WHO/HTM/NTD/IDM/2008.7

REPORT OF THE

CONSULTATIVE MEETING

ON

CUTANEOUS LEISHMANIASIS

Geneva, WHO Headquarters, 30 April to 2 May 2007

Neglected Tropical Diseases

Innovative and Intensified Disease Management
Leishmaniasis Control Programme

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1. Background

Leishmaniasis is a parasitic disease transmitted by the bite of blood suckling insects, sandflies, which have previously fed on an infected reservoir host. There are two basic clinical presentations: visceral leishmaniasis (VL) or "kala-azar" and cutaneous leishmaniasis (CL). VL is the most severe and is fatal in almost all cases if left untreated, while CL is associated with a strong tendency toward spontaneous resolution but causes important social and psychological stigma.

Leishmaniasis is prevalent in 88 countries, affecting an estimated 12 million people with approximately 2 million new cases per year, 500 000 of which are VL and l 500 000 CL (90% of them in Afghanistan, Algeria, Brazil, the Islamic Republic of Iran, Peru, Saudi Arabia and Sudan). The disease burden is calculated at 2 356 000 disability-adjusted life years (DALYs): 946 000 in men and 1 410 000 in women, representing a significant rank among communicable diseases. A third of the global figure (770 000 DALYs) is attributable to CL. Given the importance of leishmaniasis, the 60th meeting of the World Health Assembly approved a resolution for "The Control of Leishmaniasis".

In general, CL has a tendency to heal spontaneously leaving scars which, depending on the species of *Leishmania* responsible, may evolve into recidivans CL, which is difficult to treat, and leaves extensive scars. In the Americas, CL may develop into one of two possible forms, depending on the species of *Leishmania* responsible: (1) diffuse CL, which occurs in patients with a weakened immune system who fail to heal spontaneously and relapse after treatment, with disastrous aesthetic consequences for the patient; or (2) muco-cutaneous leishmaniasis (known as "espundia" in South America), characterized by the destruction of the mucous membranes and cartilage of the mouth and pharynx followed by the facial tissue.

CL is a public health, as well as social problem, in many countries. CL is endemic in 82 out of the 88 countries where leishmaniasis is transmitted. The disease affects poor and deprived populations and has an important impact on the propagation of poverty, since treatment is expensive and therefore either unaffordable or involves a great a loss of wages. The cost of treatment and implementation of prevention strategies needs sizeable investments (financial and human resources) especially for vector and reservoir control. CL is re-emerging in many settings and in different countries with a variable number of cases and outbreaks occurring in urban areas or refugee camps, especially the internally displaced populations.

Operational research is required in multiple areas for evidence-based decisions. Public sector reporting of leishmaniasis only accounts for 20% of cases. The disease burden is therefore underestimated and real figures may be 4-5 times higher than what is being reported. Since CL is not fatal, it has received little attention with respect to improving its control at the individual or social level. CL therefore continues to be disregarded among the neglected diseases, and requires enhanced support for the implementation of effective prevention and control strategies.

Middle East and Maghreb countries harbour around 15% of the global leishmaniasis burden, which is almost exclusively attributable to CL. To aid the launch of a control programme aimed at reducing the incidence of CL in the aforementioned areas, WHO arranged a consultative meeting in Geneva from 30 April till 2 May 2007, which forms the basis of this report.

2. Meeting minutes

2.1 Opening Session

Dr Lorenzo Savioli, Director, Department of Control of Neglected Tropical Diseases, WHO Headquarters, Geneva, welcomed the participants of the meeting. In his opening remarks he highlighted the importance of leishmaniasis at global and regional levels. In particular, he mentioned the WHO commitment for the control of neglected diseases, which include leishmaniasis as one of the tropical diseases of public health importance. He highlighted important parts of the speech of the Director General, WHO, on the control of neglected diseases and emphasized the aim to reinvigorate the whole area of specific disease-related strategies, especially in poor and displaced populations where it is recognized that vector-borne diseases affect the poor and marginalized with variable levels of morbidity and mortality.

Dr Jean Jannin, Coordinator, Innovative and Intensified Disease Management, WHO, Geneva, presented the objectives of the meeting. This was followed by the selection of the Chairperson:
Dr. Jaouad Mahjour, Director, Department of Communicable Diseases, WHO Regional Office for the Eastern Mediterranean (EMRO) was elected as the Chairperson for Session I. Professor Richard W. Ashford, Liverpool School of Tropical Medicine, and Dr C. M. Arif Munir, Pakistan Medical Research Council were elected Rapporteur.

Dr Jorge Alvar, Leishmaniasis Programme Manager, highlighted the global importance of leishmaniasis in his introductory remarks. He was concerned with the increasing incidence of CL in the Eastern Mediterranean region and emphasized the need for more urgent and sustained action to keep the disease under control. He stressed that, in addition to morbidity, the problem of social stigma attached to CL requires renewed efforts to review and refine the existing strategies and mobilize resources to prevent and control this very important disease. This demands serious commitment at the national and global level.

2.2 Meeting Objectives

The meeting objectives were: (i) to revisit the area-specific disease-related strategies for the control of CL, especially in poor and displaced settings, and (ii) to define and decide on common strategies for prevention and control of CL in the Eastern Mediterranean region.

The WHO guidance to the participants focussed on the following:

> Clear strategies are needed to move ahead.
> More emphasis is required on effective implementation of disease control interventions.
> Member countries need to define common strategies for the control of CL for the next five years (2007–2012).
> National programme managers should take the lead and move forward to control this very important disease. WHO would provide the maximum support in the areas of disease epidemiology, surveillance, implementation of control intervention, and research. WHO would also consider the different possibilities for strengthening the national disease control programmes.

2.3 Invited lecture

Dr Riadh Ben-Ismail, Regional Advisor, Control of Tropical Diseases, WHO, EMRO, presented the regional situation of CL (anthroponotic and zoonotic). He discussed in detail the disease epidemiology including vectors and reservoirs and emphasized the need for more organized, target-oriented and cost-effective disease prevention and control strategies. He reviewed old and existing tools and the development of new tools for wider implementation. He also highlighted the case containment strategies.

Session I: Epidemiological Review and National Programmes

Speakers from 11 countries (Afghanistan, Algeria, Iraq, the Islamic Republic of Iran, Jordan, Libya, Morocco, Pakistan, Saudi Arabia, the Syrian Arab Republic, and Tunisia) made presentations. In almost all countries anthroponotic and zoonotic CL are prevalent. At the end of the session, detailed discussions were held that helped the participants focus their attention during the working group discussions.

Session II: State of the Art

Five presentations made by the speakers (list attached) covered different topics ranging from a systematic review on the treatment of CL, drug resistance, vector and reservoir control, and control in displaced settings. These state of the art lectures provided the opportunity to share diverse experiences related to various disease control components. The presentations were followed by in-depth discussions, and the session was concluded with the identification of working groups.

Session III: Working Groups

Three working groups were formed:

Epidemiological information and policy
Cases management
Prevention (vector and reservoir control)

Prior to working groups, discussions were held to identify key areas requiring input from the working groups. At the end of the session, one member presented the findings of their group These findings were then discussed in a combined session, and recommendations were given.

3. Recommendations

3.1 To endorse all recommendations of the resolution for the "Control of Leishmaniasis", 60th World Health Assembly, May 2007.

3.2 To promote political commitment of national governments for:

Formulation of policies
Availability of appropriate allocation of resources
Intersectoral collaboration

Community mobilization
Co-ordination with neighbouring countries

3.3 To set up a network for CL for:

Sharing information and experiences
Harmonization of control measures
Capacity building
Drug access and resistance monitoring
Quality control
Sub-regional collaboration

Vote of thanks and closure of the meeting

4. EPIDEMIOLOGICAL REVIEW AND NATIONAL PROGRAMMES: COUNTRY SUMMARIES

4.1 AFGHANISTAN, presented by Kamal Mustafa

4.1.1 Epidemiological information

Anthroponotic cutaneous leishmaniasis (ACL) is a major public health problem in Afghanistan. The disease occurs in 'independent' foci in the major cities of Kabul, Herat and Kandahar, and in 'dependent' foci in Charikar, Panjsheer valley, Gorband valley, and villages around Kandahar. The causative agent is *Leishmania tropica.* The vector is *Phlebotomus sergenti.* Although infected dogs have been found they are not thought to be a reservoir host. Since 1996 the infection has been spreading to new areas. Displacement and migration of people, particularly to cities, are thought to prolong the epidemic of ACL.

Zoonotic cutaneous leishmaniasis (ZCL) occurs in the northern plains of the Amu Darya River. The causative organism is *Leishmania major*. The vector is *Phlebotomus papatasi* and, possibly, *Ph. caucasicus*. The reservoir host is *Rhombomys opimus*. There is no recent information on this infection in humans.

Previously, there was a comprehensive reporting system, with free treatment in leishmaniasis treatment centres. The formal report of just 2000 cases in Kabul in 2006 is clearly a gross understatement: the estimated number of cases is more like 40 000. The current incidence at the national level is over 200 000 cases. Given that the population of Kabul is estimated to be 4 million, and allowing for those cases of other independent and dependent foci, the total population at risk is at least 8 million.

4.1.2 Disease management

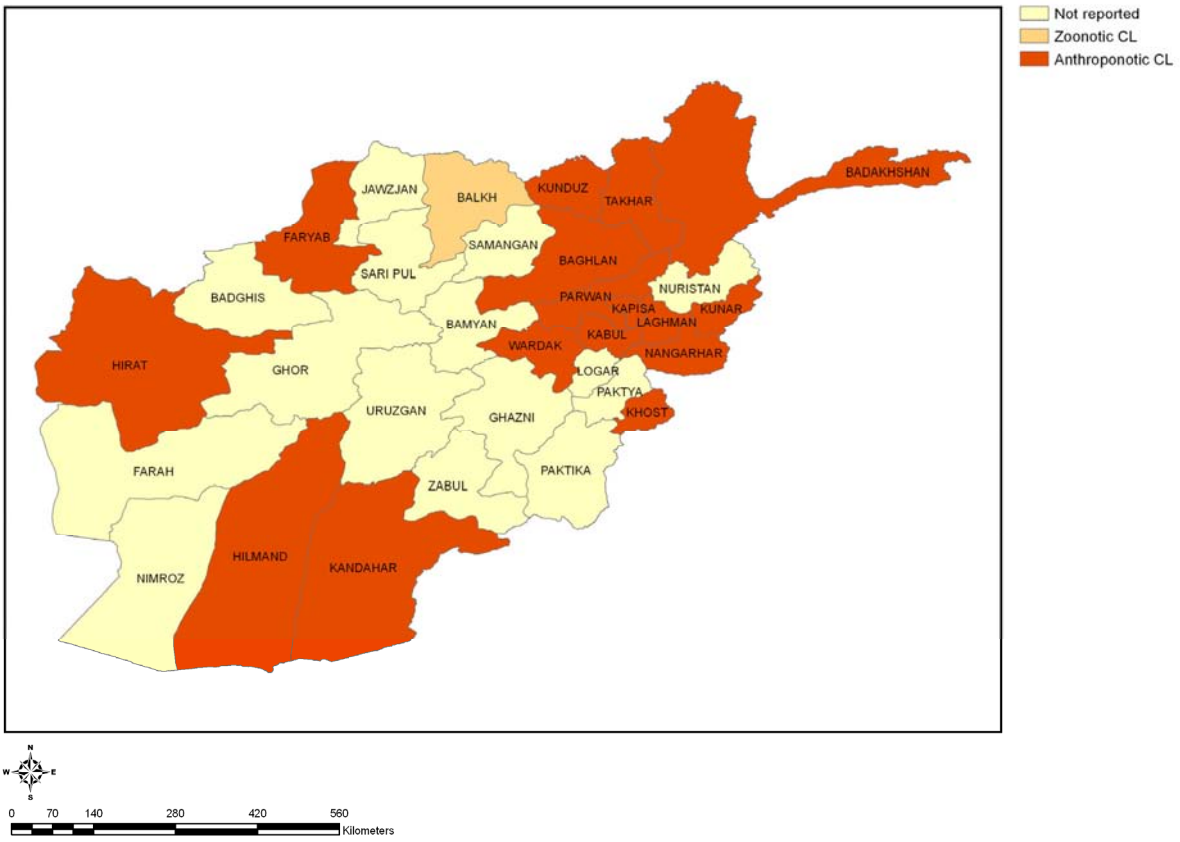
The entire health system is dependent on aid and contributions from non-governmental organizations (NGOs). The National Malaria and Leishmaniasis Control Programme (NMLCP) is currently being re-established, and a new NMLC Institute has been opened in Kabul. Leishmaniasis is not included in the Basic Package of Health Services (BPHS), but is in the Essential Package of Hospital Services. The inclusion of CL in the BPHS is of most importance.

Depending on availability, sodium stibogluconate (SSG) or meglumine antimoniate (MA) is used by intramuscular or intralesional injection. Trials with heat treatment (thermotherapy) show promising results.

ACL was reduced during the malaria eradication programme; subsequently, passive case detection with free treatment provided relief, if not control. Focal indoor residual spraying of insecticides (IRS) proved ineffective in Kabul. Insecticide treated nets (ITNs) and other insecticide-treated materials are currently showing promise.

Comprehensive reconstruction of the health system is required including the re-establishment of diagnostic and treatment services, surveillance both of the disease and vectors, development of technical capacity at all levels (i.e. clinical practice, entomology, parasitology), and training and resources for operational logistics and other fields.

Geographical distribution of Cutaneous Leishmaniasis in Afghanistan, 2007



4.2 ALGERIA, presented by Miloud Belkaid

4.2. 1 Epidemiological information

ZCL is dominant in Algeria, and distributed in a wide band across the arid zone with 10 000 cases recorded annually. Outbreaks seem to follow rainfall. *Psammomys obesus* is the reservoir host in unpopulated areas, and 'sylvatic' foci are thought to infect *Meriones shawi* in towns and villages, provoking outbreaks in settled human populations. The vector is *Ph. papatasi*.

Sporadic CL due to *Leishmania infantum* (MON 24) and *L. tropica* (MON 8) has also been isolated from further north.

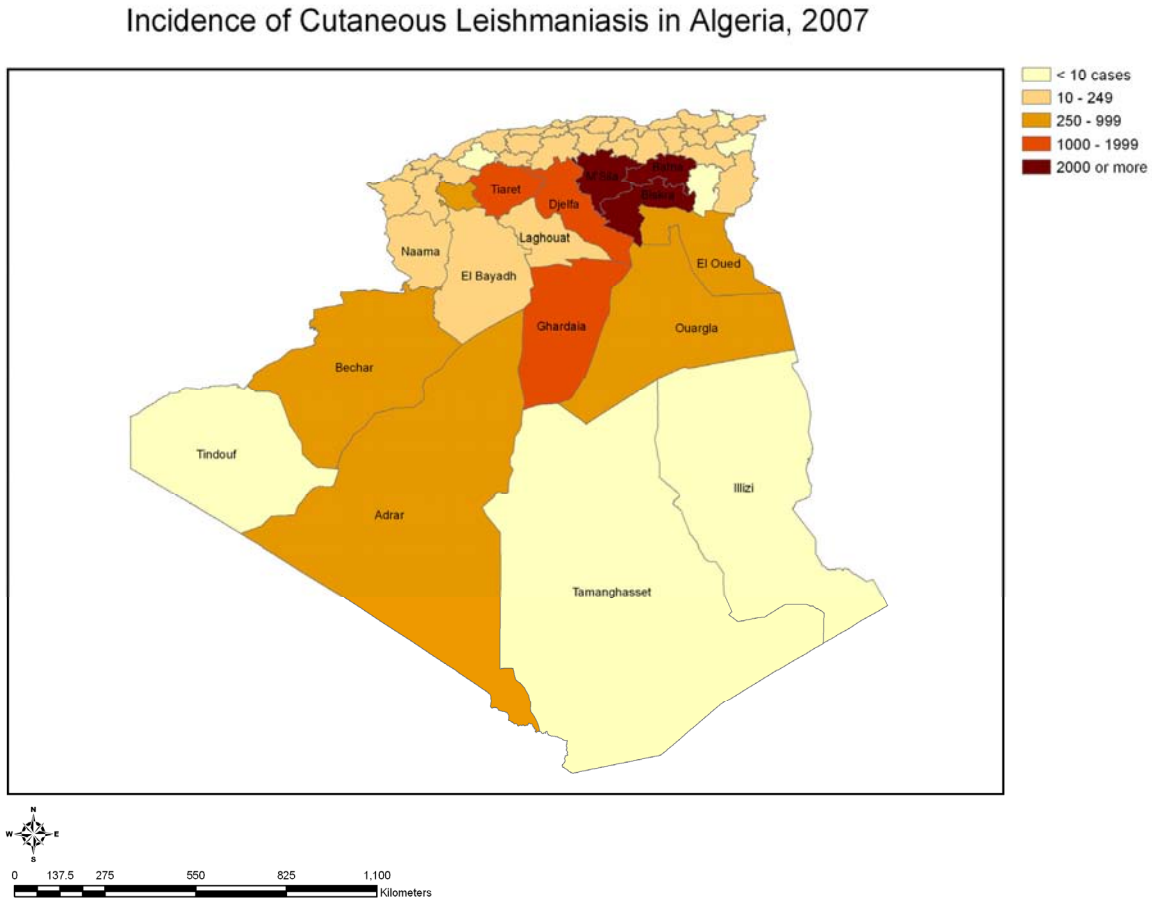
4.2.2 Disease management

A pilot control area has been identified, centred on the town of M'Sila, where intervention will be carefully monitored.

Control measures in the pilot area include the removal of succulent halophilic vegetation around population centres, environmental sanitation, burying of ruins, plastering of exterior

walls, and destruction of rodent burrows by ploughing between 500 and 1000m around dwellings.

In parallel, the risk factors for ZCL are being measured. Intrinsic factors include the polymorphism of the parasite, the biology of reservoir hosts and vector; extrinsic factors include weather conditions, soil types, vegetation and urbanisation.
CL is a serious public health problem, whose control deserves intensive action using the results of research studies.



4.3 ISLAMIC REPUBLIC OF IRAN, presented by Mohammed Reza Shirzadi

4.3.1 Epidemiological information

ACL caused by *L. tropica* occurs in 14 cities in the centre, south, south-east and north-east of the country. The vector is *Ph. sergenti* and there is no evidence of any non-human reservoir host.

ZCL caused by *L. major* is widespread in the centre, south, north and north-east. In most areas the reservoir host is *Rhombomys opimus*, but other rodents, *Meriones* spp. and *Tatera indica* may also be involved. The vector is *Ph. papatasi*.

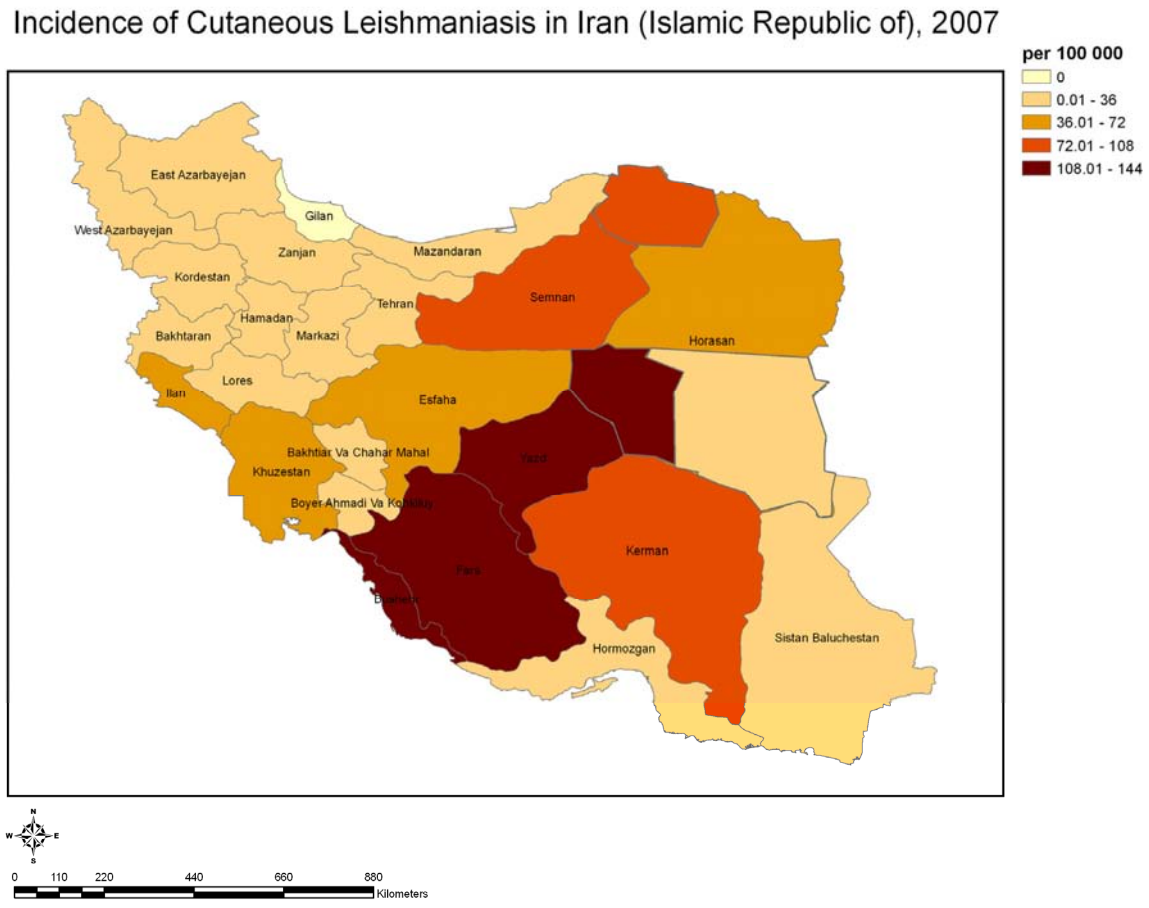
4.3.2 Disease management

CL is a notifiable disease. Surveillance is integrated into the health system. Cases detected passively in peripheral units are collated monthly at the district health centre and reported at the national level. The number of reported CL cases increased from 13 729 in 2002 to 24 092 in 2006.

There is a comprehensive network of research activities involving the Ministry of Health (MoH) and several universities, with a creditable record of important findings that are nationally and internationally relevant. Control of CL is the responsibility of the Zoonoses Department of the MoH. An increasing number of cases in recent years have necessitated revision of the national plan.

The new national plan will be piloted in some districts, such as Bam, and will include: education of health workers and the population, immediate case finding (active in new ACL-infected areas and passive in ZCL areas), standard treatment (using directly observed therapy), and free delivery of diagnosis, treatment and dressing. There is a standard register of cases by case definition and treatment, with evaluation and assessment of case-finding and treatment results.

There is a need for support from WHO in the evaluation of the leishmaniasis surveillance system.



4.4 IRAQ, presented by Sumayah Badri Hasan Al-Tuwaijari

4.4. 1Epidemiological information

CL is mainly endemic in the north of the country. Most cases occur in Diala, Kirkuk, Salahaldin, Baghdad/Kerkh, Wasit and Missan. Around 2000 cases are reported annually although cases are increasing due to the movement of people across open borders and increased surveillance.

4.4.2 Disease management

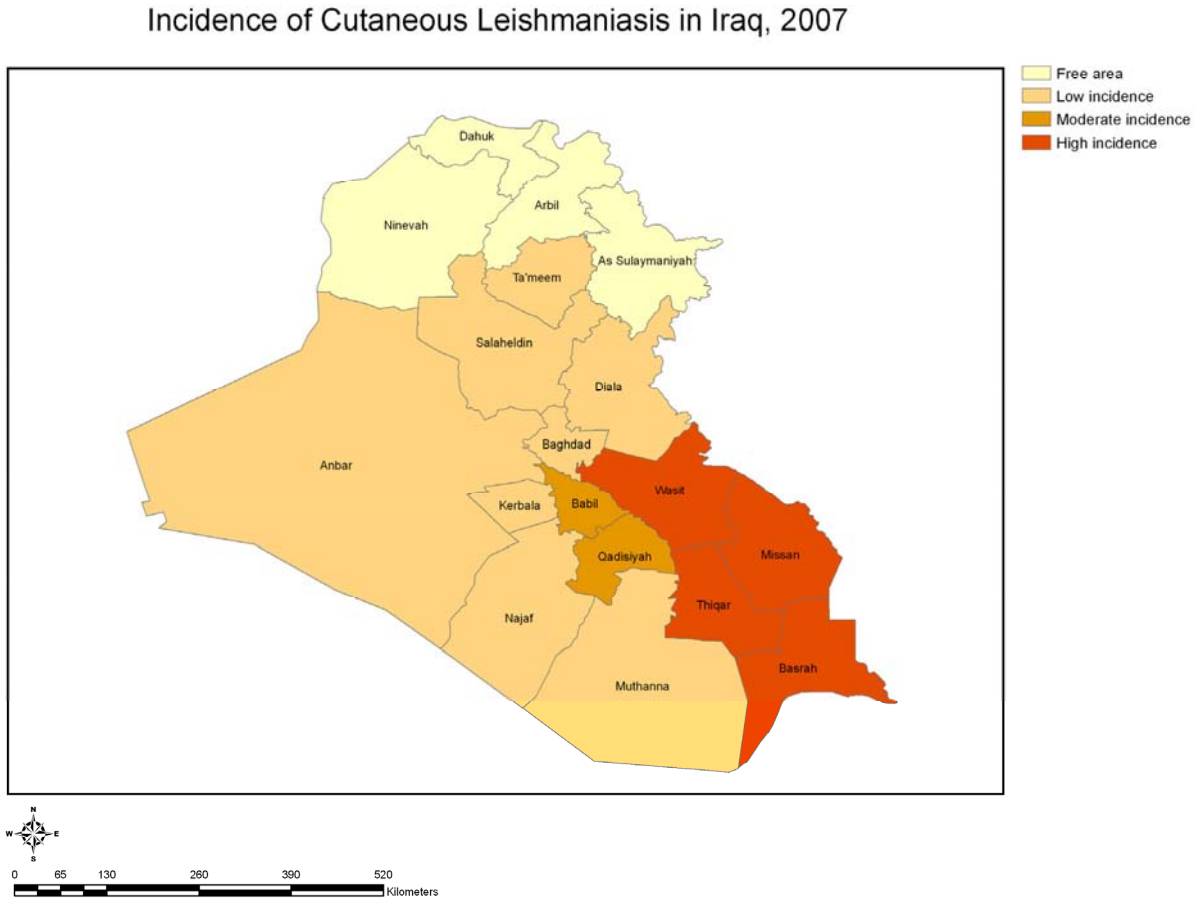
Increased surveillance is practiced as far as possible, but is limited to secure areas.

The leishmaniasis programme is the responsibility of the Zoonotic Diseases section in the department of Primary Health Care (PHC). Little control intervention is possible in the current security situation.

Diagnosis involves the examination of smears from the edges of ulcers and the culture of parasites.

Control measures include IRS (two rounds per year), fogging, and rodent control using rodenticides.

Little improvement in control measures is possible due to the current instability.



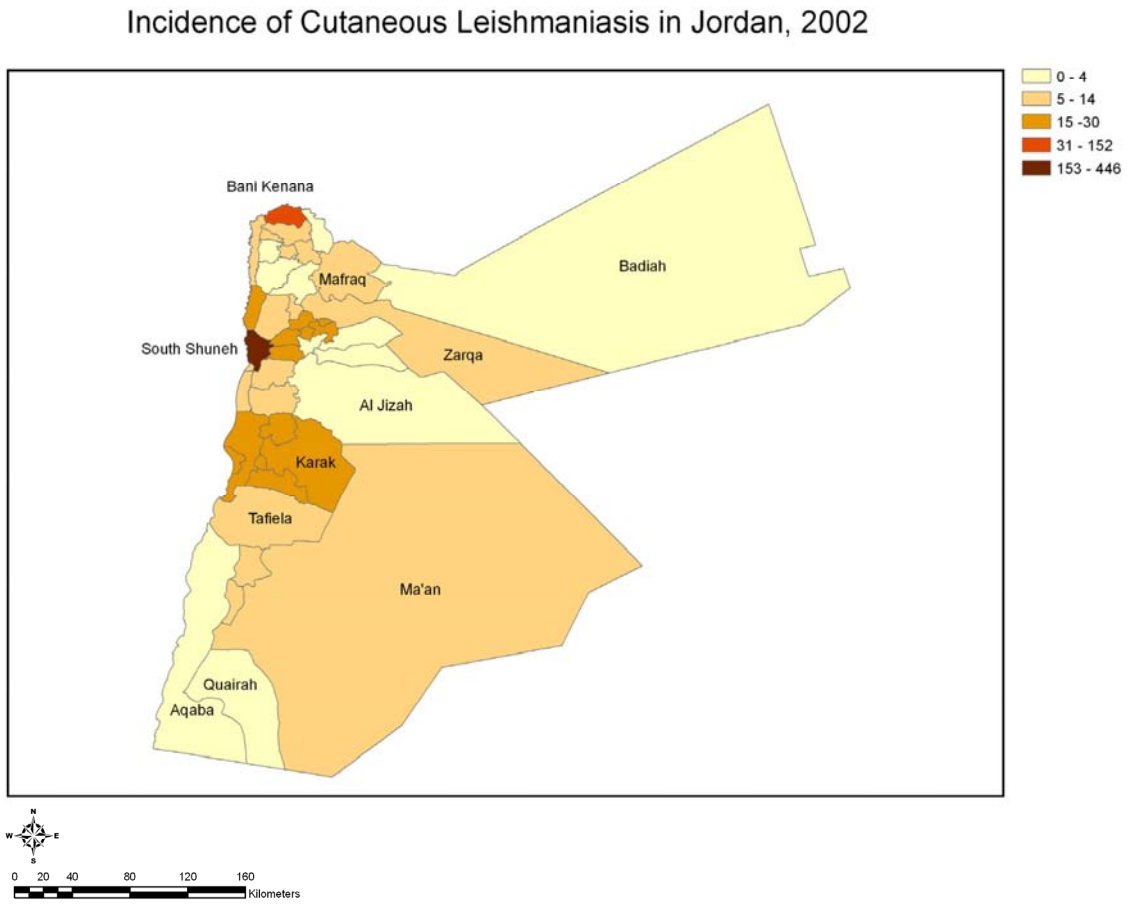
4.5 JORDAN, presented by Mahmoud Abu-Shehada

4.5.1 Epidemiological information

ACL occurs in the northern border area, where it is sporadic in rural villages, leading to the supposition that there may be a non-human reservoir host. The vector has not been incriminated.

ZCL is widespread in the Jordan valley, where the vector is *Ph. papatasi* and the reservoir host is *Psammomys obesus*. Cases are particularly concentrated in the resort area of Sweimah on the Dead Sea. In a recent outbreak at Quaira near Aqaba, there were around 150 cases, and a spiny mouse, *Acomys* sp. was found infected.

A total of 300 cases are reported annually.



4.6 LIBYA, presented by Baddereddin Annajar

4.6. 1 Epidemiological information

ZCL due to *L. major* (MON 25) is common and widespread in the north-west region except Tripoli and its suburbs. Reinfection has been reported in many areas in Jebel Nefusa.
However, only a single case of *L. killicki* (MON 8) has been confirmed. *Psammomys obesus* and *Meriones libycus* are reservoir hosts of *L. major*. The vector of *L. major* is *Ph. papatasi*.

4.6.2 Disease management

Since 2002 a National Centre for Infectious Diseases Prevention and Control (NCIDPC) was established, with responsibility for surveillance. The National Control Programme for Leishmaniasis was formed in 2006. Around 3000 cases were reported in 2006, and the disease seems to be spreading eastwards to previously unaffected areas.

The NCIDPC will contract control measures to local private pest management firms.

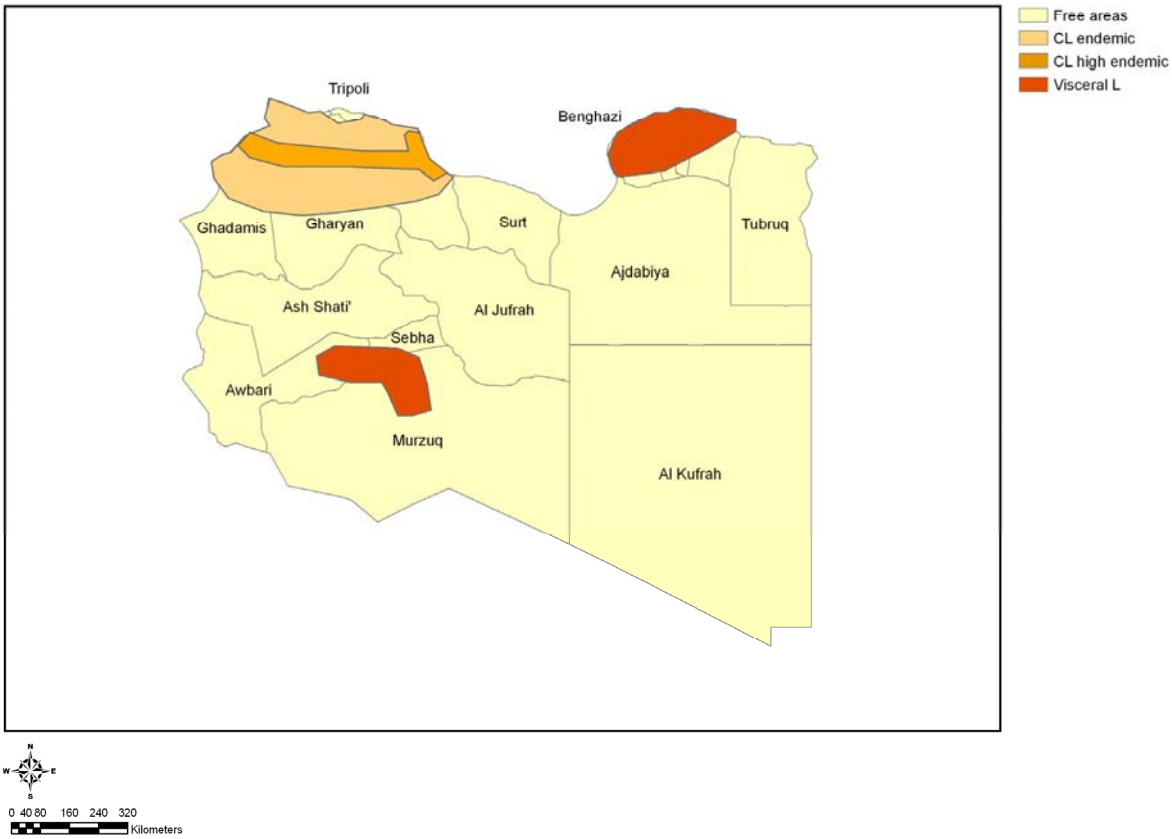
All CL patients are treated in local health centres and hospitals. There are dedicated leishmaniasis clinics with trained dermatologists in highly endemic areas. Treatment includes SSG, hypertonic saline solution administered intralesionally, and cryotherapy. Treatment is readily available and is free of charge.

Control measures are to be carried out by local pest management companies. The aim is to prevent the emergence of epidemics, to prevent spread of disease to new areas, and to reduce case numbers.

Assistance is required for the development of a comprehensive national plan to control leishmaniasis. This will include parasitology, entomology and environmental capacity building, as well as the evaluation of several treatment regimes, and may be integrated with sandfly fever surveillance.

Urgent action is required in a newly affected area close to a major city.

Geographical distribution of Cutaneous Leishmaniasis in Libya, 2007



4.7 MOROCCO, presented by Abderrahmane Laamrani El Idrissi

4.7.1 Epidemiological information

ZCL due to *L. major* occurs in unpredictable outbreaks in the south and south-east. Outbreaks seem to move in waves from west to east over several years. The reservoir host in heavily populated areas is *Meriones shawi*, and it is suggested that, as in Algeria, there is a 'sylvatic' reservoir system that 'feeds' this urban system, with *Psammomys obesus* as reservoir host. The vector is *Ph. papatasi*.

ACL due to *L. tropica* occurs in towns and villages in the centre of the country, on the Atlantic slopes of the Atlas Mountains. The vector is *Ph. sergenti*; no reservoir host other than man is known.

Occasional cases of CL occur in the north of the country, caused by *L. infantum*, with the domestic dog as reservoir host and *Ph. ariasi* as vector.

4.7.2 Disease management

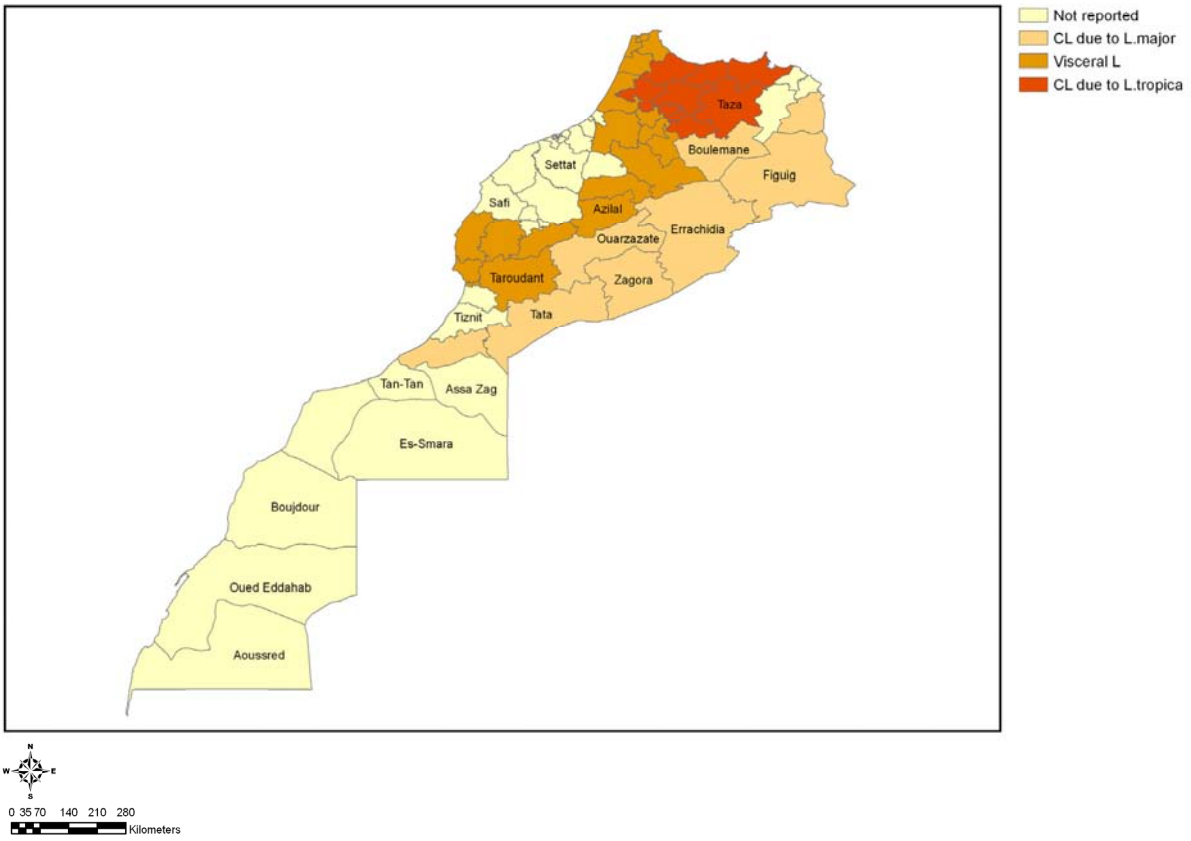
Leishmaniasis has been notifiable since 1995. Around 2000 cases of ZCL and 1000 cases of ACL occur annually.

A national control programme was established in 1997. The objectives of control are to stop transmission in active foci and prevent its geographical spread. Management of strategy and guidelines is conducted at the national level, as is the budget. Planning and operation of control activities are decentralized at the provincial level, and integrated into the PHC system.

Diagnosis is based on clinical examination and parasitological confirmation. MA is used intralesionally and intramuscularly to treat the CL patients. Diagnosis and treatment are free of charge.

Control activities involve close collaboration with the Ministries of the Interior, Education and Agriculture, and NGOs. Activities include early case detection and early treatment, vector control, reservoir host control, and health education.
Support is required for training, retraining and operational research.

Geographical distribution of Cutaneous Leishmaniasis in Morocco, 2007



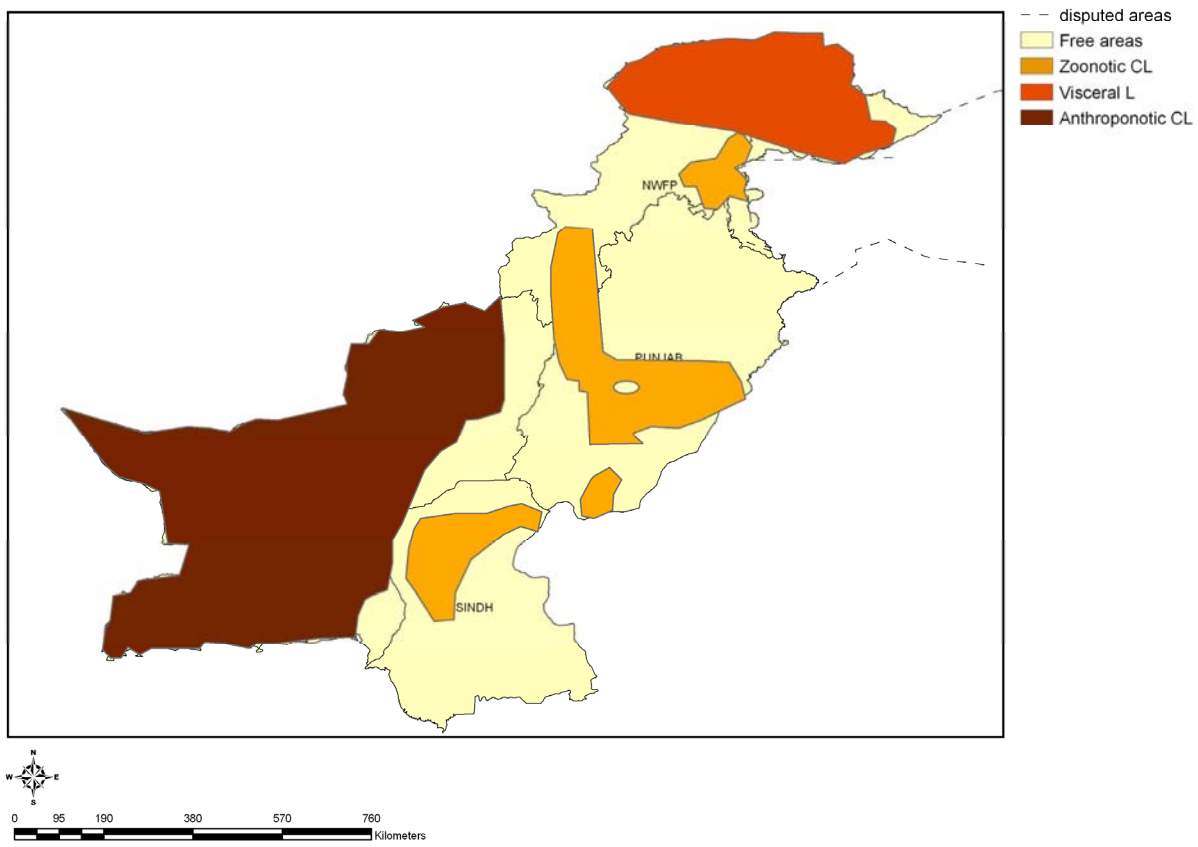
4.8 PAKISTAN, presented by Faisal Mansoor

4.8.1 Epidemiological information

ACL occurs in many parts of the country although its precise distribution and prevalence cannot be determined because of inadequate available information. Previously it was thought that the disease was restricted to urban and suburban areas, especially in the south. However, in recent years an upsurge in the number of ACL cases has been noticed and it has now been reported from many towns in the North-West Frontier Province (Peshawar, Mardan, Kohat and Abbottabad) and Baluchistan (Quetta, Mastung and Peshin), and even in the suburbs of Islamabad and Rawalpindi. Disease foci are also present in Gilgit town in northern areas and in parts of Azad Jammu and Kashmir. An epidemic occurred in Kurrum Agency in the Federally Administered Tribal Area in 2001 with an estimated 1200 cases. The main cause of the increase in cases of ACL seems to be the mass migration of the population from endemic to non-endemic areas and vice versa, and Afghan refugees from those areas of Afghanistan where disease is highly endemic. *Ph. sergenti* is considered to be the most probable vector.

ZCL occurs in many parts of the country being widespread over a large area in Baluchistan province. The incidence is high among children in the indigenous population, whereas adults are generally immune as a result of contact with the parasite during their childhood. However, non-immune adults, including military personnel and labourers, are at high risk of acquiring infection. An outbreak of ZCL occurred in two districts (Larkana and Dadu) of Sindh province in January 2001 with an estimated 4700 cases. Since then the number of cases has increased in these two districts with an estimated 15 000 new cases reported. The disease is spreading further and cases are now being reported from neighbouring districts. On the basis of its proven status as a vector elsewhere, including Iranian Baluchistan, *Ph. papatasi* is strongly suspected as the vector of disease, although a vectorial role for *Ph. salehi* cannot be ruled out. Several rodent species are candidate reservoir hosts in Baluchistan, but none has yet been incriminated.

Geographical distribution of Cutaneous Leishmaniasis in Pakistan, 2007



4.8.2 Disease management

There is no proper reporting or recording system. Cases seen by public sector hospitals are reported to central hospitals, then to an office at the Malaria Control Directorate. Some 25 000 cases are reported annually, but an estimated 70% are not seen in the public sector. Surveys among Afghan refugees showed an excess of cases in children and adult males.

The Directorate of Malaria has been assigned to take the lead role in the control of leishmaniasis, while it has also proposed incorporating responsibility for dengue control.

Diagnosis is generally clinical and, depending on availability, SSG or MA is used for treatment by intramuscular or intralesional injection.

Beyond passive case detection and treatment, no control measures are active.

A surveillance system needs to be established in order to fully evaluate the problem.
There is a general requirement for better understanding of the dynamics of the disease in Pakistan, and the measures for controlling it. Operational research is required in all aspects of case management and control including studies on vectors and reservoirs of infection.

Resources need to be allocated for case management and control.

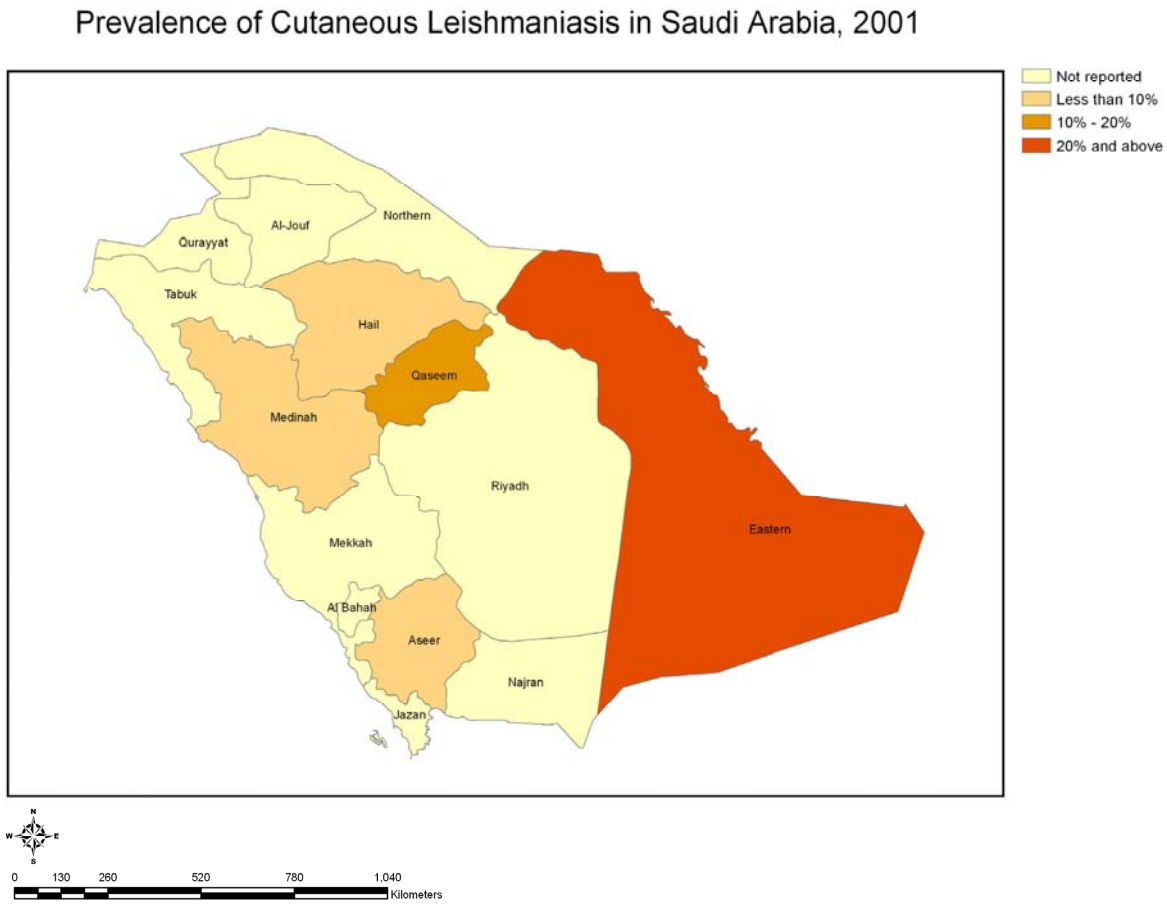
The development of a strategy that integrates leishmaniasis control with other vector-borne diseases is required.

4.9 SAUDI ARABIA, presented by Jaffar A. Al-Tawfiq

4.9.1 Epidemiological information

ACL due to *L. tropica* occurs in Aseer in the south-western part of the country. The vector is *Ph. sergenti*.

ZCL due to *L. major* occurs mainly in the east and centre of the country. The reservoir hosts for ZCL are thought to be *Meriones crassus* and *M. libycus*. The vector is *Ph. Papatasi.*



4.9.2 Disease management

CL is a notifiable disease that requires mandatory reporting of cases using a standardized form. The annual number of 4000 cases has almost halved since the early 1980s. Many more cases occur in expatriates than Saudi citizens and the former tend to have larger numbers of lesions.

A national programme was established in 1979 as the Leishmania Section, which subsequently became a department in 1983 and was integrated into the PHC.

Diagnosis is confirmed both clinically and microscopically. Treatment is mainly by administering intralesional or intramuscular SSG.

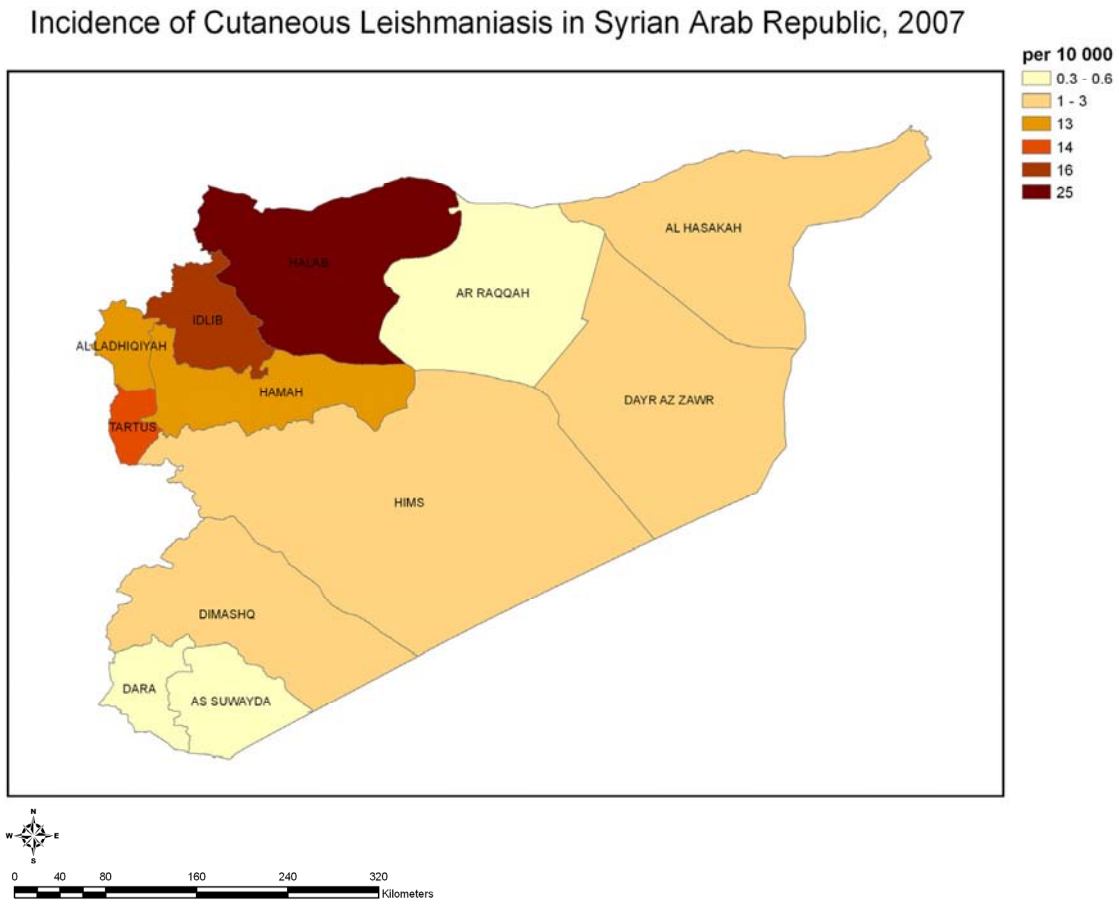
To control infection, the following activities are carried out when deemed appropriate: epidemiological surveillance of vectors and reservoir hosts; fogging and IRS; control of reservoir hosts by removal of their food source (plants) and destruction of their burrow systems; health education of health care workers.

4.10 The SYRIAN Arab Republic, presented by Nassir Ajlani

4.10.1 Epidemiological information

ACL is still endemic in its traditional home of Aleppo, and also in Edlib, Lattakia, Tortous, Hama and the city of Damascus. ACL represents about 90% of all CL cases. The vector is *Ph. sergenti*, and there is no evidence of a non-human reservoir host.

ZCL due to *L. major* occurs in rural areas close to Damascus, Deir al Zour and Al Hasakeh. The vector is *Ph. papatasi* and the reservoir host is *Psammomys obesus*. Other rodents that have been found infected include *Meriones* spp. and *Nesokia indica*. ZCL represents 10% of CL cases.



4.10.2 Disease management

Leishmaniasis is a notifiable disease in the Syrian Arab Republic. Surveillance includes both active and passive case detection. There is a peripheral centre for leishmaniasis control in each province to implement the plan of the MoH. Each of these 14 centres has branches (e.g. 35 in Aleppo) that provide diagnostic and treatment services free of charge and report monthly to the peripheral centre, including the number of registered cases. The peripheral centres, in turn, regularly report results and feedback to the central level within the MoH. The annual number of reported CL cases is approximately 19 000.

The political commitment to leishmaniasis control is at the highest level in the country. Both the President and Ministers recognize CL to be a major public health priority. Control of leishmaniasis is the responsibility of the Department of Infectious and Environmental Diseases (Malaria Control Programme). MoH policies include the control of leishmaniasis diseases and the provision of free treatment. Policies to combat and prevent leishmaniasis have been translated into actions, including the establishment of a "system for centres for the control of leishmaniasis and other parasitic diseases" at the governorate level in 1993.

Pentavalent antimonials are used for treating patients. The majority of cases are treated by intralesional injections and, in a few cases, intramuscular injections.

Control measures include early detection and treatment of cases and vector control. Vector control using IRS has been the main strategy for many years. Two insecticide spray campaigns are carried out each year according to the number of cases in the previous year, and the timing of vector appearance. The spray campaigns are conducted under the supervision of the central department in the MoH, which provides material support (insecticides, workers' payment, spraying machines, etc.). Personal protection measures include the use of ITNs. Trials carried out locally show that long-lasting ITNs are effective in reducing the number of cases.

Despite the strong policy and regulatory background, no national strategy has been implemented. The policy of a leishmaniasis control programme needs to: (i) massively reduce the use of insecticide, and (ii) adopt the use of pyrethroid-impregnated bed nets as a supportive control tool.

4.11 TUNISIA, presented by Afif Ben Salah

4.11.1 Epidemiological information

Sporadic CL due to *L. infantum* (MON 1 and MON 24) occurs in towns and villages in the north of the country. The reservoir host is the domestic dog and the vector is *Ph. langeroni*.

Sporadic CL due to *L. killicki* (MON 8) occurs further south, sometimes in limited outbreaks. The gundi (*Ctenodactylus gundi*) is suspected to be the reservoir host, and *Ph. sergenti* is the suspected vector. ZCL due to *L. major* is the main public health problem with *Psammomys obesus* as reservoir host and *Ph. papatasi* as vector.

4.11.2 Disease management

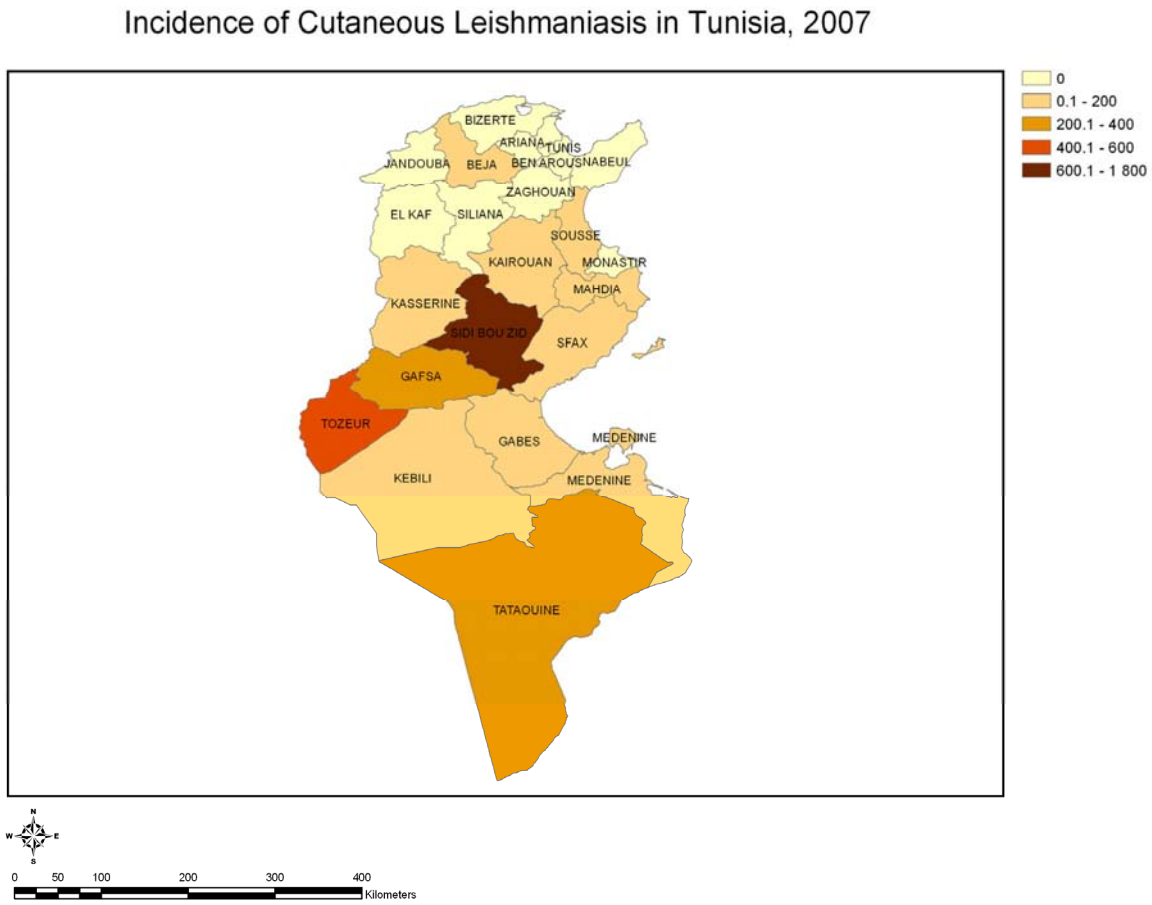
Passively detected cases are recorded on specific forms by primary care facilities; information is passed to the regional epidemiology unit at the governorate level and then to the Parasitic Disease Programme Manager at the PHC Directorate in the MoH. An outbreak started in central Tunisia in 1982 and the infection has subsequently spread to 15 of 23 governorates. Epidemics are cyclic with a periodicity of 5–6 years. Between 2000 and 3000 cases are reported annually.

The Tunisian National Parasitic Diseases Programme adopted a revised multidisciplinary control strategy for ZCL in 2000. Comprehensive research and pilot control measures have been jointly carried out by MoH units in affected areas, in collaboration with the Pasteur Institute, Tunis.

Diagnosis is based on clinical and epidemiological criteria and demonstration of *Leishmania* parasites by direct smear and culture. Treatment involves the administration of MA interlesionally (mild cutaneous cases) and intramuscularly (severe cutaneous cases).

In a pilot project at Sidi Bouzid, the area around the town was cleared and planted with trees to provide leisure facilities and prevent reinvasion by gerbils. Initially the result was ambivalent, as the incidence decreased both in the intervention area and the control site. More recent analysis has shown that over a longer period there has been a considerable reduction of cases in the intervention area. Under the new strategy, rodent populations in areas at risk are surveyed continuously so that epidemics can be predicted and prevented.

Surveillance of rodent populations by health staff presents difficulties of resource allocation.



5. STATE OF THE ART PRESENTATIONS

5.1 Ongoing Cochrane systematic review on treatments for Old World cutaneous leishmaniasis, presented by Urbà González

A Cochrane systematic review is an extensive, selective and critical review of the best available information using a systematic methodology**.** A systematic review ensures that healthcare decisions throughout the world can be informed by high quality, timely, updated research evidence. The other major bibliographic databases cover less than half the world's literature and are biased towards English language publications and, of the evidence available in these databases, only a fraction can be found by the average researcher. Textbooks, editorials and reviews that have not been prepared systematically may be unreliable. The mainstream medical databases such as Medline or EMBASE do not always capture clinical trials in the Middle East and South East Asia.

CL is a major worldwide health problem. Many treatments are currently used and a reliable and updated systematic review is needed. Since over 90% of cases of solitary or limited CL heal spontaneously within 3 to 18 months, the rationale for the use of systemic and topical treatments needs to be well established and preferably stratified for different geographic regions and *Leishmania* species.

Topical treatments are appropriate for early lesions, which are not at risk of dissemination. Systemic treatments are indicated when the patient has multiple or complicated lesions. Other reasons to consider systemic treatment are location, size, evolution, persistence, or nodular lymphangitis. Antimonials are the mainstay treatments but can cause serious adverse effects, require administration over long periods of time, and the development of drug resistance is a major concern. To limit toxicity, pentavalent antimony derivatives are used intralesionally for solitary or limited Old World CL.

The objective of the Cochrane review is to assess the effects of therapeutic interventions for CL. The criteria for inclusion of studies for this review are randomized controlled trials (RCTs) of immunocompetent people with solitary or limited Old World CL confirmed by smear, histology, culture or PCR probe. All doses and regimens of therapeutic interventions (including topical, systemic and non-pharmacological treatments) are considered, including any treatment or combination of treatments versus no treatment or placebo, and comparison of two or more therapies or combination of treatments.

The primary outcome of the review is percentage of lesions ‘cured’ at 3 months after the end of treatment. By ‘cured’, we mean that all inflammatory signs have disappeared (skin oedema and/or hardening) and that complete scarring or repair has occurred in ulcerative lesions. Lesions are not considered healed if there is no re-epithelialised skin, or if inflammatory signs remain after follow-up. Secondary outcomes include: speed of healing (time taken to be ‘cured’); duration of remission and percentage of people with treated lesions that recur within 6 months, 1, 2 and 3 years; degree of functional and aesthetic impairment; prevention of scarring; change in ability to detect *Leishmania* through PCR or other methods; emergence of resistance; microbiological or histopathological cure of skin lesions; development of cell-mediated immunity (i.e. positive leishmanin skin test); and adverse effects.

We have initially included 71 RCTs assessing the effects of different therapeutic interventions for CL, and excluded 29 for several reasons. Most RCTs contain defects in data reporting that have been considered predictors of defective study quality.

We have found RCTs of systemic treatments on intramuscular MA, intramuscular MA plus oral allopurinol, intravenous SSG, oral allopurinol, oral antifungals, oral pentoxyfiline, oral dapsone, oral zinc sulphate and oral rifampicin.

Topical therapies are attractive options offering reduced systemic toxicity and outpatient treatment for lesions not at risk of dissemination. We have found RCTs for cryotherapy, intralesional antimonials, intralesional interferon-gamma (IFN-γ), topical antifungals, topical paromomycin, intralesional hypertonic saline solution, intralesional zinc sulphate, IFN-β-containing cream, herbal extract, garlic cream, topical opium, Berenil/Savlon and thermotherapy. We found no trials on local care and treatment of secondary bacterial infection (essential for healing).

The results of this Cochrane review could be interpreted differently because information can be extrapolated from one situation to another with variable results, and each endemic area probably needs to establish its own therapeutic regimen for prompt treatment, as well as vector and reservoir control.

As an implication for research the creation of a Cutaneous Leishmaniasis Clinical Trial Network is proposed. This would be devoted to conducting high-quality, multicentre, RCTs that answer questions of importance to clinicians and patients, establishing a collaborative network of clinicians, nurses, health service researchers and patients throughout all affected countries in order to develop high-quality study proposals and trial suggestions. There is a need to search for unpublished trials, those published in local journals, and ongoing clinical trials.

5.2 Vector control: Insecticide-treated bed nets (ITNs) to prevent anthroponotic cutaneous leishmaniasis in Aleppo Governorate, the Syrian Arab Republic, presented by Lama Jalouk

Indoor-spraying campaigns apparently did not produce any impact on ACL incidence during the past ten years in the Aleppo Governorate. The disadvantages of residual house spraying and the success of impregnated bed nets technology in the control of malaria has inspired the WHO to employ the same technique to control ACL.

To evaluate the efficacy of pyrethroid-impregnated bed nets (ITNs) in controlling ACL, three trials were conducted in the Aleppo Governorate, which represents one of the oldest-known foci of the disease. Epidemiological surveys took place before the use of both, impregnated and non-impregnated bed nets, to estimate the one-year CL prevalence. In order to compare with CL incidence in the subsequent year after the use of bed nets, surveys were conducted quarterly to look for new CL cases.

Consistent studies during 10 years covering 24 257 individuals and using around 8513 impregnated bed nets and 5430 untreated bed nets, showed a clear decline in the disease incidence in three studies, supporting evidence that ITNs have produced the desired control effect. The studies have shown a sharp reduction in the incidence of ACL following the

implementation of the ITNs in the intervention villages. With a mean annual number of 15 366 ACL cases reported by the MoH in the past 10 years, the size of the public health problem presented by this figure is alarming since only one of four patients visits a public health facility (according to a 1993 study).

The success of these three studies led us to conduct the one-year study in 20 infected urban and rural districts in Aleppo during 2004 to provide baseline information that would assist the control programme in scaling up ITN strategy in the Syrian Arab Republic. Household, demonstration, commercial retails and net placement surveys were conducted. Key informant interviews and focus group discussions were also carried out.

This study provided an in-depth analysis of the community beliefs, preferences, likes and dislikes of ITNs, and their willingness to pay for them, in highly infected districts in Aleppo, where all the population was at risk and the prevalence of ACL was around 4%. The study demonstrated a real willingness to buy ITNs but related such willingness to buy with the price. The fact that each household spends between US$2.3 and US$4.7 in urban and rural areas, respectively, to buy insecticides, indicates that increasing community awareness about the efficacy of ITN will definitely result in shifting their behaviour from buying insecticides to ITNs.

The study reported the over-reliance on IRS as the main vector control method in this endemic area. It is therefore recommended to shift from this method to ITNs using the information provided by this study and its recommendations to scale up its use in this community in the most efficient way. To implement these findings, especially those related to communities' misconceptions on ITNs, will require the development of appropriate behavioural messages. The use of communication for behavioural impact methodology may be necessary.

The implication of the positive results of the four studies can lead to less dependence upon the current policy of selective spraying campaigns in endemic areas. The use of ITNs may represent the most sustainable method of reducing *Leishmania* transmission.

5.3 Reservoir Control, presented by Richard W. Ashford

In ZCL the reservoir of infection ('reservoir') is an ecological system, which includes populations of one or more species of mammalian reservoir host, populations of one or more species of sandfly vector, in sufficient density, and environmental factors permitting transmission at a rate sufficient to maintain, indefinitely, a population of the parasite.

The understanding of reservoirs involves an ecological study of populations and their interactions. It is a multidisciplinary study involving entomology, mammalogy, parasitology, population dynamics, and several other ecological subjects.

'Reservoir control' can include any intervention designed to reduce the incidence of human disease by manipulation of one or more of the components of a reservoir of infection. This might involve:

Avoidance: if a reservoir can be clearly defined and described it may be possible to protect people by keeping them away from transmission at night during any transmission season

Mammal control: reduction of populations of reservoir hosts below any transmission threshold may effectively 'sanitise' an area.

Bonification: an old term from malariology. It may be possible to reduce the risk of human disease by diverse environmental interventions, which might affect reservoir hosts, vectors, or the interactions between them.

Table 1. Nosodemiological forms of CL in the Eastern Mediterranean region.

***Leishmania* species**	**Geographical area**	**Main reservoir host**	**Habitat**	**Possible measures**
L. major	All countries from Morocco to Saudi Arabia and Syria	Fat sand rat *Psammomys obesus*	Sebchet with halophilic vegetation	Avoidance Ploughing? Poisoning? Flooding?
L. major	Parts of Iraq and south-west Iran	Uncertain	Uncertain	Uncertain
L. major	Central and north-eastern Iran, northern Afghanistan	Great gerbil *Rhombomys opimus*	Loess soils in alluvial plains	Ploughing? Poisoning
L. major	South-eastern Iran, Pakistani Baluchistan	Gerbils *Meriones* spp.?	Arid rural areas	Gerbil control?
L. tropica	Sporadic, from Morocco to northern Afghanistan, Pakistan	Man, domestic dog?	Densely populated areas	Vector control, ITNs
L. tropica	Sporadic cases Morocco, Turkey, N. Galilee, northern Jordan etc	Rock hyrax *Procavia capensis*? Others uncertain	Rural and suburban areas with large boulders	Uncertain
L. infantum	Rare cases throughout Eastern Mediterranean (usually causes infantile VL)	Domestic dog	Peripheries of towns and villages	Vector control, control of VL

Although studies have helped provide us with important knowledge, it must be recognized that there is no standard method(s) that has been shown to be effective in the reduction of ZCL due to *L. major*. Any intervention must therefore, at this stage, be preliminary and investigative.

5.3.1 Key features of L. major *infection (ZCL) in our area.*

Through much of the area (Algeria, Tunisia, Libya, Egypt, Saudi Arabia, Palestine, Jordan, the Syrian Arab Republic) the main reservoir host is *Psammomys obesus*, the fat sand rat.

In eastern Iran and Afghanistan, *P. obesus* is absent, and the main reservoir host is the great gerbil *Rhombomys opimus*.

In southern Morocco, the gerbil *Meriones shawi* is a reservoir host in and around the town of Tata. It has been suggested that there are permanent reservoirs in sylvatic areas, with *P. obesus* as reservoir host, and subsidiary (dependent) reservoirs maintained by *Meriones* spp. in towns and villages. *L. major* infection occurs in people in Iraq and south-east Iran, outside the ranges of both *P. obesus* and *R. opimus*. It is not clear which of the local rodents may be the reservoir host(s) in this area. In Pakistani Baluchistan, ZCL exists, but little is known of its ecology.

The recent confirmation that *Psammomys* has two species, *P. obesus* and *P. vexillaris,* raises possible further complications: the distribution of the two species needs to be mapped, their ecology described, and their epidemiological roles assessed.

Throughout the area, the vector is *Phlebotomus papatasi*, a sandfly that readily feeds on many types of mammalian and avian blood and lives both in human habitations and many sylvatic locations. Its breeding sites are unknown. The adults feed on juices from the leaves of plants; it has been suggested that transmission could be reduced by growing species of plants with juices that are toxic to *Leishmania*.

Transmission, at least in some areas, is seasonal and, in humans, there is an incubation period of several weeks. Therefore, by the time an epidemic becomes apparent, most of the cases have been infected and transmission has passed its peak for that year. In this case, simply responding to an outbreak when it is noticed may be much too late. It is important to recognize the factors preceding an outbreak, to predict them, and to intervene in advance.

In a settled human population living in an area of high transmission, most people become infected and immune at a very early age; if the transmission rate is reduced but not eliminated, the same number will become infected in their lifetime, but infection will occur at a later age. Since the disease is more of a problem in teenagers and young adults, reducing transmission may do more harm than good to local residents. Only when transmission is reduced to a very low level will there be a reduction in the number of people who become infected in their lifetime, or in the number of cases annually.

However, ZCL is mostly a public health problem when it occurs in unsuspecting people, either because the disease has changed its distribution, or because people have moved into a zoonotic focus. In such situations urgent action may be appropriate.

Typical situations where people have been infected by moving into a zoonotic focus include builders of housing projects close to towns, builders of projects in rural areas, workers on agricultural projects, and military activities, particularly lookout posts in border areas.

The movement of the disease to new areas is less well documented and less well understood, but it does seem to happen, as in Sahara el Jefara in Libya, the Sidi Bouzid area in Tunisia, and Tata in Morocco.

The populations of the reservoir hosts, *Psammomys obesus* and *Meriones* spp. undergo great fluctuations. These are poorly recorded and not understood. One suggestion is that since the

camel was replaced by 4x4 off-road vehicles, the succulent vegetation required by the rodent has flourished (the camel being the only competitor for this food source). Consequently, the rodent may have also flourished.

In Tunisia, we evaluated a transect method for monitoring the fat sand rat populations. It would be very cheap to set up monitoring stations so that an increase in numbers could be rapidly detected and outbreaks foreseen. *R. opimus* populations are monitored in Kazakhstan in connection with plague control, and the methods used could be adapted for leishmaniasis.

Neither the fat sand rat nor the great gerbil is an agricultural nuisance, so there has been little work on their control. Furthermore, their habitats are in marginal land that is very sensitive to disturbance. Any control measures should be environmentally friendly.

5.4 Leishmaniasis control in displaced settings: experience with Afghan refugees, presented by Muhammad Arif Munir

5.4.1 Background of leishmaniasis in Afghan refugees in the North-West Frontier Province (NWFP), Pakistan:

Form of leishmaniasis:	CL due to *Leishmania tropica* (isolated from patients and confirmed on PCR)
Vectors:	Vector species yet to be confirmed. However, on epidemiological grounds *Phlebotomus sergenti* is considered as the most probable vector involved in disease transmission.
Distribution of cases:	90% of cases are reported from southern districts of NWFP and 10% from northern districts.
Current refugee population:	1.1 million

5.4.2 Health Services Set-up

The health service situation for Afghan refugees is structurally and functionally separate. Service delivery is through Basic Health Units (BHUs). There is one BHU for a population between 5000 and 15 000**.**

Services are delivered through the network of BHUs:

Staff: medical officer, dispenser, paramedic/microscopist
Services: curative, antenatal and preventive for 5000–15 000 people
Outreach through trained volunteers – referral and ITN promotion

5.4.3 Arrangements in place

General health facilities enabled to offer *Leishmania* microscopy and treatment
A laboratory for every population between 10 000 and 15 000
Single visit to obtain the confirmed diagnosis
External Quality Assurance – linked to malaria microscopy quality control

5.4.4 Leishmaniasis control components

Rapid assessment
Case management: 90% of leishmaniasis cases diagnosed clinically (i.e. on the basis of examination of lesions) and 10% on confirmation of parasite microscopically Treatment is with SSG or MA (depending on the availability of drugs). Drug administered by intralesional and intramuscular injection following guidelines developed by HealthNet International Prevention (using focal IRS with synthetic pyrethroids, ITNs and other materials)
Community mobilization
Surveillance, outbreak detection and response
Monitoring and evaluation

5.4.5 Operational Research

Programme strategies and operations informed through operational research
Operational research built into programme implementation
Linkages with academic/research institution
Operational research disseminated widely, mainly through publication in peer-reviewed journals and inclusion in local advocacy materials

Some examples of operational research:

Trials on miltefosine against CL
Trials on impregnated nets and other materials
Disease epidemiology, prevention and control strategies

5.4.6 Outcome (last 3 years)

Incidence of CL reduced from 13.8 to 3.6/1000 population.

5.4.7 Challenges

Drug registration with host country
Expensive and painful treatment leading to poor compliance
Re-treatment of ITNs is labour intensive and costly
Stigma which the patient has to live with throughout lifeFemales with facial scars suffer the consequences of the disease and are the victims of social isolation and deprivation

ANNEX I - AGENDA

MONDAY, 30 APRIL (Salle D)

08:30-09:00 **Registration** at front desk, Main Building

09:00-09:30 **Opening session**

Lorenzo Savioli, Director, Control of Neglected Tropical Diseases, WHO; and
Jaouad Mahjour, Director, DCD, WHO Regional Office for the Eastern Mediterranean (EMRO)

Objectives of the meeting

Jean Jannin (Coordinator) and Jorge Alvar (Leishmaniasis Programme Manager), Innovative and Intensified Disease Management, WHO

Election of Chairperson and Rapporteur

09:30-10.10 **Invited lecture**

Cutaneous Leishmaniaisis: anthroponotic vs zoonotic entities
Riadh Ben-Ismail, Regional Adviser, CTD, WHO Regional Office for the Eastern Mediterranean (EMRO)

10:10-10:40 ***Coffee break***

Session 1: Epidemiological review and national programmes

10:40-11:00 **Afghanistan:** Kamal Mustafa, DCD/RBM, WHO, Kabul
11:00-11:20 **Pakistan:** Faisal Mansoor, Ministry of Health, Islamabad
11:20-11:40 **Iran:** Mohammed Reza Shirzadi, Ministry of Health, Tehran
11:40-12:00 **Iraq:** Sumayah Hasan Al-Tuwaijari , Ministry of Health, Baghdad

12:00-12:30 **Discussion**

12:30-13:30 ***Lunch break***

13:30-13:50 **Syria:** Nassir Ajlani, Ministry of Health, Damascus
13:50-14:10 **Jordan:** Mahmoud Abo-Shehada, University of Irbid, Jordan
14:10-14:30 **Saudi Arabia**: JA Al-Tawfiq, Dhahran Health Centre, Saudi Aramco, Dhahran

14:30-15:00 **Discussion**

15:00-15:30 ***Coffee break***
15:30-15:50 **Libya**: Badereddin Annajar, National Centre for Infectious Diseases Prevention and Control, Tripoli

15:50-16:10 **Tunisia**: Afif Ben Salah, Institut Pasteur, Tunis - WHO Collaborating Centre for Leishmaniasis

16:10-16:30 **Algeria:** Miloud Belkaid, Institut Pasteur, Alger

16:30-16:50 **Morocco:** Abderrahmane Laamrani El Idrissi , Ministry of Health, Rabat

16:50-17:30 **Discussion and organization of working groups**

TUESDAY, 1 MAY (Salle D)

Session 2: State of the art

09:00-10:00 **Systematic review of treatments for cutaneous leishmaniasis**
Urbá Gonzalez, Research Unit for Evidence-based Dermatology, Clinic Plató, Barcelona, Spain
Susceptibility and resistance of *L. tropica* against meglumine antimoniate. Miltefosine versus meglumine antimoniate in the treatment of zoonotoic cutaneous leishmaniasis
Mohammed Reza Shirzadi (on behalf of Prof M. Mohebali), Ministry of Health, Tehran, Iran

10:00-10:30 **Discussion**

10:30-11:00 ***Coffee break***

11:00-12:30 **Vector Control**
Lama Jalouk, Aleppo Leishmaniasis Centre, Damascus, Syria

Reservoir Control
Richard W. Ashford, Parasite and Vector Biology, Liverpool, UK

Control in displaced population settings
Chaudhry Muhammad Arif Munir**,** Pakistan Medical Research Council, Islamabad, Pakistan

12:30-13:00 **Discussion**

13:00-14:00 ***Lunch break***

14:00-16:00 **Working groups**

A. Epidemiological information
B. Case management
C. Vector and reservoir control

Summary of bullet points

16:00-16:30 ***Coffee break***

16:30-18:00 **(Room E 110)**	**Discussion and working groups' organizationWEDNESDAY, 2 MAY**
09:00-10:30	**Working groups** **A. Strengthening the National Health Programmes** **B. Strengthening a Regional Programme**
10:30-11:00	***Coffee break***
11:00-12:30	**Working groups (cont.)**
12:30-13:00	**Summary of bullet points**
13:00-14:00	***Lunch break***
14:00-15:30	**Discussion and decisions for report**
15:30-16:00	***Coffee break***
16:00-16:30	**Final remarks and end of the meeting**

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