FALCIPARUM MALARIA AND CLIMATE CHANGE IN THE NORTHWEST FRONTIER PROVINCE OF PAKISTAN

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Abstract. Following a striking increase in the severity of autumnal outbreaks of *Plasmodium falciparum* during the last decade in the Northwest Frontier Province (NWFP) of Pakistan, the role of climatologic variables was investigated. A multivariate analysis showed that during the transmission season of *P. falciparum*, the amount of rainfall in September and October, the temperature in November and December, and the humidity in December were all correlated ($r^2 = 0.82$) with two measures of *P. falciparum*, the falciparum rate (percent of slides examined positive for *P. falciparum*) since 1981 and the annual *P. falciparum* proportion (percent of all malaria infections diagnosed as *P. falciparum*) since 1978. Climatologic records since 1876 show an increase in mean November and December temperatures by 2°C and 1.5°C, respectively, and in October rainfall. Mean humidity in December has also been increasing since 1950. These climatologic changes in the area appear to have made conditions for transmission of *P. falciparum* more favorable, and may account for the increase in incidence observed in the NWFP in recent years.

In the last decade, the reported cases of *Plasmodium falciparum* malaria in the local and Afghan refugee population in the Northwest Frontier Province (NWFP) of Pakistan increased from a few hundred in 1983 to more than 25,000 in 1990. In Pakistan, the proportion of *P. falciparum* infections to all malaria infections microscopically diagnosed increased from 34% in 1987 to 54% in 1990,[1] with the NWFP showing the largest proportional increase in this period. The NWFP is presently one of the most northernmost areas worldwide where seasonal transmission of falciparum malaria occurs. *Plasmodium vivax,* more prevalent in the temperate areas, has historically been the predominant species in the province. Small outbreaks of *P. falciparum* malaria have been reported in the past,[2] but never on the scale observed in the Punjab,[3] the province that borders the NWFP on the south.

Climate change is one possible explanation for the increase in *P. falciparum.* Ambient temperature can affect malaria transmission in various ways. The growth rate of the vector population is dependent on temperature. Between 20 and 30°C, higher temperatures shorten the mosquito generation time,[4] and thus may result in higher vector densities that increase the likelihood of transmission. Temperature also affects the development of the parasite in the mosquito vector. The duration of sporogony, the time required to complete the sexual stage of the parasite in the mosquito, is inversely related to ambient temperature (logarithmic curve).[5] Below a threshold variously estimated at 16°C,[6] 18°C,[7] and 19°C,[5] for *P. falciparum,* this stage in parasite development cannot be completed, and the vector will not become infective. *Plasmodium vivax* has a lower threshold of approximately 15°C.[5] As a result, the prevalence of *P. falciparum* decreases rapidly in subtropical and temperate zones.[7] In the global distribution of malaria, small climatic changes can have a considerable effect on the transmission of malaria, and historic changes in the epidemiology of this disease appear to be related to changes in global temperature.[8] Current concern about increasing global temperature has resulted in predictions of a widening geographic distribution of malaria in temperate climates.[9] Other climatologic

parameters, rainfall, and humidity influence the transmission conditions mainly through their effect on breeding (density) and longevity of the vector population respectively.[5,10] In forecasting malaria epidemics, temperature (extrinsic incubation period) and humidity (survival rate) have been identified as the most sensitive factors.[11]

In temperate climates malaria transmission is seasonal, with usually two peaks in the incidence of *P. vivax,* of which the first is caused by true relapses.[12,13] Where *P. falciparum* transmission occurs, it has a single peak, usually after the second peak of new *P. vivax* infections.[13] The occurrence of the peak of *P. falciparum* after that of *P. vivax* has been related to the longer incubation interval (period between the occurrence of infective gametocytes in a case and their appearance in an infective form in a secondary case derived from it) of *P. falciparum.*[5] A wider and more readily acquired immunity in the population generated against *P. vivax* can account for a decrease of fresh, clinically apparent infections before *P. falciparum* reaches its peak.[13]

Given the northern locality of NWFP, the incidence of falciparum malaria would be expected to be restricted by temperature. Its occurrence is likely to vary with the altitude and latitude of the districts, and high late season temperatures are likely to result in more infective vectors and thus more annual cases of *P. falciparum.* Because of the early seasonal decrease as a result of developing immunity to *P. vivax,*[13] this malaria species is less likely to be affected by late season temperatures that would permit sporogony. Preliminary investigations have revealed a significant correlation between mean November temperature and the percentage of slides examined positive for *P. falciparum.*[14] A further analysis of climatologic variables, temperature, rainfall, and humidity, that may affect transmission of *P. falciparum* in NWFP is presented here.

MATERIALS, METHODS, AREA, AND POPULATION

Area and population of NWFP. The NWFP is located between 32° and 37° latitude North, bordered by China on the north, Kashmir on the east, the Punjab and Baluchistan
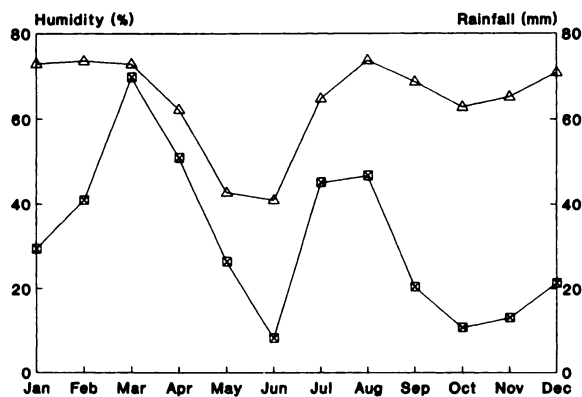
FIGURE 1. Averages of monthly total rainfall (box with x) and mean monthly humidity (△) between 1950 and 1980 for Peshawar station.
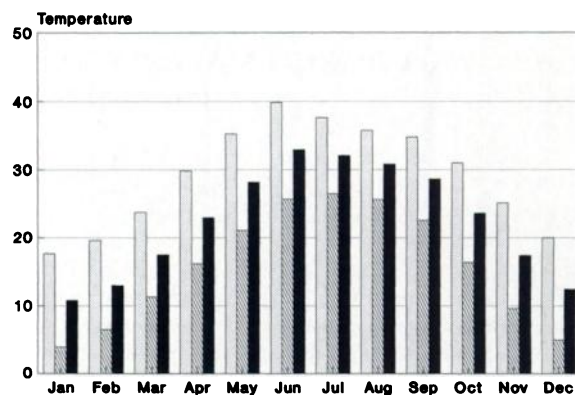

FIGURE 2. Temperature in °C (average 1950–1980) for Peshawar station. Dotted bars = mean maximum; hatched bars = mean minimum; solid bars = mean average (mean minimum + mean maximum/2).

provinces of Pakistan on the South, and Afghanistan on the west. The altitude ranges from 150 m above sea level in the densely populated Peshawar valley to more than 3,000 m in the Hindu Kush and Himalayas. Peshawar (336 m altitude), the capital of the province, is centrally situated. The population of NWFP in 1989 was approximately 14 million, consisting mainly of Pathans, and between two and three million Afghan refugees immigrating since 1979.

Climate. Except for the areas of high altitude with a highland, semi-arid climate in the districts in the south, the province is situated in a temperate climate zone, with cool winters and hot summers. Precipitation varies between less than 51 cm (20 inches) in the south more than over 152 cm (60 inches) in certain areas in the north. Normal values for Peshawar for the period 1951–1980 (Figure 1) show that monthly rainfall and average humidity are related, with minimums in June and October. There are two rainy seasons, in March and in July/August (summer monsoon); however, large standard deviations during the period indicate that rainfall varied considerably from year to year. Mean day temperatures (average of mean daily maximum and mean daily minimum) (Figure 2) were highest in June (32.9°C), and lowest in January (10.8°C).

Temperature records (1878–1890) were obtained from the annual Indian Meteorological Reports,[15] the Indian Weather Review (1891–1925),[16] and the Monthly Weather Report (1926–1936).[17] For the period 1907–1925, only deviations from the normal values (average values between 1878 and 1899) of the Peshawar district (which includes Peshawar station) were available. The monthly values for Peshawar station were estimated by adding the deviations of the Peshawar district to the normal values (1878–1899) for Peshawar station. For example, the average mean November temperature in Peshawar station between 1878 and 1899 was 61°F. The deviation for the Peshawar district for November 1907 was +2.7°F. Therefore, the estimated November temperature for Peshawar station was 63.8°F (17.7°C). Temperature data from 1940 to 1970 and precipitation data between 1876 and 1970 were obtained from the World Weather Records.[18] Data from 1970 to 1993 were obtained from the Meteorological Institute of Lahore, Pakistan.

Insecticides and spray strategies. Over the last 40 years, various insecticides and spray strategies have been used

against Pakistan's two identified malaria vectors, Anopheles culicifacies and An. stephensi. From the late 1950s to 1975, DDT (75% wettable powder [WP]) was used and applied at a delivery dosage of 1–2 g/m² often twice per year. Malathion (50% WP), an organophosphate (OP), was introduced as an alternative to DDT because of widespread DDT resistance in both mosquito species. In 1976 and 1977, malathion was used in a double round at a delivery dosage of 2 g/m². In Pakistan, this resulted in an overall reduction of 76% in the slide possitivity rate in 1976 and 1977.[19] Since 1978, malathion was used in a single round in July and August, targeted at the increasing vector population following the monsoon rains. The residual effect of malathion on the mainly mud houses in the area is approximately 4–5 weeks (Shah I, National Institute for Malaria Research and Training, unpublished data). Because the spray strategy between 1978 and 1993 remained unchanged regarding timing, this period was selected for analysis. In this period, only malathion was used, except for limited quantities of fenitrothion in 1983 and 1984. Fenitrothion, also an OP compound, (40% WP) was applied at a delivery dosage of 1 g/m². The amount of malathion (metric tons) sprayed was used as a variable in the analysis. The quantities of fenitrothion used in 1983 and 1984 were multiplied by two to equal the estimated potency of malathion per unit of weight.

Case detection and microscopic diagnosis of malaria. During the eradication period from 1955 to 1973, malaria was detected mainly through active case detection (ACD). Detection has gradually shifted towards diagnosing cases that present with clinical symptoms at health posts or passive case detection (PCD). Approximately 12% of the cases microscopically identified by Giemsa-stained thick blood smears were detected by PCD in the mid 1970s. This figure has increased to 74% in 1990.

In the epidemiologic data analyzed, mixed infections are counted both as a P. vivax and a P. falciparum infection. In selecting a variable for P. falciparum transmission, the annual incidence (absolute number of P. falciparum infections per year) appeared unsuitable due to the considerable changes in the method and intensity of malaria detection in Pakistan since provincial data were available (1970). Two dependent variables to quantify annual fluctuations in P. fal-

ciparum were chosen. The first is the annual proportion of falciparum infections to all malaria infections diagnosed between 1978 and 1993 (n = 16 years), the period that a single round of insecticide (mostly malathion) was sprayed. This variable is only dependent on the ability of microscopists to make a correct species diagnosis. Pakistan has a well-managed national training center for microscopists. The second is the *P. falciparum* rate, the percentage of slides examined from health posts (PCD) between 1981 and 1993 (n = 13 years) in NWFP that were positive for *P. falciparum*. For the second variable, all ACD data were excluded from the analysis because of the often exaggerated denominator (Georghiou GP, unpublished data) (total slides examined) that lowers the rate in an unpredictable way. The PCD data prior to 1981, when the promoting of malaria detection through health posts was in an early stage, was excluded for similar reasons.

The numerator and denominator of both variables are thus different. The numerator of the second variable (total cases of *P. falciparum* per year obtained through PCD) is a subset of all annual cases of *P. falciparum*, the numerator of the first variable.

To obtain the distribution of both species throughout the year, available provincial monthly malaria data for NWFP (ACD and PCD) between 1982 and 1990 were used to calculate, for each malaria species, the average monthly percentages; for example, the value for January is the average annual figure (nine years) for the proportion of *P. falciparum* infections diagnosed during January of a given year divided by the total number of *P. falciparum* cases during that year × 100. Data by district were available between 1985 and 1990 and were used to calculate the average proportion of *P. falciparum* infections in the districts of NWFP (the average of six years between 1985 and 1990 of the annual percentage of *P. falciparum* infections: annual cases of *P. falciparum* divided by all malaria infections × 100). The temperature difference with a reference point (Peshawar City) for all capitals of the districts was calculated using corrections for latitude, longitude, and altitude typical for the northwest part of former British India (including the NWFP) in the October–December period.[20] Temperature in the area changes in a northerly direction by −0.523°C/degree of latitude, in an easterly direction by +0.111°C/degree of longitude, and with altitude by −0.0056°C/m. For example, Chitral, located 1.85° north and 0.39° east of Peshawar, with an altitude that is 1,123 m higher than Peshawar, has a calculated temperature difference from Peshawar of (1.85 × −0.523) + (0.39 × 0.111) + (1123 × −0.0056) = −7.2°C.

Regression analysis. Following preliminary regression analysis on independent variables singly, 13 were selected for further investigation by multiple regression. These were the mean daily temperature (average of mean daily maximum and mean daily minimum temperatures) in September, October, November, and December, mean daily relative humidity (at 8:00 AM) in September, October, November, and December, total rainfall (log[x + 1]) in September, October, November, and December, and annual tonnage of insecticide applied. To make most use of available data, we performed a joint analysis of two dependent variables (analysis of covariance); the annual proportion of all positive slides that
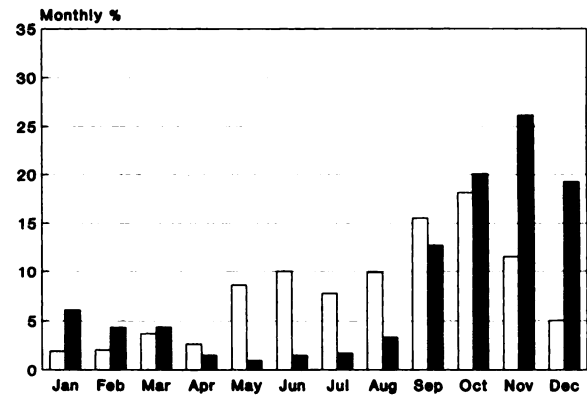

FIGURE 3. Averages of the monthly percentages of the year figures for *Plasmodium falciparum* (hatched bars) and *P. vivax* (open bars) between 1982 and 1990.

were positive for *P. falciparum* (1978–1993) and the proportion of all slides examined positive for *P. falciparum*, the *P. falciparum* rate (1981–1993). Multiple logistic regression was carried out by backward elimination from the full model, removing the least significant variable at each step, and retaining only those variables that explained a significant fraction of the variation. Because our two dependent variables are to some extent related, we carried out the same analysis on both variables separately. The methodology of the regression analysis and Williams' method to correct for the overdispersion in binomial errors are described by Crawley.[21]

RESULTS

The distribution of *P. vivax* and *P. falciparum* (Figure 3) during the year shows a seasonal trend. The early peak of *P. vivax* reflects true relapses and possibly early transmission as the mean temperature in March is above the critical temperature for this malaria species (Figure 2). In May and June, humidity is low (42.8% and 41%, respectively) and it will reduce the vector's life span and thus the capacity to transmit malaria.[22] Adult vector densities were indeed very low during these months (Bouma MJ, unpublished data). The main peaks for both malaria species were seen after the summer monsoon (July–August), in September–October for *P. vivax*, and in November for *P. falciparum*. Most interannual variation was seen in December at the end of the transmission season.

The proportion of *P. falciparum* infections detected in NWFP since 1970 and the *P. falciparum* rate since 1981 showed a marked interannual variation (Figure 4), with peaks in 1973, 1979, 1983, 1990, and 1992. Similar fluctuations were seen in the data from the Afghan refugee program since the early 1980s (Bouma MJ, unpublished data).

Multiple regression analysis of climatologic variables between September and December revealed five significant factors that were correlated with the two y variables (r^2 = 0.82), i.e., proportion and rate of *P. falciparum* infections (Table 1). Rainfall appears to have a strong impact on transission of *P. falciparum* in NWFP. At the end of the transmission season for *P. falciparum*, December humidity and mean temperatures in November and to a lesser extent in December
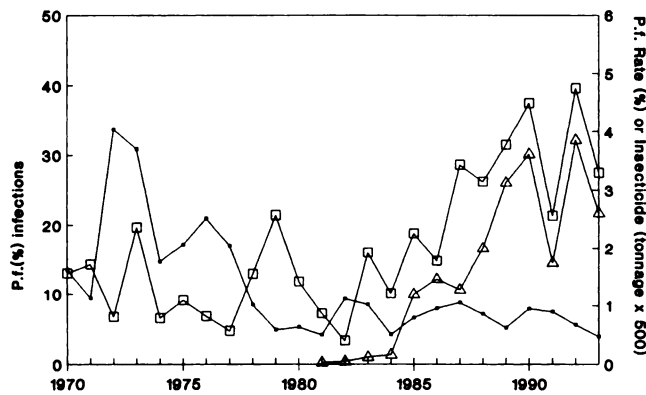
FIGURE 4. Interannual variation (1970–1993) in the proportion of *Plasmodium falciparum* (P.f.) infections to all malaria infections diagnosed (□), and *P. falciparum* rate, i.e., the percent of slides examined positive for *P. falciparum* (△). Data provided by the Provincial Malaria Control Program (refugee data not included). Tonnage of insecticide is indicated by the small squares.

were also correlated. Only September rainfall was not significant in either analysis of the separate variables (Table 1). The amounts of insecticide sprayed showed no significant correlation with the dependent variables (Figure 4). This finding is supported by the observation that the tonnage of insecticide (Figure 4) began to decrease from 1972 (DDT) and 1976 (malathion), a decade before a consistent increase in the proportion of *P. falciparum* infections. In the joint analysis, we found no significant interactions between the independent and dependent variables (the regression lines for the two y variables were indistinguishable).

Analysis of data between 1985 and 1990 on the proportion of cases of *P. falciparum* in the districts of NWFP show that this proportion decreased in the cooler districts (Figure 5). In the same figure, the proportion of *P. falciparum* cases among Afghan refugees in certain districts in 1990, when no insecticide was sprayed (except for a small trial area) in the refugee villages, showed a similar relationship with temperature. Some cooler districts in the province, such as Abbottabad and Mansera (Figure 5), had more rainfall during September and October when compared with Peshawar. Their lower proportion of infections with *P. falciparum* therefore suggests that temperature rather than rainfall or humidity was a likelier determining factor in these cooler districts.

Except for September rainfall (Figure 6), all climatic factors that appear to be of importance for *P. falciparum* transmission showed changes in the last century. The trend of October precipitation showed a more than 100% increase since 1876 (Figure 7), which is significant (t = 2.15, P < 0.05). November and December temperatures in the capital of NWFP have increased since 1876, approximately 2°C and 1.5°C, respectively (Figure 8). These trends are significant (respectively, t = 6.46, P < 0.001 and t = 5.45, P < 0.001). The average yearly temperature in Peshawar has increased only by approximately 0.5°C, which corresponds to the average increase observed in the northern hemisphere.[23] Also, the average (8:00 AM) humidity showed a significant increase (t = 4.58, P < 0.001) since 1950. There appears to be a change of variance between 1950 and 1993 (Figure 9). The small increase observed in September rainfall was not significant (t = 0.73, P > 0.05).

TABLE 1

Multivariate analysis of climate variables associated with *Plasmodium falciparum* prevalence in Northwest Frontier Province, Pakistan

Joint analysis of the rate and proportion

Variable	Estimated slope	SE	F value (1,22) Critical value = 4.30
September log rainfall	0.2239	0.0907	6.42*
October log rainfall	0.3462	0.0867	18.23†
November mean temperature	0.7740	0.2005	15.07†
December mean temperature	0.3019	0.1188	6.75*
December humidity	0.0953	0.0216	21.97†

Rate

Variable	Estimated slope	SE	F value (1,7) Critical value = 5.59
September log rainfall	0.3020	0.1697	3.250
October log rainfall	0.2827	0.1514	3.677
November mean temperature	0.9674	0.4413	4.832
December mean temperature	0.5910	0.1898	10.130*
December humidity	0.1440	0.0399	15.350†

Proportion

Variable	Estimated slope	SE	F value (1,10) Critical value = 4.96
September log rainfall	0.1695	0.0907	3.504
October log rainfall	0.3736	0.0888	19.420†
November mean temperature	0.7876	0.1916	16.480†
December mean temperature	0.0824	0.1295	0.404
December humidity	0.0693	0.0221	10.230†

* $P < 0.05$.
† $P < 0.01$.

DISCUSSION

Climatologic factors appear to have affected the transmission of *P. falciparum* in the NWFP of Pakistan between 1978 and 1993, in a period characterized by only minor changes in the malaria control strategy. The amount of rainfall in September and October, mean temperatures in November and December, and humidity in December were correlated with the two y variables ($r^2 = 0.82$). The con-
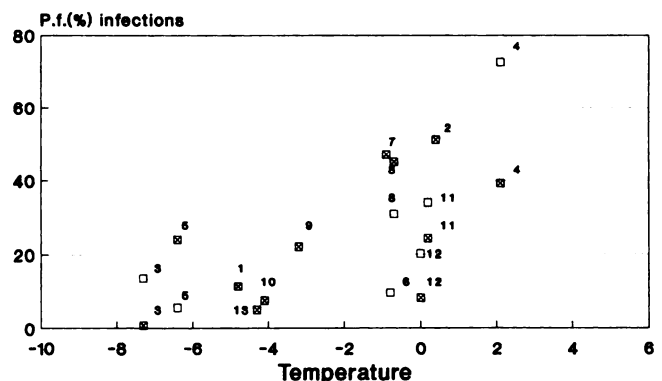

FIGURE 5. Annual proportion of *Plasmodium falciparum* (P.f.) infections in the districts of Northwest Frontier Pakistan for the local population (box with x) (average 1985–1990, insecticide sprayed) and refugees in 1990 (□) (no insecticide sprayed), and the estimated average (October–December) mean temperature difference from Peshawar, based on corrections for altitude, latitude, and longitude.[22] The districts are Abbottabad (1), Bannu (2), Chitral (3), D. I. Khan (4), Dir (5), Haripur (6), Karak (7), Kohat (8), Malakant (9), Mansera (10), Mardan (11), Peshawar (12) and Swat (13).
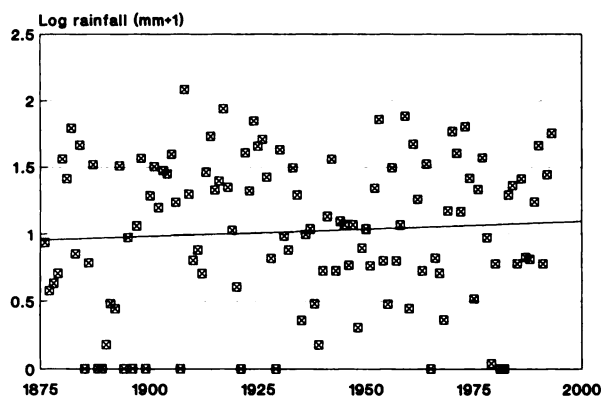
FIGURE 6. Total September rainfall (box with x) for Peshawar station (log [mm + 1] with a linear regression line) since 1876.

tribution of rainfall in September is questionable because it only appears of significance in the joint regression analysis and not in either analysis of the *P. falciparum* variables separately. Our initial hypothesis that high late season temperature affects transmission by lengthening the transmission season of *P. falciparum* was supported, albeit not as the most important factor. The temperature in November becomes critical for sporogony and in December only daytime temperatures can support completion of the parasite's life cycle. Temperature is unlikely to affect the start of the transmission season for *P. falciparum* in May and June, before the start of the summer monsoon, and low relative humidity restricts vector survival and transmission.[5, 10] The finding that the annual proportion of infections with *P. falciparum* shows a positive relationship with the ambient temperature of the district capitals (dependent on latitude, longitude, and altitude) supports the hypothesis that in the NWFP, temperature plays a critical role. Unfortunately, insufficient data per district and per month were available to analyze regional variations more closely. The size of the population and malaria cases in the colder districts are limited, and are not likely to seriously distort the analysis of the pooled data for the province. This implies that the results of the analysis are likely to be restricted to the lower (most populated) plains of the province, and extrapolation of these findings to neighboring areas should be done with care. The annual rainfall in these most populated parts of
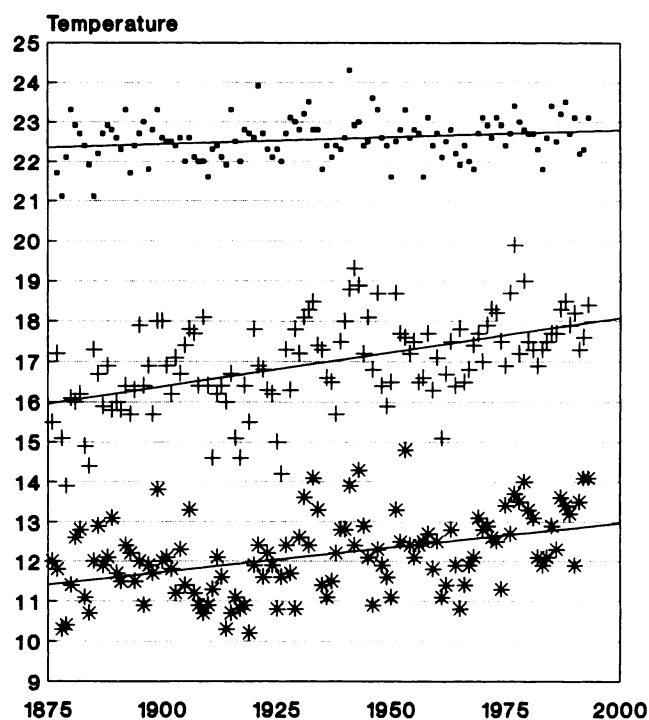

FIGURE 8. Mean November (+), December (star), and average year (small square) temperatures in °C with a linear regression line since 1876 for Peshawar station.

the province is low, particularly in September and October (after the monsoon), the months in which rainfall appears to affect transmission of *P. falciparum*. Prolonged breeding conditions are likely to enhance vector density, and thus transmission. Rainfall may also increase the human biting rate.[11] In the Punjab province of Pakistan, an increase (150-fold) of the human biting rate (indoors) of *An. culicifaciens* was observed during rainfall.[24] Relative humidity appears to be of importance for *P. falciparum* in NWFP, as has been suggested for epidemics in Pakistan's Sind province.[11]

Another factor that could possibly affect the transmission of *P. falciparum* is the level of transmission in the previous year, since more carriers can speed up transmission. When the reproduction rate (ratio: cases in year t/cases in year t − 1) was included in the multivariate analysis, none of the
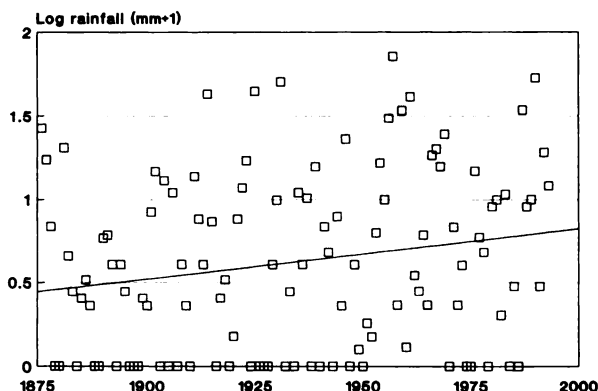

FIGURE 7. Total October rainfall (□) for Peshawar station (log [mm + 1] with a linear regression line) since 1876.
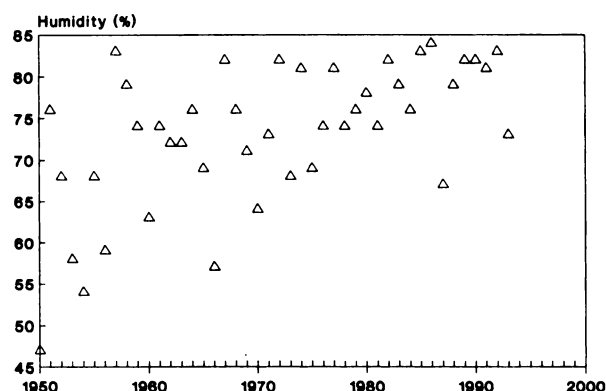

FIGURE 9. Mean relative humidity in December at 8:00 AM (△) for Peshawar station since 1950.

climate variables reached a significance level. However, apart from infections acquired late in season but diagnosed and reported in the following year, climate factors that favor transmission tend to occur in successive years (Bouma MJ, unpublished data). The identified climate variables in one year may also affect transmission in the following year through their effect on the size of the vector population that survives the winter.

It appears that the striking increase in *P. falciparum* in the NWFP in the last decade may be related to climatologic conditions favorable for transmission. Late season temperatures have been exceptionally high in the 1980s,[14] with years of high precipitation in critical months. Alternative explanations for this development have been proposed. These are the spreading chloroquine resistance in *P. falciparum* (Shah IH, unpublished data) and the increase in the vector population over time due, for example, to reduced efficacy of the malaria control program (insecticide resistance and poorly applied and ineffective control efforts). These explanations appear compatible with the gradual increase in *P. falciparum* between 1983 and 1990. However, the striking decrease of *P. falciparum* in 1991 and 1993 is difficult to explain with these alternative explanations. Drug resistance is unlikely to decrease unless the selective pressure (use of chloroquine) is removed. In the NWFP, the availability of chloroquine and prescription policy have not changed. Similarly, fluctuations in *P. falciparum* prevalence are not easily explained by variations in vector control efforts. We found no correlation between the amount of insecticide sprayed and *P. falciparum* prevalence, and insecticide resistance is, analogous to drug resistance, unlikely to change without decreases in the application of insecticide.

The Afghan refugees, with less previous exposure to malaria before their arrival,[25] and because of their vulnerability and the number of potential carriers, may have increased the parasite reservoir in the population, thus facilitating transmission. However, the local and refugee population had shown similar fluctuations of *P. falciparum* rates since the early 1980s (Bouma MJ, unpublished data), which suggests that both populations have been exposed to the same transmission conditions.

On the basis of the apparent long-term increases in November and December temperatures, October rainfall, and December humidity, conditions for transmission of *P. falciparum* may be further enhanced in the area. In particular, higher temperatures that lengthen the transmission season will result in the increase of the latitude on which *P. falciparum* can occur. This is in line with predictions made in relation to global climate change.[9, 26]

The practical implications of our findings are that more effective measures can be taken to interfere with the transmission of *P. falciparum* malaria. These include coverage of the complete transmission season of *P. falciparum* with an effective insecticide instead of a single round of spray in July–August with a residual effect of only 4–5 weeks. For assessing the impact of malaria control measures, it is apparent that climate factors, which contribute to year-to-year variations in transmission conditions, should be taken into account. The reliable prediction of climate variables that is shown here to correlate with *P. falciparum* in the NWFP may be used to develop an early warning system for severe

seasonal epidemics. This is now under investigation using the El Nino southern oscillation, a phenomenon known to be associated with climate change on the Indian subcontinent.[14]

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REFERENCES

1. WHO, 1992. World malaria situation 1990. *World Health Stat Q 45:* 257–265.
2. Hehir P, 1927. *Malaria in India.* London: Humphrey Milford Oxford University Press.
3. Swaroop S, 1949. Forecasting of epidemic malaria in the Punjab, India. *Am J Trop Med 29:* 1–17.
4. Molineaux L, 1988. The epidemiology of human malaria as an explanation of its distribution, including some implications for its control. Wernsdorfer WH, McGregor I, eds. *Malaria.* Edinburgh: Churchill Livingstone, 913–998.
5. Macdonald G, 1957. *The Epidemiology and Control of Malaria.* London: Oxford University Press.
6. Detinova TS, 1962. *Age Grouping Methods in Diptera of Medical Importance, with Special Reference to Some Vectors of Malaria.* Monograph Series 47, Geneva: World Health Organization.
7. Boyd MF, 1949. Epidemiology: factors related to the definitive host. Boyd MF, ed. *Malariology.* Philadelphia: W. B. Saunders, 608–697.
8. de Zulueta J, 1987. Changes in the geographical distribution of malaria throughout history. *Parassitologia 29:* 193–205.
9. Kalkstein LS, Smoyer KE, 1993. The impact of climate change on human health: some international implications. *Experientia 49:* 969–979.
10. Russell PF, 1946. Climatological factors. Russell PF, West LS, Manwell RD, eds. *Practical Malariology.* Philadelphia: W. B. Saunders.
11. Onori E, Grab B, 1980. Indicators for forecasting of malaria epidemics. *Bull World Health Organ 58:* 91–98.
12. Gill CA, 1938. *The Seasonal Periodicity of Malaria and the Mechanism of the Epidemic Wave.* London: Churchill.
13. Macdonald G, 1953. The analysis of malaria epidemics. *Trop Dis Bull 50:* 871–889.
14. Bouma ML, Sondorp HE, van der Kaay HJ, 1994. Health and climate change. *Lancet 343:* 302.
15. *Indian Meteorological Reports, 1878–1890.* Calcutta: Government Printing India.
16. *Indian Weather Review, 1891–1925.* Calcutta: Government Printing India; under the direction of Walker GT.
17. *Monthly Weather Report, 1926–1936.* Banerji (Dir. Gen. Observatories), Poona: Government of India.
18. *World Weather Records, 1920–1970 and Errata.* Washington, DC: Smithsonian Institute.
19. Zulueta J de, Mujtaba SM, Shah IH, 1980. Malaria control and long-term periodicity of the disease in Pakistan.' *Trans R Soc Trop Med Hyg 74:* 624–632.
20. Jagannathan P, 1948. Regression of climatic elements on latitude, longitude and elevation in India. *India Meteorol Dept Sci Notes 10:* 83–105.
21. Crawley MJ, 1993. *GLIM for Ecologists.* Oxford: Blackwell.

22. Fox E, Strickland GT, 1989. The interrelationship of *P. falciparum* and *P. vivax* in the Punjab. *Trans R Soc Trop Med Hyg 83:* 471–473.

23. Jones PD, Wigley TML, Wright PB, 1986. Global temperature variations between 1861 and 1984. *Nature 322:* 430–434.

24. Mahmood F, McDonald MB, 1985. Ecology of malaria trans-

mission and vector capacity of *An. culicifacies* species A in rural Punjab, Pakistan. *Pak J Med Res 24:* 95–106.

25. Suleman M, 1988. Malaria in Afghan refugees in Pakistan. *Trans R Soc Trop Med Hyg 82:* 44–47.

26. McMichael AJ, 1993. *Planetary Overload.* Cambridge: Cambridge University Press.