

WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR EUROPE
WELTGESUNDHEITSORGANISATION
REGIONALBÜRO FÜR EUROPA



ORGANISATION MONDIALE DE LA SANTÉ
BUREAU RÉGIONAL DE L'EUROPE
ВСЕМИРНАЯ ОРГАНИЗАЦИЯ ЗДРАВООХРАНЕНИЯ
ЕВРОПЕЙСКОЕ РЕГИОНАЛЬНОЕ БЮРО

WHODOC 2/1

HLT

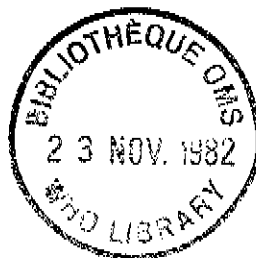
Malária, camp...
Малария, камп...
Leishmaniasis, viral...
Лейшманиозис, вирус...
Mea...
срещи нас

23 NOV 1982

MALARIA AND OTHER IMPORTED COMMUNICABLE DISEASES
IN MEDITERRANEAN COUNTRIES

Report on a WHO Coordination Meeting

Mahon
1-4 June 1982



INFORMATION COPY
ORIGINAL IN REGISTRY FILE

1748740/3



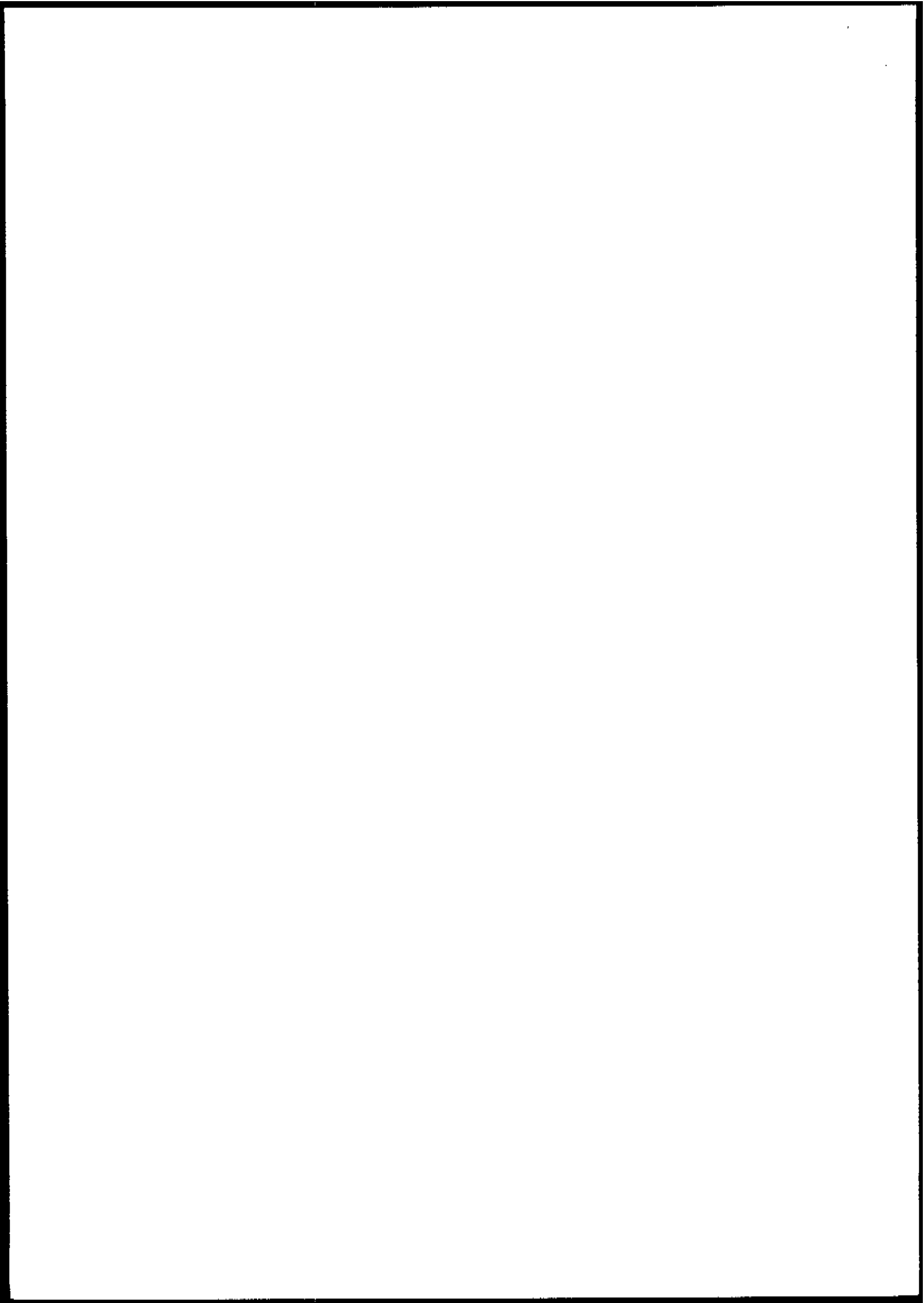
ICP/MPD 002
0016C
ORIGINAL: ENGLISH

Note

The issue of this document does not constitute formal publication. It should not be reviewed, abstracted, quoted or translated without the agreement of the World Health Organization. Authors alone are responsible for views expressed in signed articles.

CONTENTS

	<u>Page</u>
1. Introduction	1
2. Scope and purpose	1
3. Malaria	2
3.1 The present situation in Mediterranean countries	2
3.2 Classification of cases by species of parasites and by profession	3
3.3 Legislation	3
3.4 Control measures and surveillance	3
3.5 External reporting	4
3.6 Entomological activities and observations	5
3.7 Training	5
3.8 International cooperation	6
4. Haemorrhagic fevers	6
4.1 Implicated viruses and the diseases they cause	6
4.2 Geographical distribution	6
4.3 Transmission	7
4.4 Pathology	7
4.5 Clinical features	7
4.6 Serological diagnosis	8
4.7 Virological diagnosis	9
4.8 Clinical management of cases	10
4.9 Prognosis	10
5. Leishmaniases	11
5.1 General	11
5.2 The epidemiological situation in participating countries	11
5.3 Reservoir	12
5.4 Vectors	13
5.5 Control measures	14
5.6 Research	14
6. Recommendations	14
6.1 Malaria	14
6.2 Viral haemorrhagic fevers	15
6.3 Leishmaniases	15
6.4 General	15
Annex 1 Bibliography	16
Annex 2 List of participants	18



1. Introduction

The Meeting was organized by the WHO Regional Office for Europe in collaboration with the Spanish Government and the Regional Government of Menorca, as a follow-up of the Coordination Meeting on the Prevention and Reintroduction of Malaria in the Countries of the Western Mediterranean held in Erice, Italy, in October 1979, the Meeting on the Coordination of Antimalaria Activities in South-East Europe in Sofia, Bulgaria, in March 1980 and the Conference on the Role and Participation of European Countries in the Fight against Malaria in the World in Cagliari, Italy, in October 1980).

Delegations from the following 11 Mediterranean countries took part in the Meeting: Bulgaria, France, Greece, Italy, Morocco, Portugal, Spain, Syrian Arab Republic, Tunisia, Turkey and Yugoslavia. They included staff of ministries of health, officials responsible for the control of malaria and other communicable diseases, and experts from university teaching bodies in the fields of tropical parasitology, virology research and manpower training. There was a temporary adviser, who acted as Rapporteur, staff from WHO headquarters and the Regional Office for Europe, and several officials of the Spanish Ministry of Health and Consumer Affairs, who took part as observers.

The participants were welcomed by Dr M. Sequi, Director of Health and Consumer Affairs, Mahon, Dr Fernandez Nafrio, Director-General of Public Health and Consumer Affairs, Spain and Dr Mario de la Mata, Assistant Director-General of International Relations, Spain. Dr E. Lepariski, Director, Disease Prevention and Control, WHO Regional Office for Europe, greeted the authorities on behalf of Dr Leo A. Kaprio, WHO Regional Director for Europe, and Dr H. Mahler, WHO Director-General. He expressed warm thanks to the Spanish Government for its hospitality and generosity in hosting this Meeting. Dr Lepariski added that although, with regard to infectious diseases, a steady epidemiological situation existed in the Mediterranean area, importation and subsequent flareups could occur because of increasing population movement. It is important, therefore, that countries should establish multidisciplinary and multisectoral action, through the implementation of the primary health care policy, to help maintain a state of constant preparedness.

Dr F. Maroto was elected Chairman, Professor L. Dardanoni and Dr Z. Khawam Vice-Chairmen, and Dr S. Litvinjenko Rapporteur.

2. Scope and purpose

Although malaria has been eradicated from many countries and transmission brought to a low level in others, there are still countries in the Mediterranean area with a considerable level of transmission.

The tendency for malaria to be reimported into nonendemic countries is the consequence of the unprecedented increase in population movements, caused by tourism, labour migration and trade. This, together with the appearance of *Plasmodium falciparum* strains resistant to chloroquine, is a constant threat, which must be met by a sufficient level of monitoring and adequate facilities to check outbreaks of malaria if they occur.

The scope of the Meeting was enlarged to include haemorrhagic fevers and leishmaniases, as well as malaria.

Following the recent recognition of clinically serious haemorrhagic fevers, such as lassa fever, Marburg disease, Ebola fever and Rift Valley fever, and particularly as some of them (Lassa, Marburg) have already been imported in several instances into Europe, there is a need to determine what national and international efforts are necessary to minimize the risks they represent.

In recent years, leishmaniases have shown an increase in several Mediterranean countries. There have also been well documented cases imported into nonendemic European countries, suggesting that the transmission problem is more serious than was previously assumed. A considerable part of the data available on leishmaniases come from papers in the medical press and are therefore often too old to serve any surveillance purposes.

The participants of the meeting analysed the following topics.

(1) Malaria:

- the internal and external reporting of cases;
- the management of imported cases;
- the implementation of recommendations from earlier malaria coordination meetings.

(2) Hsemorrhagic fevers:

- the present status of information regarding their occurrence and their importance for public health;
- their epidemiology;
- the laboratory and clinical problems involved in their containment.

(3) Leishmaniasis:

- the present status of information regarding their occurrence;
- their epidemiology.

(4) Training, research and international coordination with regard to the above questions.

(5) Other administrative and technical (entomological) topics related to the above topics.

3. Malaria

3.1 The present situation in Mediterranean countries

Among the participating Mediterranean countries, indigenous cases of malaria exist only in Algeria, Morocco, Syria and Turkey where malaria transmission still occurs in some places. Table 1 shows an almost twofold increase of malaria cases in Turkey in the period from 1979 to 1981 and a considerable increase of cases in the Syrian Arab Republic in 1980 and 1981. This calls for the special attention of all Mediterranean and European countries that have good trade and tourist connections with near and middle eastern countries.

On the other hand, those countries that are free of transmission also import a considerable number of cases from distant countries with which they have close connections. In some cases, according to reports presented to the Meeting, imported cases from these distant countries constitute the only registered cases of malaria, and in others, a great majority of them.

In the period from 1979 to 1981, induced cases were notified only in Bulgaria (2 cases), Yugoslavia (5) and Greece (29).

In the discussion on the scope of control measures, the suggestion was accepted of making serological surveys in those localities where the donors of blood to induced cases live in order to prevent the potential spread of transmission.

An unusual epidemic of malaria tropica (*P. falciparum*) in a group of 23 refugees in Italy, caused by the use of syringes should be added to the group of induced cases. The parasite was chloroquine-resistant, and one patient died.

Table 1. Malaria - Reported cases in Mediterranean countries 1979-1981

Country	1979	1980	1981
Bulgaria	101	128	472
France	25	94	80
Greece	44	53	64
Italy	105	176	143
Morocco	397	367	98
Portugal	45	25	27
Spain	47	90	59
Syrian Arab Republic	2 544	1 460	1 828
Tunisia	9	7	1
Turkey	29 324	34 154	54 415
Yugoslavia	59	83	53

Relapses were registered primarily in countries where transmission still exists, but individual cases were reported from Bulgaria, Portugal and Yugoslavia.

3.2 Classification of cases by species of parasites and by profession

In countries where transmission still exists it is almost exclusively P. vivax that has been detected. The few existing cases of P. falciparum were imported. In the transmission-free countries, the ratio between P. vivax and P. falciparum varies from one year to another depending on the proportion of cases coming from different infected areas. In the majority of countries, the imported P. falciparum cases come from Africa south of the Sahara and from south-east Asia, and the P. vivax cases from the Asian countries infested with this species.

As for grouping the imported cases by the profession of the sufferer, the predominance differs from country to country. Therefore it is rather difficult to determine which types of professions or groups predominate in the importation of malaria into nonendemic countries. It depends, in the individual country, on a number of factors such as the degree of development of international tourism, the actual number of workers and professionals temporarily employed in infected areas, the number of students, workers, refugees, or immigrants coming from endemic countries and the number and frequency of aerial, maritime and surface connections and routes that come into contact with endemic areas.

For instance, in some countries, national or foreign tourist groups predominate, while in other areas, the highest number of imported cases occurs among immigrants, while in others again, professionals, workers, or sailors represent the most frequent group. However, as mentioned above, the contribution of individual groups also varies from one year to another within the same country.

As an example of the way malaria can spread even within Mediterranean countries themselves, the increase of imported malaria cases among truck drivers travelling from Yugoslavia or Bulgaria, for instance, through Turkey to the Middle East was mentioned. Among Yugoslav citizens, truck drivers constituted one third of all imported malaria cases in 1981. In the same year, 66 malaria cases imported from Turkey were registered in Bulgaria.

The increased opportunities for malaria to spread are illustrated by the fact that the amount of air travel between African and Asian countries and Europe increases by 250% every year. The importance of the malaria risk should therefore not be underestimated.

3.3 Legislation

The compulsory notification of malaria cases has been introduced in almost all the participating countries. In most of them, microscopic confirmation is a prerequisite for diagnosis and notification.

Some of the transmission-free countries have regulations about chemoprophylaxis for all citizens travelling to endemic areas, and a follow-up of these persons for two or three years after their return. Such regulations are also applied to incoming foreigners (such as students and temporary workers), and to immigrants, but not to transit passengers, tourists and diplomats.

In Bulgaria the frontier medical service notifies the Department of Parasitology within the Hygienic-Epidemiological Inspectorate by telex of all the arrivals of nationals from endemic countries (and foreigners who intend to stay for a long time). This department establishes a control file and immediately transmits a message to the primary health care service where the passenger lives. This service, in turn, establishes a control card, takes some blood for examination and places the person under surveillance for three years. Some countries carry out a compulsory epidemiological investigation in each case of malaria and impose compulsory hospitalization for treatment.

3.4 Control measures and surveillance

Specific activities such as residual spraying, space spraying, larvicide (and other antilarval activities), active and passive case detection, mass blood surveys, mass chemoprophylaxis, presumptive treatment and epidemiological assessments are performed to different extents in countries where malaria transmission still occurs.

The application of such measures in Turkey and the Syrian Arab Republic, however, has faced a number of difficulties of a technical, administrative or human character including the increasing cost of insecticides, equipment, vehicles and fuel, a lack of manpower during the spraying season caused for example by unsatisfactory wage levels in relation to the increased cost of living, a lack of proper supervision (for the same reasons), the hostility of the workers or of the population to the application of indoor residual spraying, delays in laboratory examination of blood slides, and gaps in the reporting of cases. The consequence of all this has been the worrying increase of malaria cases in these countries.

Some specific problems were also mentioned. Several participants stressed that there is not always good cooperation between malaria centres and public health centres or dispensaries and other public bodies. They pointed out the need for people working with malaria to have a more important role in the development of primary health care. In transmission-free countries such as France, Greece, Morocco and Tunisia, biological (antilarvae) control of mosquito density is maintained in some places by use of Gambusia affinis.

Systematic spraying is used in some transmission-free countries to reduce the malaria risk in places that are especially exposed, like main traffic routes, camping places (in Bulgaria, for instance), and in places where imported cases have been found. In addition to this, spraying is also used in the control of pests (e.g. Culex and Aedes).

After a discussion of the changing state of receptivity in different areas of the participating countries (such as the disappearance of A. labrancheae from south-east Spain and its comeback to Toscana, in Italy), it was agreed that the presence of different vectors, as well as the level of their susceptibility to insecticides (both as adults and as larvae) should continue to be monitored, while it would seem unrealistic to maintain a more complicated level of monitoring (vector density, etc.).

One very important problem related to the prevention of malaria resurgence is the lack of knowledge of the real number of (imported) malaria cases in some of the transmission-free countries. This is largely due to difficulties encountered by some practitioners in the clinical recognition of the disease mostly because they are unaware of the possibility of the reappearance of malaria in areas from which it has disappeared, and to the gradual fading of knowledge and experience in the techniques and recognition of malaria parasites in the blood, caused by long periods in which the laboratory diagnosis of malaria has not been performed.

While the health authorities are not notified of all cases of malaria it is impossible to know the real epidemiological situation in several countries.

As a special problem, it was mentioned that in some countries, especially where decentralization of the health services exists, malaria control tends to receive only little and irregular attention.

Following previous recommendations, a national centre for malaria was established, by the end of 1980, in Greece, Italy and Yugoslavia. Its purpose was to check all positive slides, to proceed and assist in epidemiological investigations, to conduct regular entomological activities, to prepare instructions on the prevention of importation and on control, to organize refresher courses in the epidemiology, diagnosis, treatment and prevention of malaria, as well as to maintain an awareness of the danger of malaria in the general population through health education. In Bulgaria, the Department of Parasitology of the national Hygienic-Epidemiological Inspectorate constitutes the national centre, and in Algeria, Morocco, Syria and Turkey, the directorates of the antimalaria services have this function.

The Meeting felt that the governments should ensure that sufficient and adequate information was made available to local health authorities, transport companies, travel agencies and vaccination centres about the risk of malaria and other tropical diseases to travellers.

This information should be prepared by a competent institution (such as the ministry of health, institute of public health, etc., or with their agreement) in order to prevent its misuse by public information media. Leaflets with information on the risk of malaria and preventive measures for international passengers, may be considered a valuable support to the health education of the public.

3.5 External reporting

It was repeatedly stressed that the registered number of malaria cases does not reflect the real situation everywhere. Differences also often exist between the official figures forwarded to WHO, the figures given at congresses and the figures presented in newspapers or published in other ways. These difficulties arose even during the preparation of this report. Which figures should be used? Those from official reports to WHO, or those submitted to the Meeting?

It was agreed that all countries in which clearly confirmed, (documented) imported cases of P. falciparum resistant malaria were found, (or any other imported cases of malaria that, according to the case history, had been transmitted in areas where, according to present knowledge, no such transmission occurs), should immediately, preferably by cable, inform WHO, which should in turn inform the exporting country concerned.

3.6 Entomological activities and observations

The relatively limited likelihood of the reintroduction of transmission of P. falciparum into the European continent raised lively discussion among the participants. P.G. Shute^a found that English specimens of A. atroparvus were completely refractory to infection with strains of P. falciparum from India and West Africa, but could be easily infected with strains from Italy and of Romanian origin. Dr J. de Zulueta et al.^b showed that the Italian A. atroparvus is refractory to P. falciparum from Kenya and northern Nigeria (the latter being demonstrated only by a small-scale experiment). Recent work carried out in the Soviet Union by N.G. Dashkova^c has confirmed the refractoriness of A. atroparvus to exotic strains of P. falciparum. The results of this work also show that three other important European vectors, A. messeae, A. typicus and A. sacharovi, are refractory to P. falciparum from tropical Africa.

Taking into account the findings mentioned, as well as greatly modified ecological, social and economic conditions in Europe, one may presume that the risk of re-establishment of P. falciparum transmission in the Mediterranean countries of Europe is limited. This was seen in Portugal after the loss of the colonies and the influx of a great number of P. falciparum cases without any reintroduction of transmission.

In the discussion it was pointed out that despite the above negative results of infecting some vectors with P. falciparum from some places, it cannot be excluded that P. falciparum from other places might be transmitted by some European anophelines, especially perhaps the P. falciparum from nearby countries like those of the Middle East. The possibility of genetic changes should also not be overlooked.

The risk of reintroduction of P. vivax is undoubtedly greater, as there is no known refractoriness to this species among the European vectors. But, due to the changes in human lifestyles mentioned above, one would expect a return in force of malaria transmission to Europe to be possible only in the event of war or some major political and social upheaval. There is however a need for constant vigilance to prevent the occasional transmission of malaria and to ensure that the potentially lethal P. falciparum is detected and correctly treated in time.

Tests of the susceptibility of Anopheles to insecticides are performed as a routine in most Mediterranean countries. It was observed, however, that not all the tests comply with WHO recommendations, so that they are not comparable. Besides this, the reports do not always reach the Vector and Biology Division in WHO headquarters in Geneva, a fact which hampers coordination in this field.

Generally the susceptibility of Anopheles to malathion and fenitrothion is almost entirely intact with the exception of a moderate or probable resistance to malathion in Spain. The results of susceptibility tests given in the papers presented point to a complete or high resistance to DDT, Dieldrin and Propoxur.

3.7 Training

In all participating countries, malaria is included, to a greater or lesser extent, in the normal curricula of medical studies at universities and in medical schools at the lower levels. Special training and refresher courses, national and/or international (e.g. in Bulgaria and Yugoslavia), exist in the majority of participating countries. In the countries with transmission, special training and inservice training goes on continuously.

In Greece, national courses in epidemiology, clinical and laboratory diagnosis, treatment and prevention are held regularly for clinicians (doctors), sanitary inspectors, microscopists, rural doctors, visiting nurses, and so on.

In Italy, following the recommendations of the meetings held in Erice, in 1979 and in Cagliari, in 1980, a training course on malaria and other tropical diseases was organized in

^a Shute, P.G. Failure to infect English specimens of Anopheles maculipennis var. Atroparvus with certain strains of Plasmodium falciparum of tropical origin. Journal of tropical medicine and hygiene, 43: 175-178 (1940).

^b Zulueta, J. de et al. Receptivity to malaria in Europe. Bulletin of the World Health Organization, 52: 109-111 (1975).

^c Dashkova, N.G. [New data on susceptibility of Anopheles mosquitoes of the USSR fauna to imported strains of the causative agents of human malaria]. Medskaya Parazit, 46: 652 (1977).

1982 and cosponsored by WHO. The theoretical part of the course was held in Italy and the practical part in Turkey with support from the respective governments. Sixteen participants, coming from 12 countries of Africa, Asia and Europe followed the course which lasted for 12 weeks. A second course is being planned.

National courses on malaria were also held in Italy in 1979 and 1981 (both of one week's duration) for medical doctors and biologists.

3.8 International cooperation

The need for the exchange of knowledge, experience, manpower and equipment among Mediterranean countries has been repeatedly expressed. Examples in recent years have fully proved that it is feasible. For instance, after the epidemic of malaria in Turkey, pumps, insecticides, vehicles, and funds were contributed from other countries. Tunisia, having just finished its own eradication programme, has lent its pumps to Algeria. The multilevel planned hispano-Moroccan cooperation is also worth mentioning.

4. Haemorrhagic fevers

Knowledge of the etiology of haemorrhagic fevers may be summarized as follows.

4.1 Implicated viruses and the diseases they cause

<u>Virus</u>	<u>Disease</u>
<u>Arenaviridae</u>	Lassa fever American haemorrhagic fevers Argentina: <u>Junin</u> Bolivia: <u>Machupo</u> Brazil: <u>Amapari</u> Colombia: <u>Pichinde</u> Paraguay: <u>Parana</u> Florida: <u>Tamiami</u> Trinidad: <u>Tacaribe</u>
<u>Bunyaviridae</u>	Crimean-Congo haemorrhagic fever Rift Valley fever
<u>Togaviridae</u> Group B arboviruses (Flavivirus)	Yellow fever Dengue Omsk Kyasanur Forest
<u>Ungrouped</u>	Marburg Ebola Korean

4.2 Geographical distribution

The natural geographic distribution of the diseases caused by class 4 viruses, and confirmed by the isolation of the virus, is the following.^a

Russian spring-summer encephalitis virus:	USSR
Kyasanur Forest disease virus:	India (Mysore state)
Omsk haemorrhagic fever virus:	USSR (Siberia)
Crimean-Congo haemorrhagic fever virus:	Asia, USSR, Bulgaria, south-east Asia (Pakistan, Iraq) west Africa (Senegal), central Africa (Uganda, Zaire, Central African Empire), east Africa (Kenya, Ethiopia)

^a Van der Groen, G. & Trexler, P.C. A look at the P4 virus containment laboratory. In: Progress in medical virology. Basle, Karger, 1982, vol. 28.

Marburg virus:	Federal Republic of Germany, Yugoslavia (laboratory accidents), South Africa (Johannesburg), Zimbabwe, Kenya (Nairobi)
Ebola virus:	northern Zaire (Yambuku area), north-western Zaire, (Tandala-Gemena area), southern Sudan (Nzara-Maridi district)
Junin virus:	Argentina (Buenos Aires)
Machupo virus:	Bolivia (Beni region)
Lassa virus:	west Africa (Nigeria, Liberia, Sierra Leone)
Korean haemorrhagic fever virus:	USSR, Czechoslovakia, Yugoslavia, Japan, Korea

4.3 Transmission

The method of transmission is seen from Tables 2 and 3 below.^a In the case of the Rift Valley fever, the possible vectors are numerous.

The animal reservoirs consist of for example, rodents (Lassa, Crimean-Congo), monkeys (Marburg), domestic animals like cattle and horses (Rift Valley, Crimean-Congo) but both with regard to animal reservoirs and vectors (or vehicles) of transmission the existing knowledge is far from complete.

Since there are also many unclear points about the contagiousness, pathogenicity and lethality of the disease in man, a series of studies are needed, particularly serological surveys both in the endemic areas and among contacts in nonendemic countries, to further the understanding of the epidemiological characteristics of the different haemorrhagic fevers. Also to further the education of the public, it is important to obtain more knowledge about the considerable number of symptomless or very light cases.

The participants felt that WHO had an important role both in the promotion of research activities and the dissemination of knowledge about the diseases and their occurrence. They also felt that periodical publication of updated knowledge (including information on the suppliers of equipment) was needed. In spite of the gaps in our knowledge about transmission, it was recommended that, in the case of transmission from man to man, a patient must be considered as contagious from the day of onset of the symptoms and it was suggested that the virus may continue to be excreted long after clinical recovery, e.g. 6 weeks or more in the urine (Lassa). The Marburg and Ebola viruses have been detected in the seminal fluid and in the anterior chamber of the eye of three convalescent patients up to two or three months after the onset of the illness. One case of sexually transmitted Marburg fever took place 80 days after onset.

The above must be taken into consideration when addressing the period of isolation required, especially when laboratory tests cannot be performed.

4.4 Pathology

The lesions caused by Rift Valley fever are nearly always much less extensive and severe than those of the other diseases, whose lesions may be seen in almost every organ, particularly the liver and spleen. Severe degeneration of lymphoid tissue, spleen and liver may result in accumulations of cellular and nuclear debris. Hyaline changes are frequently seen in the liver. Mononuclear transformation of lymphoid tissue, as well as necrotic lesions are seen not only in the liver and spleen but also in the pancreas, gonads, adrenals, hypophysis, thyroid, kidneys and skin. No lymphocytic reaction has been seen in the brain, where the pathological changes are confined mainly to the glial tissue. Rift Valley fever lesions are mostly limited to the liver with central necrosis.

4.5 Clinical features

The incubation time may vary from 3 to 16 days with an average of about one week (Rift Valley fever usually has a shorter incubation period, of 3 to 6 days). As already mentioned, there are

^a Bres, P. Models for action in major causes of epidemics; viral diseases. Geneva, World Health Organization, 1981 (unpublished document CDS/MTG/MOD/81.4).

Table 2. Method of transmission of haemorrhagic fevers

Virus	Source	Route of transmission	Spread of epidemic
<u>(a) Mosquito-borne</u>			
Yellow fever	Animal, infected persons	Indirect (mosquito bite)	Fast, limited to areas of dispersion of vector mosquitos
Dengue	Infected persons	Indirect (mosquito bite)	
Rift Valley fever	Animal, infected persons	Indirect (mosquito bite)	
<u>(b) Tick-borne</u>			
Crimean-Congo	Animal, infected persons	Direct and indirect	Slow, limited to areas of dispersion of vector ticks
Omsk	Animal	Indirect (tick bite)	
Kyasanur Forest	Animal	Indirect (tick bite)	
<u>(c) Rodent-borne</u>			
Lassa (Africa)	Animal, infected persons	Direct and indirect	Progressive, limited to areas of infected rats
Junin (Argentina)	Animal	Direct and indirect	
Machupo (Bolivia)	Animal	Direct and indirect	
Hantaan ^a	Animal	Direct and indirect	
<u>d) Unknown</u>			
Marburg and Ebola	Infected persons, unknown animal reservoir	All routes seem possible	Slow from animal or fast from man

^a Arthropods included were implicated as vectors or reservoirs by virus isolation from field collections, demonstration of laboratory transmission, and/or laboratory infection.

great variations in the severity of the disease. It starts by a period of fever (up to 39-40°C) accompanied by (great) weakness, (severe) malaise and headache, pharyngitis and general pains, sometimes most marked in the lumbar region. Vomiting and severe diarrhoea are very often present. After three or more days, jaundice and haemorrhagic symptoms may appear with petechial rashes, nasal, vaginal and/or conjunctival haemorrhages, haematemesis, melaena and pleural effusions. The patients may develop cachexia and dehydration, and may show signs of severe central nervous system involvement (paraesthesia, lethargy, confusion, instability, stupor, aggression, and signs of meningeal irritation). Other complications may be seen as well.

4.6 Serological diagnosis

The conversion from negative to positive in paired serum samples in a fluorescent antibody test is the most reliable serological test. Complement fixation tests have been much less reliable, and no satisfactory neutralization test has yet been devised for these viruses. Reverse passive haemagglutination test (RPHA), enzyme-linked immunosorbent assay (ELISA) and thin-layer immunoassay (TIA) tests are promising.

Generally it is not feasible to establish viral diagnostic facilities under field conditions at the site of the outbreak, but fluorescent antibody tests were successfully carried out during the Zaire outbreak.

Table 3. Arthropods implicated as Rift Valley fever virus vectors or reservoirs

Diptera (mosquitoes)

<u>Aedes</u>	A. dentatus, A. tarsalis, A. circumulveolus, A. lineatopennis, A. caballus, A. juppi, A. triseriatus, A. aegypti, A. africanus, A. dendrophilus
<u>Anopheles</u>	A. coustani
<u>Coquilletidia</u>	C. fuscopennata, C. microannulata, C. versicolor
<u>Culex</u>	C. neavai, C. theileri, C. univittatus, C. zombaensis, C. pipiens
<u>Eretmapodites</u>	E. chrysogaster, E. quinquevittatus
<u>Mansonia</u>	M. africana, M. uniformis

Diptera (biting midges and blackflies)

Culicoides spp.

Simulium spp.

Acarina (ticks)

Rhipicephalus appendiculatus

4.7 Virological diagnosis

Positive diagnosis by virus isolation generally takes a minimum of 5 to 7 days. Inoculation of acute samples into Vero cell cultures and intraperitoneal inoculation into guinea-pigs are the most useful methods.

Rift Valley fever may produce four syndromes: (1) influenza-like cases without any complications; (2) encephalitis; (3) retinitis; and (4) haemorrhagic fever. Generally the clinical course of this disease is much less severe than that of the manifest cases of the other haemorrhagic fevers. The symptoms of haemorrhagic fevers may resemble closely those of influenza, malaria and typhoid fever and WHO has recommended that any patient with continual fever and abnormal haemorrhages should be considered as possibly affected by haemorrhagic fevers.

Once the likelihood of such a disease has been raised, the following emergency measures for the control of communicable or unusual diseases should be taken (although admittedly more knowledge is needed about the contagiousness):

- patient isolation
- personnel protection
- isolated patient care
- patient transportation
- specimen collection and shipment
- decontamination or disposal of contaminated items
- laboratory
- insect and animal (rodent) control
- autopsy
- burial
- legal considerations

The patients should be isolated in special units. An epidemiological questionnaire should be prepared to find out about recent trips, general habits and people with whom they have been in contact during the last few weeks.

Potential patients and other recent direct contacts should be isolated and kept under strict observation.

Public health authorities should be informed at once about any suspected cases.

Personnel attending the cases should follow strict norms of asepsis using gloves, masks and special clothes at all times and disposable articles wherever possible.

All elements that have been in contact with the patient should be treated according to the norms established in each case.

The vehicles used to transport the cases to special isolation centres, should be specially treated and conditioned. The routes to be taken should be carefully chosen.

Great care should be taken to protect the specialized personnel who transport the cases and they in turn must assure the disinfection and sterilization of the vehicle used for transportation of the cases.

The collection, transportation and handling of the samples to be studied can be dangerous. They must be clearly marked with labels or other appropriate systems. From the patient's bedside to the laboratory, perfect coordination is necessary to assure a quick, correct and trouble free delivery of the samples and efficient reception of them for immediate study. During transportation these samples may fall into the hands of the inexpert (post office personnel, porters, etc.), so the samples should be clearly marked and carefully transported.

Laboratories responsible for studying the samples should provide high security measures for the handling of this material.

The control of insects and vectors should be carried out by specialized personnel particularly in suspected areas while the epidemic lasts.

An autopsy, because of the great risk of contagion, is not recommended. Should personnel have to carry out an autopsy, they should be appropriately vaccinated and protected to avoid any infection.

4.8 Clinical management of cases

Globulin and convalescence serum is used as a specific treatment. Bedrest, with the recording of all vital functions, administration of sedatives without hypotensive effects, lowering of the body temperature by antipyretics or physical means, treatment of headache and myalgiae are the general supportive measures to be applied. Oral intake of food or drugs should be avoided as nausea and/or vomiting are very frequent symptoms. Antiemetics may be required. It is essential to supervise and maintain the fluid balance carefully. The treatment used on haemorrhages must also be selected carefully. In some cases a tendency towards disseminated intravascular coagulation has been observed. Monitoring of the coagulation factors should take place. Transfusion of fresh platelet concentrates or fresh blood, fibrinogen, vitamin K and amino caproic acid have been used to treat the tendency to bleed and heparin has been given as a prophylactic to prevent coagulation (this should only be done after careful monitoring of the coagulation factors). Finally, specific complications must be treated in accordance with the individual needs.

4.9 Prognosis

Mortality may be 10% to 50% among Arenavirus cases, while in many hospital patients with Marburg fever, 30% mortality has been observed. In Crimean Congo fever, 10% mortality is reported. In outbreaks of Ebola fever, there is a high mortality though there are no exact figures. However, it should be remembered that much information is still lacking about symptomless and mild cases. Rift Valley fever outbreaks show a lower mortality of about 0.3%. Death usually occurs after large haemorrhages and shock, one to two weeks after onset of the disease. If recovery occurs, a slow return to normal starts to take place after the end of the acute febrile phase, about two weeks after onset. Periodic headaches, chest pains, abdominal cramps, fatigue, cachexia, anorexia and stooping gait continue for three to four weeks, and some patients have suffered prolonged psychotic disturbances.

In Rift Valley fever, the course of the disease is usually, as mentioned above, less severe. After two to four days the temperature usually returns to normal. Then a second febrile period of two to three days may follow, after which there is usually a rapid recovery. Outbreaks of Rift Valley fever may include many persons, as it did in the outbreak in Egypt in 1977 and 1978 when the disease appeared for the first time north of the Sahara and caused 200 000 cases (with about 800 deaths). The same was seen in Cuba in 1981 when Dengue II haemorrhagic fever produced 300 000 cases and 150 deaths.

Since the haemorrhagic fevers manifest themselves in a very dramatic way, with high mortality or great epidemics, they are bound to cause severe upheavals in society, especially when it is unprepared for them.

A discussion of the problems of maximum containment regarding laboratory, ward, disposal, and manpower focused on three main points: (1) the need to collect information concerning contagiousness, pathogenicity, and virulence, as soon as possible; (2) mobile containment units versus fixed units; and (3) training and duties for the emergency team during periods when there are no cases of haemorrhagic fevers.

Trials on mobile units and fixed units are taking place. For economic reasons, the units will not be used only for haemorrhagic fevers. For this reason, as well as to avoid alarm among the public, it was felt that countries should determine:

- (1) possible and probable agents that produce emergencies in the country;
- (2) diseases that if introduced, can cause alarm;
- (3) a plan of transportation of prepared units at home or abroad with help from WHO;
- (4) the preparation of nursing, medical and laboratory staff to diagnose and look after these patients; and
- (5) connection with WHO to obtain urgently diagnostic, therapeutic or preventive elements (sera, vaccines, etc.) and if necessary, experts to help cope with the problem.

A Rift Valley fever formalin-inactivated vaccine is available for persons exposed to a high risk of infection, such as veterinarians, butchers, herdsmen and laboratory workers. However, this vaccine is expensive and there are no readily available stocks of it. It may be obtained from the US Army Medical Research Institute of Infectious Diseases or from the Virus Disease Unit, WHO headquarters in Geneva. Live attenuated vaccines may become available at low cost in the future through genetic molecular techniques.

5. Leishmaniasis

5.1 General

It can be concluded from reports presented to the Meeting that both visceral leishmaniasis (VL) and cutaneous leishmaniasis (CL) exist to a greater or lesser extent in the whole Mediterranean region. Given that the data on incidence originate from different sources (official data, hospitals, surveys, articles) and do not always refer to the same periods, it is not possible at present to make a reliable comparison of the size of the problem in the participating countries. It was generally agreed that the numbers presented constituted only a general part of the real incidence.

The number of reported cases usually refers to hospitalized patients. A large number of cryptic infections, both VL and CL, are probably always present in leishmaniasis foci. Thus, the number of reported human cases is not an adequate tool for evaluating the importance of leishmaniasis foci, especially not those of VL. Serological surveys are needed to answer such questions and more knowledge about the pathogenicity and virulence of leishmaniasis is needed.

5.2 The epidemiological situation in participating countries

In Bulgaria, the disease became very rare after the reduction of the number of dogs and only VL is found. During the last 30 years, a total of about 70 cases have been notified (though reporting is not compulsory).

In France, in the period from 1970 to 1980, 159 cases of VL were registered in two foci, on the eastern and western side of the lower part of the Rhone. In a third focus, on the island of

Corsica, there were two to three cases a year. Two foci of CL exist, one in the Pyrénées orientales and another one in Cévennes in the Languedoc with one to two cases a year. In 1981, in Nice, 12 cases of VL were reported, but otherwise VL and CL are only found very rarely and sporadically outside the mentioned foci (reporting is not compulsory).

In Greece, in the period from 1979 to 1981 around Athens, in Attica, the Ionian islands and in some other areas, a total of 153 VL and 15 CL were registered (most of them in Attica). The majority of cases were registered in 1981. There is no compulsory notification.

In Italy, from 1956 to 1976, a total of 306 VL and 459 CL cases were reported. Most CL cases originated in regions on the Adriatic side of the Appenines and in Calabria and most VL cases in the southern insular regions, except in the Emilia-Romagna region where an outbreak occurred in 1971 and 1972. Notification is compulsory but is considered to be incomplete.

In Morocco, the disease was considered rare until 1975, when great foci of LC were discovered in the south of the country. Now it is known that although VL is only found sporadically in the semi-desert area north of the Atlas mountains, CL is widespread in the south. From 1975 onwards, 1230 cases of CL were registered in the focus of Alnif. In 1981, two new foci were detected: one in the province of Tata with 2659 cases (around 10% of the population) and another in the province of Quarzazate with 797 cases (2.8 % of the population).

In Portugal, there are foci in the north where 1134 cases were found from 1960 to 1976. In 1981 a total of 46 VL and 6 CL were notified. Reporting is considered to be reasonably good.

In Syria, CL exists in the semi-desert areas, there being about 500 cases a year although reporting is incomplete). No VL has been seen for many years.

The number of detected leishmaniases cases of both forms (CL and VL) in Tunisia is gradually increasing. VL and CL are considered endemic, and in the period from 1978 to 1981, a total of 95 cases (not specified) were detected, most of them in 1980 when an epidemic in the region of Medenine was reported (29 cases).

In Turkey about 300 cases of VL were reported by different investigations in the period from 1939 to 1964. A. Corradetti, during his visit to Turkey in 1964 and 1965, reported 16 cases of kala-azar (VL) (unpublished data). Most of the cases were on the Marmara, Aegean and Mediterranean sea coasts as well as in the eastern part of the Black Sea region. Few cases were observed in central Anatolia. The number of CL patients treated in the Clinic of Dermatology in Ankara in the period from 1945 to 1965 amounted to 453. In 1981, a resurgence of the disease was observed, and between 500 and 600 cases were reported from the eastern and south-eastern part of the country.

An increase in the incidence of leishmaniases, especially CL, has been observed in Spain since the 1960s. According to surveys carried out in dermatological clinics and hospitals in the country from 1976 to 1978, a total of 256 CL and 17 VL cases were diagnosed. The majority of cases, of both forms, were detected in the Mediterranean provinces of Alicante and Murcia.

In Yugoslavia, two zones of VL and CL exist: a coastal and a continental one. In the coastal Mediterranean zone, both forms used to be endemo-epidemic in the past. In this zone, the total number of VL cases was 773 in the period from 1930 to 1980, and that of CL was 210 in the period from 1945 to 1957. In the continental zone in the period from 1940 to 1980, there were altogether 1349 cases of VL reported, as well as under a hundred of CL. In the period from 1976 to 1980 in the whole of Yugoslavia (where there is no compulsory notification), a total of only 11 cases of VL was registered. It is considered that residual spraying carried out during the malaria eradication campaign probably eradicated the human parasitic reservoir.

5.3 Reservoir

The dog is considered to be the principal reservoir of *Leishmania* parasites in most Mediterranean countries. At the beginning of this century, the prevalence of canine leishmaniases in the southern regions of Italy was as high as 80%. Still in 1981, S. Mansueto et al. (unpublished data) found canine leishmaniases in 37% of dogs examined in some parts of Sicily. E. Pozio et al.^a found a prevalence of 24% in the period from 1979 to 1980 in Tuscany, in the

^a Pozio, E. et al. *Acta Tropica*, 38: 383-393 (1981).

Grosseto province. S. Bettini et al.^a also found, in the same region, that the black rat (Rattus rattus) and the fox (Vulpes vulpes) were naturally infected.

In Morocco, wild rodents constitute the main reservoir.

In Tunisia, it has been found that the geographical distribution of CL follows that of phlebotomid flies and rodents. Among rodents, the Gerbillus pyramidum, Meriones shawi and Jaculus orientalis are considered as most receptive.

In a survey carried out on a population of 40 000 dogs in Spain, the infestation with Leishmania parasites was found to amount to between 1.7% and 7.8%.

The animal reservoir in Syria is unknown but both dogs and wild rodents are suspected.

In Turkey, dogs have been found to be naturally infected.

5.4 Vectors

The participants acknowledged the high value of the efforts laid down in a WHO paper on leishmaniases vectors/reservoirs^b, to which reference is made regarding details about the vectors.

Phlebotomus perniciosus are the sandflies which are most widely incriminated as (suspected) vectors of VL and Phlebotomus papatasi as vectors of CL.

Regarding suspected and confirmed vectors in the individual participating countries, the following information is available.

In Bulgaria, the suspected vectors are P. major and P. sergenti.

In France P. ariasi is the main vector up to 1400 metres above sea level and P. perniciosus occurs up to an altitude of 650 metres.

In Greece, the main vector is believed to be P. major, but P. sergenti, P. alexandri, and perhaps other vectors occur too.

In Italy, the suspected vectors of leishmaniases are P. perniciosus, P. perfiliewi and P. papatasi. Final determination of the vectors awaits confirmation from a series of investigations.

In Morocco, according to investigations performed in 1972, 17 species of sandflies were found, among which the most frequent were P. papatasi (26%), P. alexandri (24%), S. falax (16%) and P. sergenti (8%).

In Syria, the suspected vectors are P. sergenti and P. papatasi.

In Tunisia, the transmission of CL is attributed in the south to P. papatasi, P. sergenti and P. alexandri, and in the north to P. perfiliewi, P. sergenti and P. papatasi.

In Turkey it is believed that P. perniciosus is the main vector of leishmaniases, owing to its habits and wide distribution. The other very common sandfly species are P. major, S. dentata, S. dentata dentata, S. pawlowsky and S. theodori. P. papatasi is very rare in Turkey.

In Spain, the following are mentioned as possible vectors of Leishmania parasites: P. papatasi, P. sergenti, P. alexandri, P. perniciosus, P. ariasi, P. longicuspis and S. minuta.

In the regions of Yugoslavia where the cases of VL and CL were detected, the sandfly species that have been found most often are P. major, P. tobbi, P. perniciosus and P. chinensis var. simichi.

In summary, it may be said that the picture regarding the vectors in the Mediterranean countries is not entirely clear. This problem is one of many that need solving before a complete understanding of the epidemiology can be obtained.

^a Bettini, S. et al. Transactions of the Royal Society of Tropical Medicine and Hygiene⁹ 74: 77-83 (1980).

^b Zshar, A.R., Studies on leishmaniasis vectors/reservoirs and their control in the old world. Geneva, World Health Organization, 1979 (unpublished document WHO/VBC/79.749).

5.5 Control measures

The present increase of the disease must be attributed mainly to very rapid urbanization and to the increased number of dogs, but the reduction of indoor spraying and the increased tendency of outdoor camping are other contributing factors.

In some countries the only tool so far used for the control of leishmaniasis has been the reduction of the dog population. However, the positive experiences from antimalarial campaigns and the observation that the foci of leishmaniasis are not situated in zones where spraying aimed at pest control is performed, suggest that measures taken against the vector could also be a useful way of controlling leishmaniasis. A word of warning against the reduction of the dog population must be mentioned in places where insufficient wild animals exist on which the vector will voluntarily feed.

In areas of high incidence, integrated efforts to control the disease would seem the best solution, with provision of diagnostic facilities, and treatment, and appropriate measures against phlebotomid flies and mammalian reservoir hosts.

5.6 Research

Immunological surveys of schoolchildren are being carried out to determine the most appropriate control measures in the focus of the Pyrénées orientales.

A study of 400 dogs started in 1979 in Turkey. Two were found to be infested with leishmaniasis. Further study is being carried out on 200 dog sera.

Research in Italy has the following aims:

- the obtainment of reliable data on sandfly distribution;
- the determination of the vector's breeding places;
- the attraction of the vector to the host;
- the infectiousness of the sandfly on the experimentally infected host;
- parasite development in infected flies;
- classification and behavioural studies of sandfly populations; and
- leishmania transmission studies.

In general, research needs to be oriented towards better determination of: (1) the foci of the disease and their characteristics; (2) the animal reservoir; (3) the vectors; (4) the pathogenicity and virulence of Leishmania and possible variations; and (5) the factors which may affect the epidemiological picture.

It was pointed out that in spite of the need for a rapid application of control measures, it would be wise first of all to accelerate the epidemiological studies needed to establish the correct and most efficient control methods. WHO has an important role to play in the coordination of research and the dissemination of knowledge.

6. Recommendations

On the basis of the reports submitted by each participating country and the ensuing discussions, the Meeting made the following recommendations.

6.1 Malaria

(1) The compulsory notification of malaria cases should be introduced in all participating countries.

(2) In countries where malaria transmission still continues, existing antimalarial activities should gradually be integrated with primary health care and thereby receive multisectoral and multidisciplinary support. It is recommended that, in these countries, people experienced in malaria control should have an important role in the development of primary health care in order to ensure that information systems are adequate and decisions are made at the appropriate levels.

(3) Countries in which malaria is nonendemic, but in which transmission could be re-established, should have an adequate system of vigilance for malaria operated by a small group of trained, competent people, who, inter alia, should check positive slides, perform epidemiological and entomological investigations, and provide treatment, as well as maintain knowledge and awareness of the potential malaria risk.

(4) It is recommended that border meetings be encouraged, particularly if no other coordination meetings are held.

6.2 Viral haemorrhagic fevers

(1) Further studies need to define more precisely the public health importance of this problem, especially in terms of the transmissibility, severity and lethality of these diseases in endemic and nonendemic areas.

(2) An information system for special pathogens should be set up by which all countries in the Region would immediately be notified of any news about these pathogens (new cases, outbreaks, etc.).

(3) Countries should establish contingency plans in case of importation, specifying in particular the measures required for the transport, rapid diagnosis, isolation and management of cases, disinfection, the surveillance of contacts and the training of a nucleus of personnel. Countries may wish to explore the organizational steps necessary for possible regional cooperation in the use of the existing facilities instead of or before deciding to construct maximum containment laboratories.

(4) A clear guide should be prepared with indications as to what to do and how to proceed in the event of a suspected case. This guide should be continuously updated through information sheets.

(5) The occurrence and distribution of other vector-borne viral diseases should be monitored and their importance assessed.

6.3 Leishmaniases

(1) Obligatory notification of all human leishmaniases cases, both visceral and cutaneous.

(2) Epidemiological investigation on Leishmania reservoirs and isolation of the parasites from their reservoirs, and from man, for identification of the etiological strains.

(3) Research should be carried out on phlebotomid flies considered as vectors of leishmaniases in different foci.

(4) Establishment of a national focal point in each participating country, which should be concerned with the analysis of all data related to the above aspects of leishmaniases.

6.4 General

Before planning another coordination meeting, WHO should carefully consider the value of such meetings by determining the degree of implementation of the recommendations of the present Meeting.

Annex 1

BIBLIOGRAPHY

Malaria

- Blazquez, J. & Zulueta, J. de The disappearance of Anopheles labranchiae from Spain. Parassitologia, 22: 161-163 (1980).
- Boyd, M.F. Malariology, 2 Vols. Philadelphia, Saunders, 1949.
- Broce-Chwatt, L.J. & Zulueta, J. de The rise and fall of malaria in Europe. Oxford, Oxford University Press, 1980.
- Butzer, K.W. Environment and archeology, 2nd ed. London, Methuen, 1972.
- Coluzzi, A. Dati recenti sulla malaria in Italia e problemi connessi al mantenimento dei risultati raggiunti. Riv. Malar., 44: 153-178 (1965).
- WHO Official Records, No. 221, 1975, p. 78.
- Frenzel, B. Die Klimaschwankungen des Eiszeitalters. Braunschweig, Vieweg, 1967.
- Hadjinicolaou, J. & Betsios, B. Resurgence of A. sacharovi following malaria eradication. Bulletin of the World Health Organization, 48: 699-703 (1973).
- James, S.P. et al. A study of induced malignant tertian malaria. Proceedings of the Royal Society of Medicine, 25: 1153-1186 (1932).
- Macdonald, G. The epidemiology and control of malaria. Oxford, Oxford University Press, 1957.
- Messerli, B. Die eiszeitliche und die gegenwärtige vergletscherung in Mittelmeerraum. Geographica helvetica, 105: 20 (1967).
- World Health Organization, Information on the world malaria situation, 1979. Weekly epidemiological record, 19: 145-149 (1981).
- Zulueta, J. de et al. Aspectos entomologicos sobre la receptividad al paludismo en la zona de Navalmoral de la Mata (Caceres, Espana). Rvsta. Sanid. Hig. publ., 47: 853-870 (1973).
- Viral haemorrhagic fevers
- Instruction for health institutions-based surveillance of monkeypox and VHF. Geneva, World Health Organization, 1980 (unpublished document CDS 80/2).
- Simpson, D.I.H. Marburg and Ebola virus infections. A guide for their diagnosis, management and control. Geneva, World Health Organization, 1977 (WHO Offset Publications, No. 36).
- Mccgan, J.M. & Shope, R.E. Emerging concepts on Rift Valley fever. In: Pollard, A.R., ed. Perspectives in Virology IX. New York, Liss, 1981.
- Procedures for the surveillance and management of monkeypox and VHF. Seminar on the surveillance of monkeypox and VHF, Brazzaville, WHO Regional Office for Africa, 1980.
- Rift Valley fever: An emerging human and animal problem. Geneva, World Health Organization, 1982 (WHO Offset Publications No. 63).
- Westwood, J.C.N. The hazard from dangerous exotic diseases. Ottawa, The MacMillan Press, 1980.
- WHO Technical Report Series, No. 661, 1981 (Rapid laboratory techniques for the diagnosis of viral infections: report of a WHO Scientific Group).

Leishmaniases

- Adler, S. & Theodor, O. Proceedings of the Royal Society London, 108: 453-463 (1931).
- Adler, S. & Theodor, O. Ann. Rev. Entomol., 2: 203-226 (1957).
- Basile, C. Atti R. Accad. Lincei, Rend., 19: 158-160 (1910).
- Bettini, S. et al Transactions of the Royal Society of Tropical Medicine and Hygiene, 71: 73-79 (1977).
- Bucci, A. et al. Parassitologia, 17: 25-37 (1975).
- Colella, G. & Casamassima, E. Veter. Ital., 26: 393 (1975).
- Colella, G. et al. Clin. Veter., 102: 35-41 (1979).
- Corradetti, A. Scient. Rep. Int. Sup. Sanità, 2: 103-109 (1962).
- Corradetti, A. & Neri, I. Rend. Int. Sup. Sanità, 18: 376-379 (1955).
- Gradoni, L. et al. Transactions of the Royal Society of Tropical Medicine and Hygiene, 1982 (in press).
- Gramiccia, M. et al. 1st English-Ital. Meet. Trop. Subtrop. Dis., Perugia, 1982.
- Killick-Kendrick, R. et al. Ecologie des Leishmanioses, Colloques Internationaux du CNRS, Montpellier, 1977.
- Mansueto, S. et al. 1st English-Ital. Meet. Trop. Subtrop. Dis., Perugia, 1982.
- Maroli, M. et al. Atti X Congr. Naz. Soc. Ital. Parass., Parassitologia, 22: 331-332 (1980).
- Mizcevic, Z. Acta Paras. Jugosl., 11: 25-37 (1980).
- Pampiglione, S. et al. Transactions of the Royal Society of Tropical Medicine and Hygiene, 68: 349-359 (1974).
- Pampiglione, S. et al. Transactions of the Royal Society of Tropical Medicine and Hygiene, 70: 62-65 (1976).
- Pampiglione, S. et al. Transactions of the Royal Society of Tropical Medicine and Hygiene, 69: 60-68 (1975).
- Pampiglione, S. et al. Transactions of the Royal Society of Tropical Medicine and Hygiene, 68: 447-453 (1974).
- Pozio, E. et al. 1st English-Ital. Meet. Trop. Subtrop. Dis., Perugia, 1982.
- Pozio, E. et al. 12 Congr. Ital. Entom., Rome, 1981
- Quilici, M. et al. Bull. Soc. Pathol. Exot., 72: 118-124 (1979).
- Rioux, J.A. et al. Rec. Med. Vet., 147: 489-498 (1971).
- Vanni, V. Ann. Igiene, 49: 65-67 (1939).
- Ward, R.D. et al. Ann. Trop. Med. Paras., 75: 653-661 (1981).
- Zivkovic, V. et al J. Paras., 59: 1150-1151 (1973).

Annex 2

LIST OF PARTICIPANTS

BULGARIA

- Dr I. Nakov-Dikov
Department of Infectious Diseases, Presidium, Medical Academy of Science, Sofia
- Dr P. Petrov
Institute for Infectious and Parasitic Diseases, Sofia

FRANCE

- Professor G. Saimot
Claude Bernard Hospital, Paris
- Professor R. Van Damme
Officer in charge of malaria control, Directorate-General of Health, Paris

GREECE

- Professor U. Marcelou-Kinti
Dean, Athens School of Hygiene

ITALY

- Professor S. Bettini
Department of Parasitology, University of Cagliari
- Professor L. Dardanoni
Institute of Hygiene, University of Palermo (Vice Chairman)

MOROCCO

- Mr M. Bennouna
Department of Environmental Hygiene, Directorate of Technical Affairs, Ministry of Public Health, Rabat
- Mr M. Laaziri
Office of Research and Evaluation, Ministry of Public Health, Rabat

PORTUGAL

- Dr L. Amarchande
Director of Rural Hygiene and Malaria Control Services, Lisbon

SPAIN

- Dr J.J. Fernandez Maruto
National School of Health, Madrid (Vice Chairman)
- Dr R. Najera Morrondo
National Centre for Microbiology, Virology and Immunology, Madrid

SYRIAN ARAB REPUBLIC

Dr Z. Khawam
Director, Malaria Eradication Project, c/o Ministry of Health, Damascus (Vice Chairman)

TUNISIA

Dr A. Zemzari
Head, Service of Social Welfare, c/o Ministry of Foreign Affairs, Directorate of International Cooperation, Tunis

TURKEY

Dr S. Gultekin
Director, Adana Malaria Institute

Mr U. Unsal,
General Director, Malaria Eradication Service, Ministry of Health and Social Assistance, Ankara

YUGOSLAVIA

Dr S. Ristic
Department of Health Care, Federal Committee for Labour, Health and Social Welfare,
Novi Beograd

OBSERVERS

Dr J. Blazquez
c/o Ministry of Health and Consumer Affairs, Madrid, Spain

Dr A. Lozano
National Centre for Microbiology, Virology and Immunology, Madrid, Spain

Dr F. Martin Luengo
c/o Ministry of Health and Consumer Affairs, Madrid, Spain

Dr J. Quiles
c/o Ministry of Health and Consumer Affairs, Madrid, Spain

Dr J. de Zulueta
c/o Ministry of Health and Consumer Affairs, Madrid, Spain

TEMPORARY ADVISERS

Dr S. Litvinjenko
Infectious Diseases Section, Federal Institute of Public Health, Belgrade, Yugoslavia
(Rapporteur)

WORLD HEALTH ORGANIZATION

Regional Office for Europe

Dr E. Leparski
Director, Disease Prevention and Control

Dr K. Lassen
Regional Officer for Malaria (Secretary)

Dr B. Velimirovic
Regional Officer for Communicable Diseases

Headquarters

Dr R.O. Darwish
Ecology and Control of Vectors, Vector and Biology Division

Dr A. Noguera
Chief, Programming and Training, Malaria Action Programme