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Epidemiology of Malaria and future perspectives for control (**)

Since the global malaria eradication programme was reverted to the control strategy, the malaria situation has progressively deteriorated in several countries.

In this presentation the global malaria epidemiological situation and its trend during the last eight years will be briefly reviewed. An attempt will then be made to analyze those factors which might have contributed to the worsening of the epidemiological global picture since the reversion from eradication to control (1969 to-date). In the final section, perspectives for control will be explored on the basis of the present epidemiological situation, the persistence and worsening of operational and technical problems and taking into account recent technological advances.

The present global epidemiological situation

In 1981, some 7.6 million malaria cases were reported from Member Countries to WHO excluding Africa, south of the Sahara, compared with 8.0 million cases in 1980 and 7.0 million in 1979 [1]. According to estimates, 1800 million people were exposed to the malaria risk and the disease was endemic in 103 countries of the world.

The evolution of the malaria situation on a global basis during the last eight years (1974-81) is summarized in Table 1 and Graph 1. The African tropical region, south of the Sahara (AFRO) is not represented either in the Table or in the Graph; this is due to the fact that well organized malaria control programmes have never been conducted in this large part of the continent and

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TABLE 1 - Number of malaria cases reported (in thousands).[1]

Region	1974	1975	1976	1977	1978	1979	1980	1981
Africa[2]	5.120	4.209	5.390	4.477	6.682	5.847	1.119	2.039
Americas	269	357	379	399	469	515	603	638
South-East Asia	4.162	6.105	7.304	5.540	4.790	3.658	3.561	3.351
Europe	7	13	41	119	93	34	38	60
Eastern Mediterranean	480	429	348	227	162	125	137	144
Western Pacific	179[3]	188[3]	211[3]	4.457	3.422	2.706	3.634	3.430
Total (excl. Africa)	5.097	7.092	8.283	10.742	8.936	7.078	7.993	7.643

[1] The information does not cover the total population at risk in some instances.
[2] Mainly clinically diagnosed cases; does not cover majority of chronic infections.
[3] Excluding China.

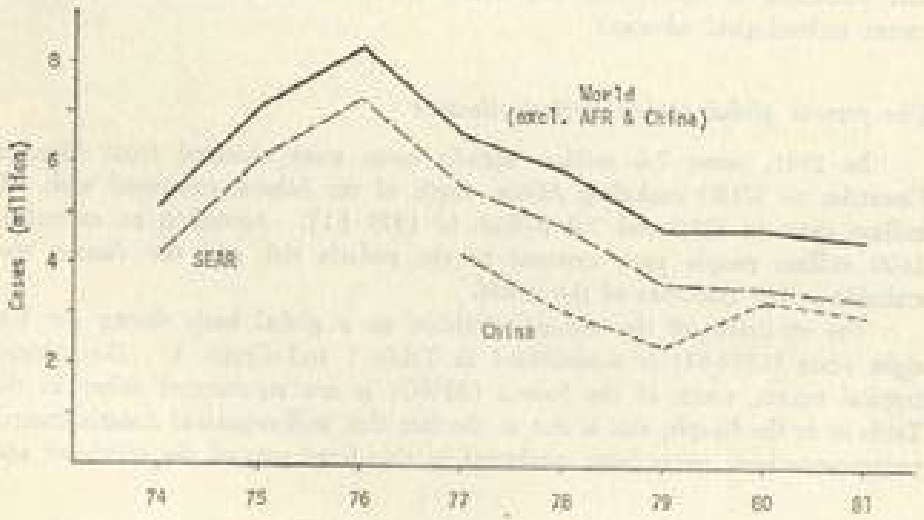

Fig. 1 — Malaria Cases Reported.

therefore the lack of precise and detailed epidemiological information. The amount of malaria prevailing in this part of Africa was estimated however in 1980 on the basis of data collected in the course of research or pilot projects conducted during the sixties and seventies [2] and on a classification of the malaria endemicity corresponding to different ecological zones. The conservative estimate made at that time indicated that the number of infections (with or without clinical manifestations) amounted to 190 million and the number of acute infections to approximately 67 million.

From Figure 1, it can be noted that: (i) the countries of the South-east Asia Region (mainly India) make a significant contribution to the number of malaria cases reported yearly in the world; (ii) the number of malaria cases in China varied from 4.2 million of 1977 (when the information was first made available to WHO) to the 3.1 million of 1981; (iii) the epidemiological situation, excluding AFRO and the People's Republic of China, has not changed significantly during the years 1974-1981 in the other regions of WHO, namely the Americas, Europe, the East-Mediterranean Region and the Western Pacific Region, if taken together.

It should be borne in mind, however, that the figures provided represent general epidemiological trends and are in reality an underestimate of the true picture, for the following reasons: (i) some countries do not report cases or the reports are incomplete; (ii) the search for cases has been drastically reduced in some countries due to high costs of maintaining a surveillance system on a total coverage basis; (iii) the type of information collected in malaria control programmes is often inadequate for correct assessment of these programmes; and finally (iv) only laboratory-confirmed cases are reported.

With regard to Europe, although special legislations make it compulsory to report all malaria cases to the national authorities of the Ministries of Health in nearly all countries of the region, only a portion of the malaria infection is reported to the health authorities and from them to WHO.

The number of malaria cases which were reported from the European Member States to WHO during the period 1972-1981 is shown in Figure 2. It can be noted that the total number of malaria cases which were imported to Europe was on the increase from 1972 to 1978 when the number of infections reached 4531. In 1979, 1980 and 1981 the malaria cases reported to WHO were 4039, 3852 and 3947 respectively.

Factors which may have determined or contributed to the worsening of the epidemiological situation during the malaria control strategy (1969 to date)

The decision to re-examine the global strategy of malaria eradication was inspired by both political and technical considerations. In the late 1960s the global eradication effort had lost momentum and many governments had shown concern about the slow rate of progress of operating programmes, a concern which was soon shared by international organizations and bilateral agencies.

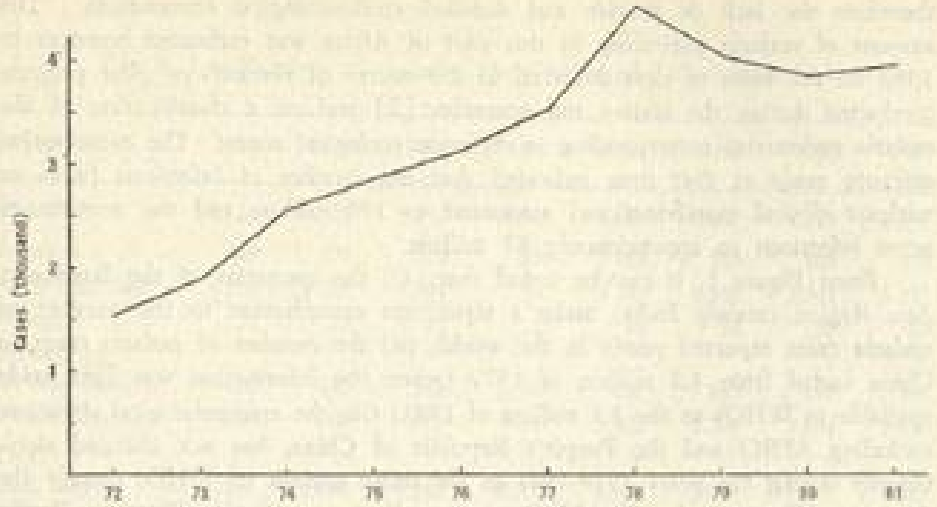

Fig. 2 — Imported Malaria Cases in Europe.

The end of the global malaria eradication programme came in 1969 when the Twenty-second World Health Assembly adopted a resolution [3] stressing the need to re-examine the global strategy of malaria eradication and to adjust the objectives, the planning and the methodology of malaria control to available resources. In other words, countries with endemic malaria were requested to develop their long-term malaria control plans within their overall health and socio-economic development plans, adjusting the antimalaria action to the local conditions and available resources. It had to be soon realized that many health authorities and policy makers were not in a position to implement the new policy, either because the necessary tools were not available or because of the existence of insurmountable obstacles. At times, the inter-related and inter-dependent administrative, operational, financial and technical problems, which adversely affected the eradication campaign, continued to persist, occasionally reaching new dimensions. It was not surprising therefore, that the switch from eradication to control was accompanied by a deterioration of the malaria situation in different geographical areas of the world.

Factors which have been recognized as important in determining or contributing to the worsening of the epidemiological situation are:

(a) The antimalaria functional structures at national and international levels instead of being strengthened to enable the application of the more complex methodology of malaria control began to be drastically reduced. For example, the advisory services of WHO at country, regional and headquarters level were cut by 34%, 42% and 33% respectively, during the decade 1967-1977, and a number of key malaria personnel were transferred to the communicable disease or environmental sanitation divisions, both at headquarters and WHO regional offices.

In 1973, at both WHO headquarters and regional offices, the malaria eradication structure was annexed by or integrated into the Parasitic Disease structure under the Division of Malaria and other Parasitic Diseases. This dismantling of the malaria organization was similarly practiced by many governments, so that the technical guidance, promotion and coordination of the antimalarial efforts that were competently carried out in the past could not keep pace with the deteriorating situation [4].

(b) International and bilateral agencies' financial commitments were drastically reduced. It has been reported that international funds (adjusted to constant dollar value) allocated to antimalaria activities in 1976, represented no more than one fifth of the amount available ten years previously [5]. Many countries of the Third World, greatly suffered from the drastic reduction of international financial assistance. It must be realised that whatever may be the planned level of malaria reduction, a certain investment is necessary and this cannot always be found within national resources.

(c) The training of specialized personnel, previously carried out at six International Malaria Eradication Centres, came practically to an end in 1969 with the closing down of the last Centre. As a substitute for this training, post-graduate courses, carried out in a few institutions, were not successful in producing the required expertise.

(d) With the limited know-how available in several developing countries, realistic objectives for the newly oriented control programmes could not be defined and national strategies taking into account local available resources could not be selected. At times, lack of knowledge was also accompanied by lack of willingness as in many instances there was reluctance to substitute the impressive gains of the eradication policy with long-term, continuous, unspectacular commitments.

(e) With the shortage of financial resources and the limited expertise available, field operations continued to be carried out in many countries without adequate planning and under much reduced supervision. Control programmes were very often confused with a patchwork of scattered eradication efforts, superimposed over a background of uncontrolled transmission [6].

Flexibility in the selection of programme objectives, of priority areas and population groups and the choice of antimalarial measures and evaluation methods have often been interpreted as permissible relaxation in the application of intervention measures [7].

(f) In line with the new control policy, malaria had to be considered as a problem among others and, as such, to be dealt with in the general framework of the country's health programme. A separate structure of the health services for the implementation of a malaria control programme was to be considered unrealistic and/or a luxury which only a few countries in the world could afford. In many instances, the malaria service was integrated with other health services without adequate planning and preliminary feasibility studies. The incorrect implementation of the process of integration always resulted in a rise of the malaria

incidence, linked to the worsening standard of the work and to the insufficiency of epidemiological surveillance.

(g) One of the most important social phenomena of recent years has been the massive exodus of poverty-stricken, underprivileged people from depressed rural areas to large cities or to new lands where large agricultural or industrial development schemes offer job opportunities and, therefore, the prospect of a better life. Since a large reservoir of endemic malaria remains in the depressed areas of the tropical and sub-tropical world, these transhuman movements or population resettlements have been responsible for the introduction of malaria into areas where the disease had never existed or for the resumption of transmission in areas where it had been controlled or greatly reduced under the impact of intervention measures and/or the improvement and consolidation of the health services. Some of these seasonal movements of the labour force have been the major cause for epidemic explosions, such as those experienced in the Cukurova and Amikova areas of Turkey [8] and in the Gezira irrigated areas of Sudan.

In Central and South America, population movements associated with socio-economic development projects and construction of highways, dams, exploitation of ore deposits, have been a serious obstacle for the smooth running of the anti-malaria campaign, especially in El Salvador, Nicaragua, Perú and Brazil.

Similar uncontrolled movements have been made responsible for the resurgence of the disease in many malaria freed areas of India.

(h) Security problems, due to political unrest, have been responsible for the isolation of important malarious areas in several countries, both in the eastern and western hemispheres of the globe. In these areas control operations could not be carried out according to plans or, at best, had to be drastically reduced. In these circumstances, which may continue to prevail in some countries for some time, spectacular or even satisfactory results cannot be expected in the near future.

Political upheavals have certainly had an adverse impact on several well-organized malaria control programmes, especially in some countries of south-east Asia. The movements of hundreds of thousands of refugees in this part of the world seem to have greatly contributed to the fast spread of *Plasmodium falciparum* resistant strains [9].

(i) Due to the reduced or confused control efforts made during the last decade, technical problems have constantly grown in size and magnitude, to the extent that they represent today major obstacles and a real threat to a successful implementation of control operations.

In 1980, a total of 51 anopheline species have been reported to be resistant to one or more insecticides: 34 are resistant to DDT, 47 to dieldrin and 30 to both DDT and dieldrin. Organophosphate resistance has been recorded in 10 species and resistance to carbamates in 4 species [10]. Striking developments have been the appearance of multiple resistance to organophosphorous and carba-

mate insecticide in *A. albimanus* in Central America and in *A. sacharovi* in Turkey and to organophosphates in *A. culicifacies* in India [11].

As already mentioned, resistance to organochlorines, organophosphates, carbamate and even to newly developed synthetic pyrethroids, has developed in areas of great economic value where agricultural pesticides are intensively and often indiscriminately used for the protection of cotton and rice-crops [12]. Suggestions for the promulgation and application of rules for a rational use of pesticides in agriculture have often been met with opposition or disregard [13, 14].

Another ever increasing problem encountered both in endemic and non-malarious countries, is the resistance of *P. falciparum* to drugs.

Resistance of *P. falciparum* to pyrimethamine and proguanil, or to both, is present in many endemic regions of the world and its appearance can be forecast in any area where the drugs have been given or are going to be administered on a large scale.

Today, *P. falciparum* resistance to 4-aminoquinolines, which was first demonstrated in Colombia [17] and Thailand [18] had been identified in six countries of south-east Asia (Bangladesh, Burma, India, Indonesia, Nepal and Thailand) in nine countries of the Western Pacific Region (China, Kampuchea, Lao People's Democratic Republic, Malaysia, Papua New Guinea, Philippines, Solomon Islands, Vanuatu and Vietnam) and in ten countries of South America (Bolivia, Brazil, Colombia, Ecuador, French Guiana, Guyana, Panama, Peru, Suriname and Venezuela). In Africa, after the discovery of *P. falciparum* resistance among non-immunes visiting East Africa, the same has been recently documented among the semi-immune indigenous populations in Tanzania, Zanzibar, Kenya, Gabon and Sudan. (See Map 1).

The appearance of *P. falciparum* drug resistance in Africa will have immense practical implications for both the African countries and all the receptive areas of the other continents exposed to the risks of the reintroduction of the disease from Africa.

The list of problems and constraints mentioned above, though far from being exhaustive, provides sufficient evidence and explanations for the massive return of malaria after the revision of the malaria eradication strategy.

In order to attempt a reversion of this trend, the Thirty-first World Health Assembly adopted a malaria control strategy and established a Malaria Action Programme which was defined as "a cooperative effort of Member States affected or threatened by malaria, WHO and international and bilateral agencies to implement antimalaria activities with the objective of reducing the impact of malaria on the health and productivity of the population" [19].

The objectives of the Malaria Action Programme are the formulation, promotion, implementation and coordination of a dynamic control/eradication programme on a world wide scale. Malaria control at country level, however, is to be based on the adjustment of the antimalaria action to local constraints and available resources. For every specific situation realistic medium-term objectives and different levels of achievements had to be set up, to be regularly revised

Areas and countries with chloroquine-resistant *Plasmodium falciparum*: status at December 1982.

in the course of programme implementation, following periodical reappraisal of progress and assessment of technological advances. In order to plan and implement a malaria control programme along the lines mentioned above, it is necessary to possess a deep knowledge and understanding of the local transmission dynamics. Such epidemiological knowledge and the expertise required to build it up, are not always available.

The impediments to effective malaria control experienced in recent years still persist and have become more acute in some instances: increased costs of essential commodities, global inflation, lack of trained personnel, increased technical problems, inadequate administrative management, uncontrolled population movements and logistic difficulties.

The evolution of the epidemiological situation during the past eight years revealed hardly any true progress in the global malaria situation. The resurgence of the 1970s has been put down to some extent and a further spread prevented in some areas with a reduction in the number of cases during the period 1977-1979. However, in most areas with programmes, the number of cases has not been reduced to the pre-1970 levels that had been achieved through the national eradication efforts, and in 1980 and 1981 globally the situation was stagnant, whilst individually some countries even experienced a worsening of the situation. Moreover, the disruption of surveillance activities in certain areas had resulted in under-reporting of cases. The epidemiological situation remains precarious.

Future perspectives

Considering the evolution of the malaria situation in the world from the days of eradication to the present time and the persistence and worsening of many operational and technical problems, spectacular results in the control of the disease cannot be expected in the forthcoming years. Much will depend on how the endemic countries and international communities will react towards the resurgence of the disease and its control. At the moment, attitudes and approaches vary greatly in the different corners of the hemisphere. While all governments have declared themselves ready to attempt to establish a new social order in the field of public health by accepting the report and declaration of the International Conference on Primary Health Care, held in Alma Ata, USSR in 1978 [20] and endorsing the resolution which was adopted in 1979 by the Thirty-second World Health Assembly [21] great differences exist in the formulation of national strategies. Malaria control as part of primary health care systems will require technical adjustments as well as a considerable amount of organizational and administrative readjustments. Experience has already shown that those countries which will carry out the readjustment mentioned above, may experience a worsening of the malaria situation for some years, until an adequate organizational structure to deal with the malaria problem has been established and/or an equilibrium between man and parasites has been reached. Other governments will continue to pursue a malaria eradication programme in order to safe-guard the

gains obtained and eventually improve them, utilizing for this purpose a well-established vertical system and feeling reluctant to integrate it with any other public health services. The successes in these cases will depend on the timely introduction of corrections in the management and planning of the programme, on the proper assessment of important socio-ecological factors calling for multi-sectoral cooperation, and, of course, on the continuous availability of financial resources.

In all circumstances, however, satisfactory progress in malaria control will be achieved whenever appropriate technical guidance, a sound public health administration and resources commensurate with the degree of malaria control defined at the time of planning, are and will continue to be made available to governments which intend and actually invest in a malaria control programme.

In this respect, there is an urgent need for the World Health Organization and other international and/or bilateral agencies to further strengthen, develop, coordinate regional training programmes so that national training capabilities will be upgraded to their needs and the multidisciplinary group of experts needed to plan and implement malaria control within the overall health and socio-economic development plans of the country, can finally be made available.

The future may look less gloomy, if the remarkable technological advances which have been made in recent years in the fields of chemotherapy and immunology and towards the development of an immunizing agent are considered.

Potentially valuable new drugs are now available and are already in different stages of development. The most promising and in the most advanced developmental stage is mefloquine, a 4-quinoline methanol which is a highly active blood schizontocide, especially against chloroquine-resistant falciparum malaria, and has a long half-life in man. Preliminary results of various phase II and III studies with regard to tolerance and efficacy are very promising [22]. It may be expected that mefloquine, either alone or in combination with sulphadoxine/pyrimethamine, will soon be available on the market.

Another group of promising compounds are artemisinine (Qinghaosu) and its derivatives which have been isolated in China and found to have an extremely short half-life and, therefore, very useful in severe malaria cases including chloroquine-resistant falciparum malaria [23]. Yet, it must be recognized that available preclinical data do not fully comply with internationally accepted standards required for the performance of clinical trials and further research is still needed.

A 9-phenanthrenemethanol, Halofantrine (WR 171, 669) is undergoing clinical trials aiming at determining optimum dosages and regimen for a one day treatment [24]. New candidate 8-aminoquinolines show a higher chemotherapeutic index than primaquine and hold promise with regard to a simplification of radical curative use in vivax malaria [25].

In the field of immunological methods in malaria, the introduction of functionally characterized monoclonal antibodies and purified antigens should produce major progress in the field of immunodiagnostic tests [26].

Important recent advances have been made in the development of malaria

vaccines [26, 28]. Protective parasite antigens have been identified in several plasmodium species, including human plasmodia, and in some cases the corresponding genes have been cloned and expressed in bacteria. It can be envisaged that research on potential vaccines will soon progress from the stage of laboratory investigation to that of developmental research involving pilot-scale production and preliminary testing.

The real value of a vaccine, however, will be known only after well planned and well organized trials are conducted in humans under different epidemiological conditions in the field. An "ideal" vaccine should give rise to a long-lasting sterile immunity against malaria after one inoculation and this may still require a lot of efforts and a considerable period of time.

We believe that malaria being a disease deeply rooted in the poorest rural areas of the world, often associated with highly depressed socio-economic conditions, reliance for success should not be based solely on miraculous vaccines, drugs or insecticides.

Control of the disease will very probably continue to depend on the application of different attack measures, i.e., the control of the vector, the rational use of chemotherapeutic agents and, when available, the use of mono or polyvalent malaria vaccines.

Attempts to find solutions to technical problems should be made through a well planned applied field research programme, whilst financial resources should continue to be made available for fundamental research.

While countries should continue to mobilize their own resources to the maximum possible extent, technical and financial inputs from international or bilateral agencies should be made available and possibly increased.

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References

[1] WHO Weekly Epid. Rec. (1983) - *World Malaria Situation, 1981.* August 1983.

[2] Kouznetsov R.L. (1977) - *Malaria Control by indoor spraying of residual insecticides.* « Trop. Doctor », *7*, 81-91.

[3] WHO (1975) - WHA 22.39 Handbook of Resolutions and Decisions of the World Health Assembly and Executive Board, Vol. 1, 80, Geneva.

[4] Farid M.A. (1979) - *Malaria: reflections of a veteran malariologist.* « World Health Forum », *1*, 9-22.

[5] Bruce-Chwatt L.J. (1979) - *Man against malaria: conquest or defeat.* « Trans Roy. Soc. Trop. Med. Hyg. », *73*, 605-617.

[6] Najera-Morrondo J.A. (1979) - *A suggested approach to malaria control and to the methodology applicable in different epidemiologic situations, based on experiences in the Americas.* « Bull. Pan. Am. Health Org. », *13*, 223-234

[7] Oshoa E. (1980) - *Experience gained during review of antimalarial programmes.* « Trop. Doctor », *16*, 195-199.

[8] Oshoa E. and Grab B. (1980) - *Quantitative estimates of the evolution of a malaria epidemic in Turkey if remedial measures had not been taken.* « Bull. Wld. Hlth. Org. », *58*, 321-326.

[9] Beales P.F. (1982) - *Biomedical and physiological consequences of migration: population movements and the evolution of drug resistant malaria.* Paper presented at the East-West Center Conference on Migration and Adaptation to Environmental Changes: Processes in Socioeconomic and Biological Evolution. Honolulu, 25-31 August 1981.

[10] WHO (1980) - *Resistance of vectors to insecticides.* « Techn. Rep. Series », No. *655*, Geneva.

[11] WHO (1976) - *Resistance of vectors and reservoirs of disease to insecticides.* « Techn. Rep. Ser. », No. *561*, Geneva.

[12] Chapin G. and Wasserstrom R. (1981) - *Agricultural production and malaria resurgence in Central America and India.* « Nature », *293*, 181-185.

[13] WHO (1975) - *Ecology and control of vectors in public health.* « Techn. Rep. Series », No. *561*, Geneva.

[14] WHO (1979) - *Safe use of pesticides.* « Techn. Rep. Series », No. *583*, Geneva.

[15] Peters W. (1970) - *Chemotherapy and drug resistance in malaria.* London and New York: Academic Press.

[16] Oshoa E. (1982) - *Resistance of* Plasmodium falciparum *to antimalarials: practical implications and perspectives of control.* « Parasitologia », *XXIII*, 31-62.

[17] Young M.D. and Moore D.V. (1961) - *Chloroquine resistance in* Plasmodium falciparum. « Am. J. Trop. Med. Hyg. », *10*, 317-321.

[18] Harinasuta T., Migasena S. and Bunnag D. (1962) - UNESCO Its Regional Symposium on Scientific Knowledge of Tropical Parasites *148*, Singapore.

[19] WHO (1983) - WHA. 31.43 Handbook of Resolutions and Decisions of the World Health Assembly and the Executive Board. Vol. II Fifth Edition (1973-82), 124-125, Geneva.

[20] WHO (1978) - Report of a joint WHO/UNICEF International Conference on Primary Health Care Alma-Ata 6-12 September 1978. Geneva-New York.

[21] WHO (1983) - WHA 29.74 Handbook of Resolutions and Decision of the World Health Assembly, Vol. II, Fifth Edition 54-55, Geneva.

[22] Development of mefloquine as antimalarial drug UNDP/World Bank/WHO Update (1983). « Bull. Wld. Hlth. Org. », *61*, 169-178.

[23] WHO (1981) - *The development of Qinghaosu and its derivatives as antimalarial drugs*. Offset document TDR/CHEMAL - SWG(4) (QHS) 81.3.

[24] Cosgriff T.M., Boudreau E.F., Pamplin C.L., Doberstyn E.B., Dejardins R.E. and Canfield C.J. (1982) - *Evaluation of the antimalarial activity of the phenanthrenemethanol Halofantrine (UR 171, 669)*. « Am. J. Trop. Med. Hyg. », *31*, 1077-1079.

[25] Davidson D.E. Jr., Ager A.L., Brown J.L., Chapple F.E., Whitmire R.I. and Rossan R.N. (1981) - *New tissue schizontocidal antimalarial drugs*. « Bull. Wld. Hlth. Org. », *59*, 463-479.

[26] WHO (1981) - Immunological Methods in Malariology Report and Working Papers of a meeting held under the auspices of the Mérieux Foundation and the World Health Organization, Lyons, France 9-12 September 1981, WHO/MAL/81. 948-972.

[27] Wernsdorfer W.H. (1981) - *Prospects for the development of malaria vaccines*. « Bull. Wld. Hlth. Org. », *59*, 335-341.

[28] *Development of malaria vaccines*. Memorandum from a USAID/WHO meeting (1983). « Bull. Wld. Hlth. Org. », *61*, 81-92.