubation period of viruses like dengue and yellow fever may be

shortened. These altered factors could result in increased transmission of vectorborne disease in temperate climates where vectors already occur but where development of the parasite is limited by current temperature conditions (4,5).

The sandfly, *Phlebotomus papatasi*, is a vector throughout Southwest Asia of two important infectious diseases, sandfly fever and leishmaniasis. Sandfly fever is a viral infection characterized by rapid onset, with a 3- to 4-day course of high fever and severe debility, but mortality is low with this infectious disease. Cutaneous leishmaniasis, also known as Oriental sore or Baghdad boil in Southwest Asia, is caused by a protozoal infection, either *Leishmania tropica* or *Leishmania major*. The primary manifestation of this disease is nonfatal ulcerating skin lesions after an incubation period of several days to many months. Visceral leishmaniasis, or Kala azar, is a chronic systemic infection caused by *Leishmania donovani*. It has an incubation period from 2 to 4 months and can be fatal if untreated.

The distribution of *P. papatasi* is not well understood but is known to be highly dependent on environmental conditions. Both sandfly adults and larvae are sensitive to high temperatures and low humidities. In laboratory experiments, all adult sandflies died within 2 hr at temperatures above 40°C, and temperatures below 10°C are unfavorable for survival (6).

Besides temperature, laboratory studies have demonstrated that as the relative humidity increases, the number of sandfly

survivors increases. Studies also have shown that the larvae, pupae and adult sandflies must have a habitat with a constant, relatively high humidity (6).

Rodent burrows, like those created by the gerbil, *Psammomys obesus*, provide the high humidity and cooler temperatures necessary for sandfly survival. Caves, deep cracks in walls, and dark corners in houses also provide favorable environmental conditions for the sandfly to survive and reproduce, even in areas of extreme temperature and aridity (6). With the onset of cold weather, however, sandfly larvae undergo diapause, permitting them to survive the winter and emerge as adults the following spring (7). *P. obesus* also serves as a reservoir of the parasite that causes cutaneous leishmaniasis (8).

Information on the seasonal distribution of *P. papatasi* indicates a definite seasonal occurrence which is consistent with environmental experiments: absent in all locations in the cold winter period of January and February, with a population increase beginning in most areas by April or May and declining in October (9-11). Also, most sandflies are nocturnal, probably due to environmental factors. The biting activity of *P. papatasi* starts immediately after sunset and increase afterwards, reaching a maximum around midnight when the temperature tends to be lower and the humidity higher (12). Biting activity has been observed in Central Iraq to decrease to 13% at 0300 hr and to almost stop after sunrise (12).

Using a computer model based on temperature, relative humidity, dew point, and previously reported vector surveys, this study explores the potential effect global warming could have on the seasonal and geographic distribution in Southwest Asia of the sandfly, *P. papatasi*.

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This research was supported by the U.S. Naval Medical Research and Development Command, workunit number 62787A001.01EAX1288.

The opinions and assertions contained herein are those of the authors and are not to be construed as official or as reflecting the views of the U.S. Departments of the Navy or Defense.

Received 16 January 1996; accepted 2 April 1996.

Initial Model

A model based on monthly weather and vector occurrence data was developed previously to predict the geographic and seasonal distribution of *P. papatasi* in Southwest Asia (13). For the model, information was compiled from 136 articles on the presence or absence of the vector, *P. papatasi*, as well as on the presence or absence of human cases of cutaneous and visceral leishmaniasis and sandfly fever. Weather data were obtained from the International Station Meteorological Climate Summary, version 2.0, June 1992 (Federal Climate Complex, Asheville, North Carolina). Data were available for 115 weather stations in 10 countries: Saudi Arabia, Kuwait, Yemen, Iraq, Iran, Syria, Jordan, Lebanon, Israel, and Egypt. These data encompassed measurements of mean high temperature, mean minimum temperature, mean temperature, extreme high temperature, extreme minimum temperature, relative humidity, and dew point.

Precipitation values were available for only 40% of the 115 weather stations. There were no precipitation values for any of the 21 stations in Saudi Arabia, the 6 weather stations in Jordan, or the 1 station in Kuwait. Mosquitoes require standing water for reproduction; however, sandflies lay their eggs in small batches in protected places with high humidity and a high content of organic matter (14). Pools of water are not necessary for reproduction, and therefore precipitation data were not considered critical to the development of a model for sandfly activity.

The major determinant of disease risk in this model is the dichotomy between environmental conditions where the vector is found and conditions where the vector does not occur. Therefore, for this exercise, negative data, the absence of the vector and disease, were given the same weight in the analysis as were positive data. Numerous articles which reported that *P. papatasi* is not found during January and February provided much of the negative data for the model.

The model was developed using the SAS stepwise discriminant analysis procedure to determine which variables were most useful in discriminating between vector presence and vector absence (SAS Institute, Cary, North Carolina). Six of the seven weather variables were selected by the stepwise analysis to be included in the model: mean minimum temperature ($F = 2.225$, Prob = 0.14), mean temperature ($F = 8.236$, Prob = 0.004), extreme high temperature ($F = 5.049$, Prob = 0.025), extreme minimum temperature ($F = 9.073$, Prob = 0.003), relative humidity ($F = 10.268$, Prob 0.001), and dew

point ($F = 18.114$, Prob = 0.0001). Wilk's λ values ranged from 0.7553 to 0.7905.

Using the selected weather variables, the discriminant analysis function classified locations as vector present or absent and calculated probability of occurrence values for each location during each month of the year. The model classified the 1742 observations into presence or absence and probability of membership: 74% of the 416 observations indicating absence of the vector were classified as absent by the model; 67% of the 414 observations indicating presence of the vector were classified as present by the model.

Simulation of Global Warming

To simulate global warming, the temperature values for all weather stations were increased by 1°C, 3°C, and 5°C, and the dependent variable was listed as unknown. Dew point and relative humidity values were not changed because it was not possible to accurately predict these parameters in the isolated habitats of vectors and animal hosts. The model was then run, and probability of occurrence values were computed for higher temperatures at the 115 weather stations during the 12 months of the year.

Sandfly Survival and Disease Transmission

Laboratory studies of the sandfly have found that, depending on the temperature and relative humidity, *P. papatasi* eggs

hatch in 4–14 days, larval development takes 3–27 days, and the pupal stage lasts 6–20 days. The entire life cycle requires 2–9 weeks (12). In Jerusalem, because of cooler temperatures, only one generation of sandflies reach the adult stage during the summer, with the larvae of this single generation going into hibernation and not hatching until May of the following year (6,11). Transmission of either leishmaniasis or sandfly fever rarely occurs in Jerusalem because the sandfly population apparently is insufficient to maintain endemicity. These infectious diseases appear to occur primarily in those areas where favorable temperatures and other environmental conditions allow at least two life cycles to be completed (4–18 weeks), creating larger sandfly populations and a greater probability of contact with both infected and noninfected host (6,8,11,12).

In those locations where the model predicts positive values for 1 or 2 months only in the summer, it is questionable whether *P. papatasi* would have sufficient time to complete more than one life cycle. Consequently, these areas were considered to have a low probability of transmission in this study and not endemic for sandfly-transmitted diseases. In contrast, weather stations with positive probability of occurrence values for at least 4 months (May, June, July, and August) were considered locations that could support endemic disease transmission.

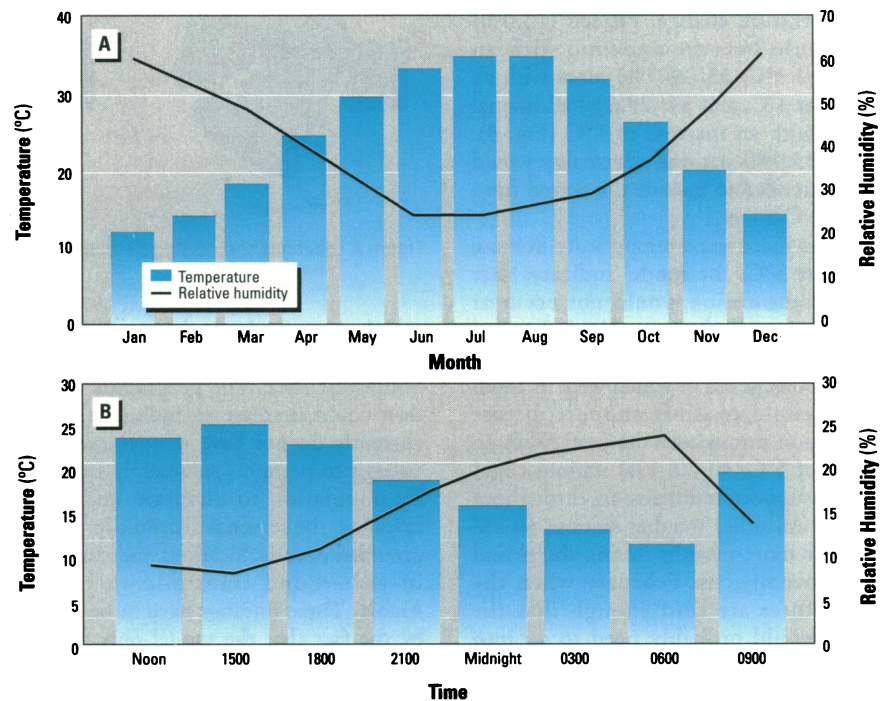


Figure 1. (A) The relationship of temperature and relative humidity by month for locations positive for sandfly activity in Southwest Asia. (B) The diurnal relationship between temperature and relative humidity at 3-hr intervals at Kuwait International Airport.

The temperature and relative humidity pattern of those locations considered to have a high probability of occurrence indicates that as monthly temperature rises, relative humidity declines (Fig. 1A). However, as the diurnal temperature declines, the relative humidity rises (Fig. 1B). This could explain the reason sandflies are nocturnal. During the day when the temperature is high and the relative humidity is low, the sandflies survive in isolated habitats, venturing outside to feed only during the evening and early morning hours when the temperature is lower and the relative humidity is higher (11).

Results

With current temperatures, 71 (61.7%) of the 115 weather stations would be considered by the model as endemic for disease transmission, permitting 2 or more life cycles of the sandfly. Fourteen (12.2%) could become endemic if the temperature was increased by 1°C, 17 (14.8%) more with a 3°C temperature rise, and 12 (10.4%) more, or all but one station, could become endemic with a 5°C rise in temperature. The one station that was not predicted to be warm enough, even with a 5°C increase in temperature, was Les Cedres in Lebanon at an altitude of 1916 m (Fig. 2).

Seasonality also could be markedly changed by global warming. Of the 115 stations, the model indicates that 17 (14.8%) would be endemic for the 8-month period from March to October with no temperature change. Fifteen (13.0%) more could become endemic with an increase of 1°C, 33 (28.7%) more with an increase of 3°C, and 34 (29.6%) additional stations with an increase of 5°C (Fig. 3). For 16 (13.9%) stations, seasonality would not be extended to include the period from March to October.

Unless there was a temperature increase of at least 3°C, the model indicates that disease transmission would not occur at any of the stations between November and February (Fig. 4). With an increase of 3°C, eight stations, seven of which were in Saudi Arabia, could possibly support disease transmission throughout the year. With an increase of 5°C, 30 (26.1%) stations could possibly support transmission throughout the year. All other weather stations would have 1 or more months during the period from November to February when the temperatures are cold enough that the sandfly would probably need to go into diapause to survive.

Discussion

This predictive model indicates that higher temperatures due to global warming could

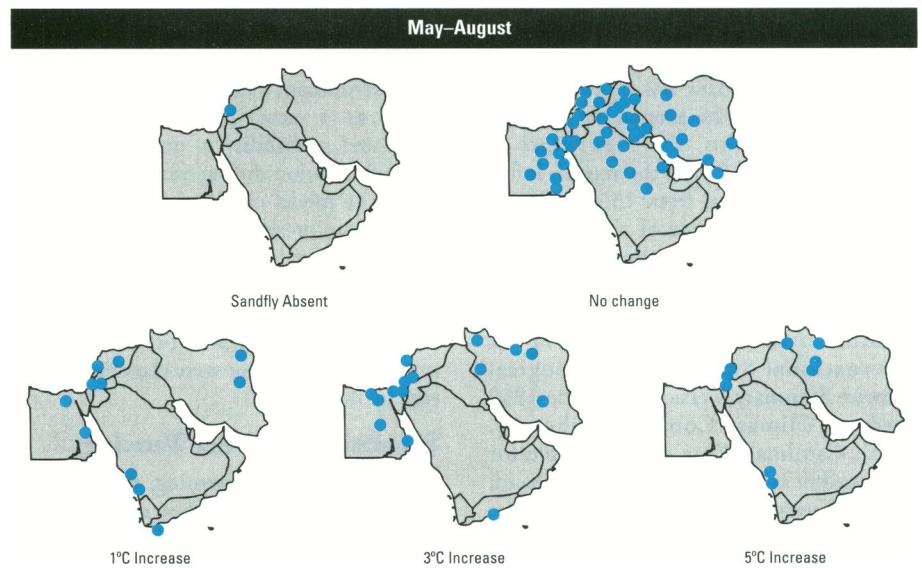


Figure 2. Locations of predicted distribution of *P. papatasi* between May and August.

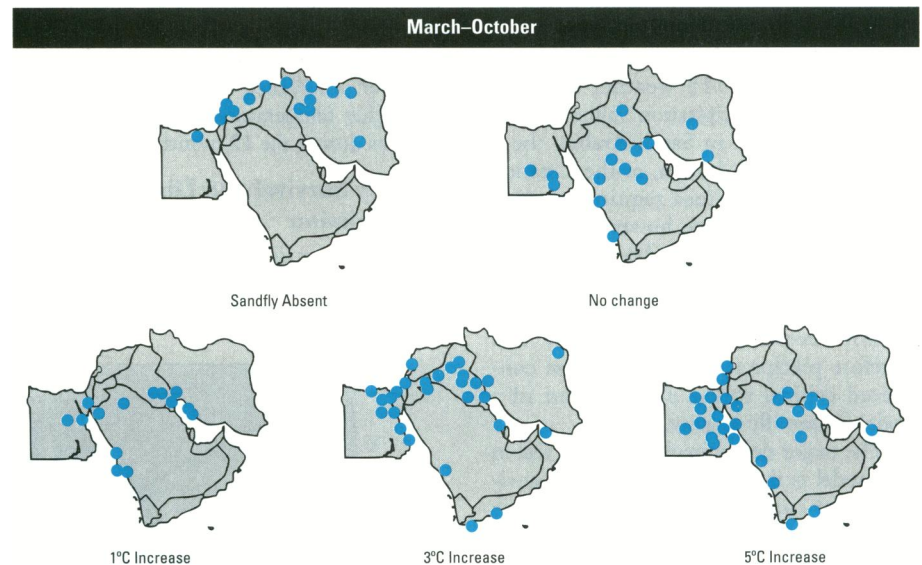


Figure 3. Locations of predicted distribution of *P. papatasi* between March and October.

greatly increase both the geographic and seasonal distribution of sandfly vectors in Southwest Asia. The geographic distribution could increase to include areas that currently do not have temperatures warm enough to permit a sufficiently large sandfly population to maintain endemicity. Likewise, the seasonal distribution could be extended in most locations and could result in year-round transmission in Saudi Arabia. These findings have to be qualified by the fact that the model only evaluated temperature increases and no other climatic factors, such as humidity and rainfall.

Unlike mosquitoes, sandflies do not need pools of water for breeding (3). The increased humidity in rodent burrows,

deep cracks in walls and dark corners in houses, where sandflies usually reside during the day, provide not only lower temperatures but also increased humidity needed for survival even with higher daily outdoor temperatures. Nocturnal activities, however, could be shortened if temperatures remain high and humidity low during evening hours.

Sandfly fever is caused by viruses belonging to the phlebotomus fever serogroup, with serotypes Naples and Sicilian occurring in Southwest Asia. Temperature can affect the rapidity of the life cycle of arboviruses because as the temperature increases, the extrinsic incubation period decreases (3). Consequently, some

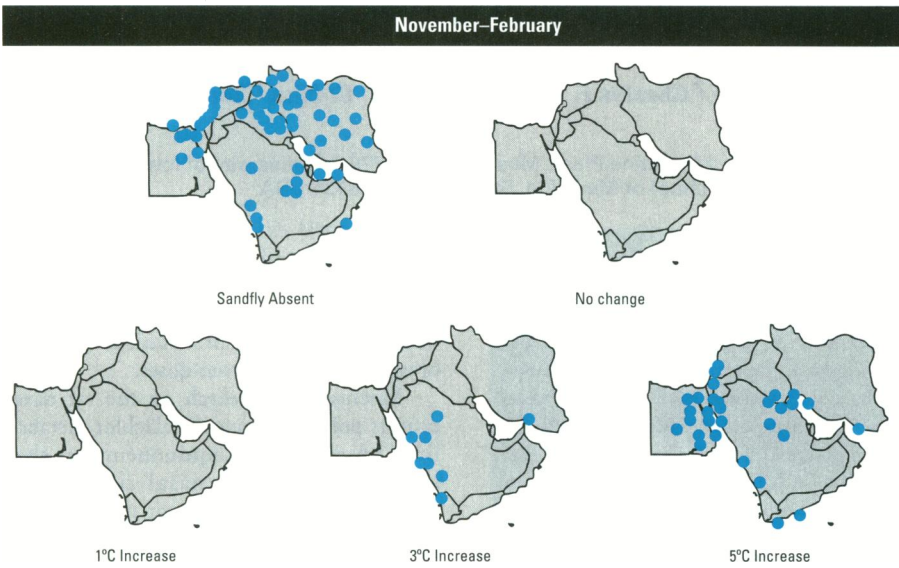


Figure 4. Locations of predicted distribution of *P. papatasi* between November and February.

viruses could replicate much more rapidly with global warming, which could also increase disease transmission. The effect of increased temperature on the phlebotomus serogroup of viruses, however, is unknown.

Leishmaniasis is caused by *Leishmania* spp., a protozoan infection. *Leishmania* spp. have acquired thermotolerance, experiencing temperatures of 22–28°C in their mammalian hosts, 31–35°C in skin lesions, and up to 37°C in visceral organs (15). Therefore, increased temperatures due to global warming probably would have little effect on these protozoans, and in those locations where sandflies can find habitats to survive the daytime heat, global warming should have little adverse effect on survival and on transmission of these infectious agents. Whether higher temperatures would adversely affect the rodent hosts of the sandfly vector has to be considered, but could not be evaluated in this analysis.

To determine the effects of global warming and validate this model, field collections of the vector and monitoring for increased disease distribution will have to be conducted. In locations that are on the periphery of current endemic areas, studies to ascertain if the vector has become established or if there is a marked rise in disease occurrence could indicate that global warming has increased temperatures sufficiently to permit the establishment of new endemic foci. Furthermore, detecting sandfly activity during the winter months in areas previously free of the vector during

this period could provide strong evidence of the effect of global warming.

Malaria has been the disease most often studied in relation to the impact of global warming on human health. As with this model, the malaria mosquito models project an increase in the geographic distribution of the disease, particularly at the borders of current endemic malaria areas, at higher elevations within endemic malaria areas, and with current temperate climate zones (5).

Because *P. papatasi* is the vector for both sandfly fever and cutaneous and visceral leishmaniasis, several different diseases could be affected with an increase in this vector. In a nonimmune population, sandfly fever can easily reach epidemic proportions (11). Although usually not fatal, sandfly fever does cause high fever, headache, and general debility similar to influenza. Cutaneous leishmaniasis causes polymorphic skin lesions which can be disfiguring and a nidus for bacterial infection. Visceral leishmaniasis is a chronic systemic disease that can be fatal.

Sandfly fever, cutaneous leishmaniasis, and visceral leishmaniasis, are difficult to diagnose and to treat. Use of insecticide for vector control can be expensive and can be harmful to the population. If an increased geographic and seasonal distribution of *P. papatasi* occurs due to global warming, the impact of these diseases on human health could be substantial.

REFERENCES

1. Stone R. If the mercury soars, so may health hazards. *Science* 267:957–958 (1995).
2. National Science and Technology Center. Report of the NSTC committee on the international science, engineering, and technology (CISSET) working group on emerging and re-emerging infectious disease. Washington, DC:National Science and Technology Center, 1994.
3. McMichael AJ. Human population health. In: *Climate change 1995. The IPCC second assessment report, version 2. Scientific technical analysis of impact, adaptations, and mitigations of climate change* (Watson RT, Ringwera MC, Moss RH, eds). New York:Cambridge University Press. In press.
4. Shope R. Global climate change and infectious diseases. *Environ Health Perspect* 96:171–174 (1991).
5. Martens WJM, Niessen LW, Rotmans J, Jetten TH, McMichael AJ. Potential impact of global climate change on malaria risk. *Environ Health Perspect* 103:458–464 (1995).
6. Theodor O. On the relation of *Phlebotomus papatasi* to the temperature and humidity of the environment. *Bull Entomol Res* 27:653–671 (1936).
7. Saidi S, Tesh R, Javadian E, Sahabi Z, Nadim A. Studies on the epidemiology of sandfly fever in Iran. II. The prevalence of human and animal infection with five phlebotomus fever virus serotypes in Isfahan province. *Am J Trop Med Hyg* 26:288–293 (1977).
8. Schlein Y, Warburg A, Schnur LF, Le Blancq SM, Gunders AE. Leishmaniasis in Israel: reservoir hosts, sandfly vectors and leishmanial strains in the Negev, Central Arava and along the Dead Sea. *Trans R Soc Trop Med Hyg* 78:480–484 (1984).
9. Killick Kendrick R, Leaney AJ, Peters W, Rioux JA, Bray RS. Zoonotic cutaneous leishmaniasis in Saudi Arabia: the incrimination of *Phlebotomus papatasi* as the vector in the Al-Hassa oasis. *Trans R Soc Trop Med Hyg* 79:252–255 (1985).
10. Abul Hab J, al Baghdadi R. Seasonal occurrence of man-biting *Phlebotomus* (Diptera: Psychodidae) in the Baghdad area, Iraq. *Ann Trop Med Parasitol* 66:165–166 (1972).
11. Theodor O. Observations on the hibernation of *Phlebotomus papatasi*. *Bull Entomol Res* 25:459–472 (1934).
12. Mohsen ZH. Biting activity, physiological age and vector potential of *Phlebotomus papatasi scopoli* (Diptera: Phlebotomidae) in central Iraq. *J Biol Sci* 14:79–94 (1983).
13. Cross ER, Newcomb WW, Tucker CJ. Use of weather data and remote-sensing to predict the geographic and seasonal distribution of *Phlebotomus papatasi* in Southwest Asia. *Am J Trop Med Hyg* (in press).
14. Strickland GT. *Hunter's tropical medicine*. Philadelphia:W.B. Saunders, 1984.
15. Zilberstein D, Shapira M. The role of pH and temperature in the development of *Leishmania* parasites. *Annu Rev Microbiol* 48:449–470 (1994).