Current status of kala-azar and vector control in China

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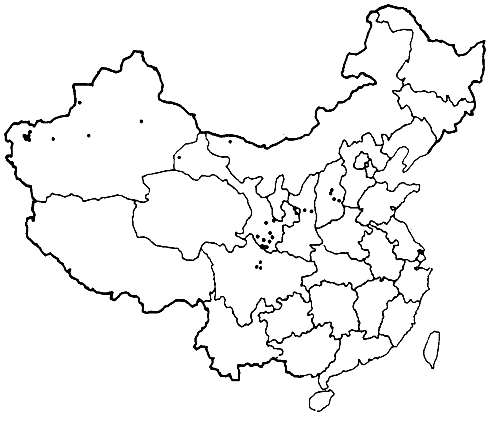
Kala-azar, which was prevalent in the vast area of China that lies to the north of the Yangtze River from the 1920s to the 1950s, is now effectively under control as a result of strenuous intervention since the founding of the People's Republic of China in 1949. Apart from 15–20 new cases that occur annually in the Keshi plain, Xinjiang Autonomous Region, the achievements of control practised in other former endemic areas in the plains have been significant and consolidated. In the mountainous areas in north-west China, where the vector, Phlebotomus chinensis, *is abundant and canine visceral leishmaniasis is common, there are still sporadic cases of kala-azar. Also, in recent years, new infections have often occurred in the deserts of Xinjiang and western Inner Mongolia, although the reservoir of the infection has not been identified.*

Before the founding of the People's Republic of China in 1949, kala-azar was one of the major parasitic diseases in the country. The disease prevailed in more than 650 counties in 12 provinces and three autonomous regions north of the Yangtze River, and in 1951 affected around 530 000 individuals. As a result of great efforts to combat kala-azar on a large scale over the period 1950–58, it has been virtually controlled in most of the former endemic regions (*1*).

Cumulative data indicate that, since 1985, newly infected cases have occurred in 32 counties in four provinces (Gansu, Shaanxi, Sichuan, and Shanxi) and two autonomous regions (Xinjiang and Inner Mongolia) (Fig. 1). A total of 200–300 cases have been reported annually (*2*).

Fig. 1. **Geographical distribution of kala-azar in China, 1985–89. Each dot indicates a focus.**



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Current status of kala-azar

In China the areas where kala-azar is endemic can essentially be stratified into three types (Fig. 2), based on geographical and epidemiological features (*3*). The effectiveness of treatment with a given set of control measures varies with geographical areas, as described below.

Plains region

In the plains region, kala-azar is anthroponotic, and in the 1950s its prevalence was 29.7–50.4 per 10 000. Concurrent or consecutive cases often occurred in one household. Mostly juveniles were affected, with 8.3–38.9% of cases involving under-5-year-olds. Post-kala-azar dermal leishmaniasis (PKDL) was frequently present, and *Leishmania donovani* was detected in the normal skin of 0.83–8.0% of post-kala-azar cases. The vectors were *Phlebotomus chinensis* (endophilic species) and *P. chinensis longiductus* (peridomestic species). Cases of canine visceral leishmaniasis were rare, and in 1950 the infection rate was 0–0.33% among 93 736 dogs examined (*3*).

Because the treatment of patients was integrated with house residual spraying of insecticides (DDT and BHC), the prevalence of the disease was substantially controlled. It has been established that the intervention measures used had optimal efficacy. For

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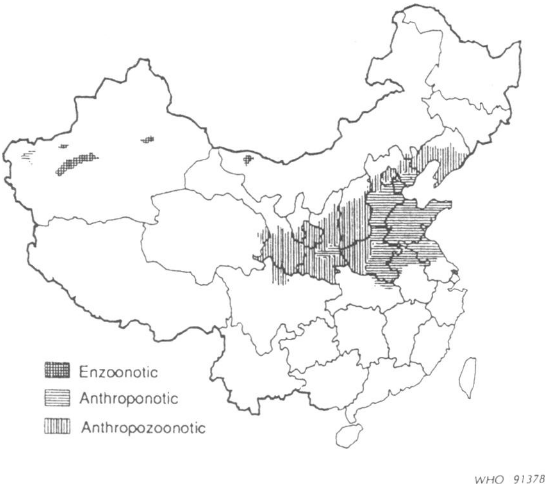
Reprint No. **5213**

Fig. 2. **Geographical distribution of the three types of kala-azar in China.**



example, in 45 villages in Taian County (Shadong Province) the number of cases of kala-azar declined from 95 to 60 over the period 1954–57, after case treatment only, while following the introduction of residual spraying in 1958 the numbers declined from 56 to zero in 1961 (*4*).

In the eastern part of the plains region (Shandong, Jiangsu, Henan, Hebei and Shaanxi Provinces) only 19 cases of visceral kala-azar and 19 cases of PKDL have occurred since 1970. All the patients were adults, mostly aged 25–55 years, who commonly had contracted the disease in childhood (*2, 5*).

Over the period 1975–84, leishmanin intradermal tests in formerly endemic areas (Shandong, Shaanxi, and Jiangsu Provinces) were positive only for over-30-year-olds, which is evidence for the interruption of transmission *in situ* (*5, 6*).

In 1975–79, investigations of sandfly populations in 31 counties of Shandong Province revealed that *P. chinensis* had been controlled by residual spraying (*6*). Field surveys in other former endemic areas of the plains region, such as south Hebei, east Henan, northern Jiangsu and Anhui, as well as Guanzhong District in Shaanxi Province, failed to detect *P. chinensis* (*5*). On the other hand, in four counties in the Keshi plain, Xinjiang-Uygur Autonomous Region, 15–20 new cases of kala-azar have been reported annually since 1985. Here, the vector, *P. chinensis longiductus*, is peridomestic and is more difficult than endophilic species to target with insecticides.

Mountainous and hilly region

In this region, kala-azar is anthropozoonotic, and in the 1950s was hypoendemic (prevalence, 0.1–16.0 per 10000). Under-5-year-olds represented 71.5–86.5% of cases. Only one case of PKDL has been reported, in Gansu Province. The vector was *P. chinensis* (semiwild species). There was a high reservoir of infection in dogs (0.65–7.3% among 16980 dogs examined in the 1950s) (*3*), and natural infection has been found in a racoon dog (*Nyctereutes procyonoides*) in Miyun County, a suburb of Beijing (*7*).

Integrated control measures, including treatment of patients, spraying of insecticides, and extermination of infected dogs, were not particularly promising, and new cases still sporadically occur in four provinces (Table 1).

Canine visceral leishmaniasis was prevalent in the mountainous region, and was the main source of human infection (Table 2) (*2, 5*).

The results of leishmanin intradermal tests indicated that transmission of kala-azar had not been interrupted, since positive reactions were exhibited by each age group of the human population (Table 3) (*8, 9*).

Considerable numbers of the sandfly vector, *P. chinensis*, were found in villages as well as in various holes and caves in the wilds (*10*).

Desert region

This region had been uncultivated desert for a considerable period of time before it was populated by immigrants who introduced agriculture and other

Table 1: **Number of new cases of kala-azar in four north-west provinces of China, 1981–89**

	No. of cases								
Province	1981	1982	1983	1984	1985	1986	1987	1988	1989
Gansu	21	21	47	144	205	226	222	194	178
Shaanxi	11	9	7	4	2	0	0	—	—
Sichuan	1	0	5	6	33	38	26	39	60
Shanxi	1	1	1	1	0	0	5	5	1

Table 2: **Number of cases of canine visceral leishmaniasis in three provinces of north-west China, 1974–88**[a]

Year	Province	No. of dogs examined	No. of positive dogs
1974–78	Shaanxi—4 counties	892	12 (1.4)[b]
1981–88	Sichuan—2 counties	276	12 (4.3)
1981–88	Gansu—7 counties	582	43 (7.4)

[a] See ref. *2, 5*.
[b] Figures in parentheses are percentages.

Table 3: **Results of leishmanin intradermal tests in two provinces in north-west China**[a]

Age of subjects (years)	Shaanxi Province (1974) No. examined	Shaanxi Province (1974) No. positive	Shanxi Province (1975–84) No. examined	Shanxi Province (1975–84) No. positive
1–5	70	2 (2.9)[b]	295	14 (4.7)
6–10	59	3 (5.1)	377	18 (4.8)
11–15	143	15 (10.5)	344	15 (4.4)
16–20	40	3 (7.5)	196	7 (3.6)
≥21	36	5 (13.9)	144	64 (44.4)
Total	348	28 (8.0)	1356	118 (8.7)

[a] See ref. *8, 9*.
[b] Figures in parentheses are percentages.

activities; consequently, autochthonous infantile kala-azar occurs, and the region is considered to be a natural nidus of kala-azar—wild animals presumably being the source of infection (*3, 11*).

The prevalence of the infection is sporadic, and affects mainly children (in the dry desert region, 92% of cases are aged <2 years, with no adult cases, and in the stony desert 90% of cases are aged <10 years and there are few adult cases). PKDL is absent. Lymphoglandular leishmaniasis occurs frequently in adults migrating to the dry desert region of Ejne Banner from nonendemic areas. The vectors are *P. major wui* (exophilic) in the dry desert region and *P. alexandri* (exophilic) in the stony desert. Visceral examination of rodents, hedgehogs, foxes, dogs, and bats failed to detect *Leishmania* spp. in either the dry or the stony deserts (*3, 11–13, 16*).

New cases continue to occur sporadically in the region. Abundant numbers of *P. major wui* and *P. alexandri* vectors were found (*14, 15*), with 0.88% of *P. major wui* being infected with *L. donovani* promastigotes in 1977 (*16*) and 1.04% of *P. alexandri* being infected in 1988 (Guan Li-ren, unpublished data, 1988). These two species of sandflies are extensively distributed in the field and bite at night.

Leishmanin intradermal tests carried out in 1972, 1982, and 1983 on local residents were strongly positive for all age groups (Table 4).

Further studies are needed to investigate the distribution of the foci of infection and the necessary effective control measures in such endemic regions.

Biological studies of sandflies

Soil type and vector distribution

Analysis of the study data indicated that the physicochemical characteristics of the soil are an essential factor that governs the distribution of sandflies. The soil of the vast area north of the Yangtze River is fundamentally alkaline (cinnamon, fluviogenic, and loessial soils, etc.), and *P. chinensis*, the main vector of kala-azar is abundant, while to the south of the Yangtze River the soil is essentially acidic (red and yellow soils, etc.), and *P. chinensis* is scarcely present.

Table 4: **Results of leishmanin intradermal tests in the dry desert, Ejne Banner, Inner Mongolia,**[a,b] **and in the stony desert, Turfan County, Xinjiang**[c]

Ejne Banner: Age group (years)	1972 No. examined	1972 No. positive	1982 No. examined	1982 No. positive	Turfan County: Age group (years)	1983 No. examined	1983 No. positive
≤2	7	1	6	1	1–5	80	14 (17.5)
3–5	16	8 (50.0)[d]	13	9 (69.2)	6–10	193	51 (26.4)
6–10	34	26 (76.5)	51	44 (86.3)	11–15	145	65 (44.8)
11–15	87	57 (65.5)	100	84 (84.0)	≥16	18	12 (66.7)
16–20	20	15 (75.0)	10	9 (90.0)	—	—	—
≥21	19	19 (100)	29	29 (100)	—	—	—
Total	183	126 (68.9)	209	176 (84.2)		436	142 (32.6)

[a–c] See ref. *8, 17*, and *12*, respectively.
[d] Figures in parentheses are percentages.

Table 5: **Vertical distribution of sandflies in south Xinjiang**[a]

Landscape zone	Soil type	No. of sandflies collected	No. of sandflies: *Phlebotomus chinensis longiductus*	*P. alexandri*	*P. major wui*	*Sergentomyia minutus sinkiangensis*
Mountainous: 1580–2100 m	Brown calcareous	442	406 (91.8)[b]	30 (6.8)	6 (1.4)	0
Stony desert: 1400–1650 m	Brown desert	1863	106 (5.7)	1704 (91.5)	53 (2.8)	0
Ancient oasis: 1200–1320 m	Whitish oasis	4978	4605 (92.5)	17 (0.3)	346 (7.0)	10 (0.2)
Dry desert: 980–1000 m	Scrubby meadow	29 588	0	0	22 901 (77.4)	6687 (22.6)

[a] See ref. *19*.
[b] Figures in parentheses are percentages.

Table 6: **Horizontal distribution of sandflies in Ejne Banner desert area, Inner Mongolia**[a]

Soil type	No. of sandflies collected	No. of sandflies: *Phlebotomus major wui*	*P. mongolensis*	*P. andrejevi*	*Sergentomyia minutus sinkiangensis*
Scrubby meadow	3899	3841 (98.5)[b]	0	0	58 (1.5)
Saline-alkaline	3646	1687 (46.3)	1317 (36.1)	538 (14.8)	104 (2.8)

[a] See ref. *18*.
[b] Figures in parentheses are percentages.

The soil type is therefore an important factor in restricting endemic kala-azar to the zone north of the Yangtze River (*18*).

A survey of the vertical and horizontal distributions of sandfly fauna in Xinjiang and Inner Mongolia in 1981–84 provided further evicence for the importance of soil type on the distribution of sandflies (Tables 5 and 6) (*18, 19*).

The main factor that influences the geographical distribution of sandflies is therefore the type of soil, and, depending on the landscape zone, different sandfly species play different roles in the transmission of kala-azar (*19*).

Autogeny in Phlebotomus chinensis

The *P. chinensis* populations in the loess plateau of Shaanxi and Shanxi Provinces are mostly autogenous. As such, they do not take a blood feed immediately after emerging as adults, but depend rather on the nutritional supply of their own fat-bodies to develop ovarian follicles. Blood meals commence only after the first oviposition (*20*). In contrast, in the mountainous area of south Gansu and north Sichuan, *P. chinensis* are apparently not autogenous.

Vector control

Use of 3,5-dimethylphenyl carbamate

The effectiveness of residual spraying with "Hunmiewei" (3,5-dimethylphenyl carbamate (3,5-MC)) in controlling *P. chinensis*, a semiwild species, was examined in Yichuan, Shaanxi Province. In 1976 after both vacant caves and caves used to hold livestock were sprayed with the insecticide, *P. chinensis* could scarcely be found in the treated caves during daytime throughout the sandfly season, although the numbers increased markedly at night because of invasion by *P. chinensis* from the wild. A follow-up study 2–3 years after the spraying operation showed that the sandfly density had returned to its previous level (*21, 22*).

In an experiment that was carried out 2 months after the residual spraying with 3,5-MC, sandflies were placed in contact with the sprayed cave walls; the knock-down time for all the sandflies was over 90 minutes. The reduction in the effectiveness of 3,5-MC was further demonstrated by observations on engorged sandflies. In 1976, the year that the spraying was carried out, engorged sandflies caught in the treated caves amounted to only 28.6% of the total; however, in 1977 and 1978 the proportions of such flies caught (82.0% and 82.8%, respectively) were similar to those of engorged flies caught in the control caves (90.1%) (*22*).

Use of deltamethrin

Residual spraying with deltamethrin (12.5–25 mg/m^2) to control *P. chinensis* was carried out in livestock caves and field caves within a 10-km^2 area surrounding Yichuan County, Shaanxi Province, in 1985–86. The sandfly density in the sprayed caves was significantly lower than that in the control area in daytime throughout the sandfly season (*23*).

In general, residual insecticide spraying for the control of periwild *P. chinensis* in the loess plateau area was less effective than in the plains area; nevertheless, in as far as it leads to a decrease in the sandfly density, the method can be included in the integrated intervention measures in the loess plateau area to reduce the transmission of kala-azar.

Aerial spraying with BHC

Aerial spraying with BHC was carried out in Ceke, Ejne Banner, Inner Mongolia. In 1972, before the spraying was performed, *P. major wui* sandflies were collected in the southern and northern parts of Ceke (1178 (in 7 sessions) and 184 (in 3 sessions), respectively). In the southern part of Ceke, BHC (6% wettable powder) was sprayed at a coverage of 1 kg per mu (1 mu ≈ 668 m^2) once per year during the peak sandfly season (June and July) from 1974 to 1979, covering forests and villages over an area of 80 km^2. The northern part of Ceke remained untreated. In 1980 an investigation was carried out to evaluate the effectiveness of BHC aerial spraying, the results of which are outlined below (*14*).

- Density of *P. major wui* sandflies caught on sticky-paper traps: 1.1 per sheet in the sprayed area; and 43.1 in the control area.
- Man-bait experiment: in July 1980, volunteers were exposed at night to biting sandflies. The number of *P. major wui* caught per person per hour in the sprayed area was 0–1 and that for the control area, 33–48.5.
- Sandflies in gerbil burrows: in late July 1980 a total of 27 *P. major wui* were caught in 30 gerbil burrows in the sprayed area and 311 in 10 burrows in the control area. These data provide evidence for a dramatic decline in the exophilic sandfly, *P. major wui*, following aerial spraying with BHC. The number of patients with kala-azar in the area also fell, but did not completely disappear, as indicated by the following incidences: 24.4 per 10 000 (1973); and 5.0–13.1 per 10 000 (1974–79) (*17*). Transmission of the disease had therefore not been interrupted.

Action of repellents

The action on *P. alexandri* of repellent liquor, *N,N*-diethyl-3-methylbenzamide, mosquito repellent, dimethyl phthalate, and dibutyl phthalate in laboratory and field studies is shown in Table 7 and Table 8, respectively (*24*).

Further experiments showed that *P. major wui* was more sensitive than *P. alexandri* to the above repellents and the repellence time was 1–2 hours longer.

Our findings indicate that the application of repellents to inhibit the action of sandflies in the transmission of kala-azar in the desert of north-west China is effective and practical.

Table 7: **Effect of various repellents on *Phlebotomus alexandri* sandflies in the laboratory**[a]

Repellent[b]	No. of sandflies	Effective repellence time (hours) at doses of of µl/cm^2: 0.1	0.25	0.5	1.0	No. of sandflies caught in 1 hour on an untreated volunteer	No. of engorged sandflies[c]
RL	564	4.75	7.50	8.25	10.25	225	173 (76.9)[d]
m-DETA	441	2.00	5.00	6.75	10.25	200	150 (75.0)
MR	419	2.25	3.75	5.25	8.00	172	129 (75.0)
DMP	184	0.75	1.25	3.00	6.50	125	100 (80.0)
DBP	223	0.75	1.00	1.75	3.0	125	100 (80.0)

[a] Experimental conditions: temperature: 24–29 °C; relative humidity: 40–50%. See ref. *24*.
[b] RL = repellent liquor; *m*-DETA = *N,N*-diethyl-3-methylbenzamide; MR = mosquito repellent; DMP = dimethyl phthalate; and DBP = dibutyl phthalate.
[c] Number caught in 1 hour on a volunteer.
[d] Figures in parentheses are percentages.

Table 8: **Effect of various repellents on *Phlebotomus alexandri* sandflies in the field**[a]

Repellent[b]	Dose ($\mu l/cm^2$)	No. of persons	Mean repellence time ± SD (hours)	No. of sandflies caught per hour on control person
RL	0.25	79	6.94 ± 0.67	16
m-DETA	0.25	24	5.19 ± 0.32	24
MR	0.25	43	4.98 ± 0.89	25
DMP	0.25	12	3.77 ± 0.43	32
DMP	0.20	16	1.94 ± 0.52	24

[a] Experimental conditions: temperature: 26–30 °C; relative humidity: 40%; wind velocity: 0.02–0.04 m/sec. See ref. *24*.
[b] See footnote *b*, Table 7.

Conclusions

Kala-azar, which was prevalent in the vast area of China north of the Yangtze River from the 1920s to the 1950s, is now effectively under control as a result of strenuous intervention since the founding of the People's Republic of China. With the exception of 15–20 new cases that occur annually in the Keshi plain in Xinjiang Autonomous Region, the achievements of control practices in other former endemic areas in the plains region have been significant and consolidated, and no new infections have been reported for more than 18 years. In the mountainous areas of north-west China, where *P. chinensis* is abundant and canine visceral leishmaniasis is common, there are still sporadic cases of kala-azar. In recent years, new infections have often occurred in the deserts of Xinjiang and western Inner Mongolia; however, the reservoir has not been identified.

Prospective investigations should be carried out to investigate the wild animal reservoirs of kala-azar and devise sandfly control measures suitable for use in the mountainous and desert regions of the country. Also efforts are needed to develop a vaccine for the prevention of kala-azar in these regions.

Résumé

Le kala-azar et la lutte antivectorielle en Chine: situation actuelle

Avant la création de la République populaire de Chine en 1949, le kala-azar était dans ce pays l'une des parasitoses les plus importantes. La maladie était présente dans plus de 650 comtés de 12 provinces et dans trois régions autonomes au nord du Yangtze. En 1951, elle touchait 530 000 personnes. Les efforts de lutte considérables déployés à grande échelle de 1950 à 1958 ont abouti à une maîtrise presque totale de la maladie dans la plupart des anciens secteurs d'endémie.

D'après les données cumulées, le kala-azar a été observé depuis 1985 dans 32 comtés de quatre provinces (Gansu, Shaanxi, Sichuan et Shanxi) et dans deux régions autonomes (Xinjiang et Mongolie intérieure). Le nombre de cas signalés chaque année est de 200 à 300.

La mise en place d'études prospectives permettrait d'étudier les réservoirs animaux et d'envisager des mesures de lutte anti-phlébotomes adaptées aux régions montagneuses et aux déserts de ce pays. D'autres efforts sont aussi nécessaires pour mettre au point un vaccin destiné à la prévention du kala-azar dans ces régions.

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