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1. RESISTANCE TO 4-AMINOQUINOLINE DRUGS OF A STRAIN OF PLASMODIUM FALCIPARUM FROM COLOMBIA, SOUTH AMERICA

Dr Martin D. Young of the National Institute of Allergy and Infectious Diseases, United States Public Health Service, Bethesda, has kindly permitted us to use the following note from him summarizing recent work on the resistance of a strain of P. falciparum from Colombia, South America, to 4-aminoquinoline drugs.

"The resistance to normal (0.6 g and 1.5 g) and above-normal doses (2.1 g) of chloroquine of a strain of Plasmodium falciparum originating in Colombia, South America, was recently reported (Young, M. D. & Moore, D. V. (1961) Chloroquine resistance in Plasmodium falciparum, Amer. J. trop. Med. Hyg. 10, 317-320). This strain has since been challenged with amodiaquine (Camoquin^(R)), and hydroxychloroquine (Plaquenil^(R)).

"The malaria infections were induced into neurosyphilitic patients either by the injection of infected blood or by the bites of infected mosquitos. The drug was given under supervision either during the first part of the primary attack or after several weeks of clinical activity. The results are summarized in Table 1:

Strains	Dose in grams	Parasite cleared from blood stream - average range in days
Amodiaquine		
* Colombia <u>P. falciparum</u> Susceptible strains	0.6 s.d. 0.6 s.d.	Not cleared in 14 days (3 patients) 1.2-5.3
* Colombia <u>P. falciparum</u> Susceptible strains	1.4 in 3 days 1.4 in 3 days	Not cleared in 14 days (3 patients) 1.1-2.8
Hydroxychloroquine		
* Colombia <u>P. falciparum</u> Susceptible strains	1.2 s.d. 1.25 s.d.	Not cleared in 14 days (4 patients) 1.3 (2 of 70 were failures)

* Compiled from personal experience and the literature.

s.d. - single dose.

"These results show the poor response of the Colombia strain to amodiaquine and hydroxychloroquine as compared to the rapid response of other strains.

"Several of the patients received quinine and gave a normal response.

"An experiment was done to determine if weekly suppressive doses of 300 mg chloroquine or 400 mg amodiaquine, started three days before exposure to the bites of infected mosquitos, would suppress, or suppressively cure, the infections of the Colombia strain of P. falciparum. In one group, three patients received the chloroquine and one did not; all four were bitten by the same group of mosquitos. A similar test was done with the amodiaquine. The patients taking the drug received five weekly doses.

"The parasitaemias appeared in both the patients receiving suppressive doses of chloroquine or amodiaquine and in the controls, who took no drug, at about the same time, all within the normal range, and ran similar courses. The fever patterns were similar also.

"The urines of the patients taking chloroquine and hydroxychloroquine showed a positive Haskins test. The plasma levels of chloroquine were in the normal ranges.

"Three of the above cases appeared to respond normally to 50 mg single dose of pyrimethamine. Two cases responded normally to a total of 1.5 g proguanil given over a five-day period. This indicates no cross-resistance to these drugs. Six cases appeared to respond normally to a 2.8 g regimen of mepacrine but four have relapsed.

"These results indicate that a strain of P. falciparum from Magdalena Valley, Colombia, South America, which is resistant to chloroquine, is resistant also to amodiaquine and to hydroxychloroquine, which are other members of the 4-aminoquinoline group. The resistant quality persisted after mosquito passage.

"Weekly doses of 300 mg of chloroquine or 400 mg of amodiaquine failed to cure or to suppress mosquito-transmitted infections of the Colombia, South American strain of P. falciparum.

"In areas where resistance to one of the above 4-aminoquinolines appears, it would appear unwise to depend upon another of this group for treatment, especially in acute cases; until evidence to the contrary appears, it seems desirable to use some other drug, perhaps quinine."

2. THE JUNE 1961 SESSION OF THE UNICEF EXECUTIVE BOARD

A session of the Executive Board of the United Nations Children's Fund was held in New York on 8-19 June 1961 at the United Nations headquarters. Among other matters, the Board discussed its policy on aid for malaria eradication and a report by the Director-General of WHO on malaria eradication was presented to the Board (Document E/ICEF/417, 3 May 1961).

In this report attention was called to the progress made over the last two years during which time areas of total population of 27 million people had entered the consolidation phase. It was shown in the report that the most important factors leading to delays and partial failures in the campaign were basically organizational or administrative failures.

The results of some successful pilot projects in tropical Africa have demonstrated that it is technically feasible to interrupt transmission there and WHO recommended that these pilot projects be discontinued as such and converted, if possible, to eradication or pre-eradication programmes. However, success in eradication depends on the meeting of administrative and operational requirements and on the availability of adequate finance. It was emphasized that the most essential elements in a campaign were sound planning and thoroughness of execution.

A number of delegates hoped that there would be a gradual reduction of UNICEF expenditures on malaria eradication, but the majority doubted whether this would be possible in the immediate future and recognized that, as UNICEF allocations rose, the \$ 10 million ceiling for malaria eradication would gradually constitute a smaller proportion of the total allocations.

The decision of the World Health Assembly in March to include in its regular budget the costs formally met from the malaria eradication special account was noted and it was thought that it might therefore be possible for WHO to assume a larger responsibility in the financing of malaria campaigns. However, the Director-General of WHO advised that the World Health Assembly, at the time of adopting this new policy, had expressed the hope that UNICEF would maintain its current level of aid. WHO intended to maintain its assistance until campaigns reached the point where expenditure could be reduced. It was essential, in his opinion, for WHO, UNICEF and the governments concerned to continue and to intensify their campaigns against this disease.

Delegates emphasized the responsibility of countries with malaria campaigns to develop, at the same time, their basic health services to the fullest extent. It was clear that the development of such health services, into which the surveillance activities of the maintenance phase of campaigns could be integrated, was not only important for the efficiency and economy of the campaign, but also related to the prime interest of UNICEF in mother and child welfare.

The Board decided to maintain the \$ 10 million per year ceiling for allocations for malaria programmes and approved the following statement of policy:

1. In countries where the chances of eradication appear to be good, where the government has made every effort to establish an efficient organization and where the programme is assured of regular financial support, UNICEF assistance may be extended and prolonged until the eradication criteria have been fulfilled under the conditions laid down by the Board at its September 1959 session.
2. In countries where the chances of eradication appear to be extremely remote, the UNICEF Secretariat, in consultation with WHO, shall open negotiations with the governments with a view to:
 - (a) The suspension of the programmes in all or part of the territory if they appear to be of no appreciable benefit to the people; or,
 - (b) The conversion of eradication programmes into pre-eradication programmes, assistance being provided in such circumstances for a limited period.
3. In countries where additional means can be mobilized, but where there are still serious difficulties, negotiations shall be resumed with the governments with a view to ensuring that the necessary efforts shall be made to remedy the financial, administrative and organizational deficiencies of the programmes.
4. A formal warning shall be addressed to those governments, impressing upon them the importance of the goal and the need to provide adequate resources for programmes and stating that assistance will not be renewed if the situation remains unchanged by the end of the succeeding operational year.

In this connexion, the following points might be considered in the course of future negotiations:

- (a) Existing legislation;
 - (b) the budget of the eradication organization;
 - (c) the administrative organization and the degree of independence of the eradication organization;
 - (d) shortcomings in the spraying operations;
 - (e) the surveillance organization;
 - (f) measures the government intends to take, particularly with regard to the recruitment and retention of staff for the duration of the malaria eradication programme;
 - (g) assurance that the government will continue the programme to the end, whatever its duration and financial implications.
5. The Secretariat shall continue, as in the past, to work in close co-ordination with WHO and the United States International Cooperation Administration.
6. The Secretariat is authorized, within the limits of the stipulated ceiling, to submit for consideration as new programmes:
- (a) Recommendations for assistance for pre-eradication programmes, in special circumstances, in countries where malaria control is a priority need for child welfare and only in cases where basic public health service projects are undertaken by the governments;
 - (b) recommendations for assistance for eradication programmes in countries where programmes have already received UNICEF assistance (Zanzibar, North Borneo) or for which formal undertakings have been made (Tunisia and Egypt).
7. The Board shall re-examine the question of UNICEF aid for malaria campaigns again in 1963 in the light of the progress made and the priority needs of children in countries affected by malaria.

The Board approved allocations totalling \$ 2 771 000 for assistance to projects for the eradication of malaria. This allocation represented almost 31% of the total long-range aid recommended at this session.

3. PREVENTION OF MALARIA ON A LARGE HYDROELECTRIC DEVELOPMENT PROJECT IN MEXICO

The following report has been received from Dr. Donald J. Pletsch, Chief Technical Adviser, Pan American Health Office (WHO) in Mexico, regarding control of a malaria situation in Malpaso area, Chiapas, Mexico, and may be of interest to those faced with similar situations in other parts of the world.

In 1960 the work undertaken by the Comision del Grijalva in the region Malpaso, Chiapas, included the completion of an 80 km all-weather road giving access to this area from the closest railhead. Preliminary work was begun for the construction of a gigantic dam across the Rio Grijalva in a heavily forested mountainous area of Chiapas. Large numbers of workers recruited by the 10 contracting companies involved in the development of the dam site began to arrive from other parts of the Republic. The magnitude of the project is indicated by the employment of 20 engineers by the Grijalva Commission and 40 engineers by the contracting companies, who live with their families and with labourers in seven camp sites along the margins of the river. Because the area was newly opened, without services of any kind, numerous commercial interests, particularly in the form of small shops, have entered in order to exploit the presence of workers and their families. The total number of residents is nearly 3000 persons at the present time, and will be approximately 7000 with the intensification of work following completion of the diversion tunnels.

Houses of Grijalva Commission personnel are very well constructed, including screen windows and doors, in camp sites, and there is fairly good drainage. The housing of contracting personnel is reasonably well constructed of wood and sheet metal, but the houses of small shop owners and other persons attracted by the development of the area are definitely substandard, frequently consisting of logs and thatching cut from the nearby forest.

A medical officer employed by the Grijalva Commission has been in the area since the initiation of exploration work two and a half years ago. He is assisted by a nurse who shares responsibility for medical services of Commission employees and their

families. The Commission doctor and nurse have been aware of the potentially dangerous malaria situation and have collaborated closely in the taking of blood smears from persons suspected of having malaria. A second doctor, employed jointly by the contracting companies, has been fully occupied in treatment of workers injured in construction and has had neither time nor interest in collaborating in control of the malaria situation.

Five malaria cases were discovered in the Malpaso area in 1960 (one in February, three in August and one in September). In view of the threat posed by the presence of infection, by the constant arrival and movement of workers inside the area and between that area and other parts of the country, agreement was reached with the Grijalva Commission to establish a check point on the only access road then existing into the area. This control post was situated at a point sufficiently remote from the camp site so as to minimize evasion by persons descending from vehicles making an enforced stop at the control station. A sign was conspicuously posted announcing a compulsory review of individual malaria control cards issued to all personnel. The control post has two police officers paid by the Grijalva Commission and two employees paid by the malaria service, providing 24 hours' service. A microscopist was stationed in a laboratory installed at the main camp site, sharing a building with the shortwave radio transmitter, permitting immediate communication to the Grijalva Commission headquarters in Villahermosa of any malaria cases or other problems associated with maintenance of the check point service.

An initial blood smear was taken from all individuals - officials or non-official - presenting themselves at the check point for the first time. Persons seeking employment were given a provisional card indicating that a blood smear had been taken. After securing employment, or in the case of persons arriving officially for permanent residence in the area, a formal "Tarjeta de Control" was issued giving the individual's name, age, sex, occupation, contracting company (if pertinent), date of taking each blood smear, record of administration of drugs, and results of parasitological examinations. Additional data include the recording of the place, and house address from which the individual has come, his address in the Malpaso area, the camp site and number of his dwelling, and information reference, the giving and completion of radical treatment in case of positivity. All individuals are required to show the control card each

time they enter the area, to avoid the taking of an additional blood smear. In the event of their absence from the area for one month or more, another blood smear is automatically taken at the time of re-entry. As far as possible slides are taken from fever cases within the area by the medical service of the Grijalva Commission or by the technicians. Following the initial insecticidal coverage of the houses constructed in 1960, spraying of newly constructed houses has been the responsibility of the two technicians assigned to the check point. This re-checking of house construction has required constant attention, principally because of the occasional transfer of housing from one camp site to another by contracting companies, and the mushrooming construction of substandard housing by non-official personnel utilizing locations as close as possible to the official camp sites.

During discussion with the resident engineer in charge of construction, it was evident that the Grijalva Commission actively appreciates the importance of the anti-malaria measures being taken in the area, including the necessity to intensify vigilance in the near future when the population will approximate 7000 people.

The Grijalva Commission has also shown active interest in the establishment of a second check point in a nearby area where surveillance and development work are being initiated associated with construction of the spillways into the Coatzacoalcos River.

The systematic spraying operations carried out in the area have apparently eliminated the immediate transmission threat, inasmuch as the 4000 slides taken in the area between last December 1960 and March 1961, did not reveal any positives.

The well co-ordinated measures taken by the National Commission for the Eradication of Malaria and the Grijalva Commission constitute an excellent example of the refinement which can be achieved in an area where movement into and within a virgin area of rapid development can be feasibly controlled.

4. OPENING OF THE MALARIA ERADICATION TRAINING CENTRE IN BELGRADE

The first course of the new Malaria Eradication Training Centre (IR 89) at Belgrade started on 2 March 1961 for French speaking students. It was attended by 13 fellowship holders from 10 countries - Cambodia, Cameroun, Dahomey, Gabon, Haiti, Iran, Malagasy, Morocco, Togo and Turkey .. covering five of the six regions of the Organization.

The official opening of the Centre was carried out by Dr Vojo Djukanović, Director of the Yugoslavia Federal Institute of Public Health.

After a short introductory speech by Dr Ivan Grujić, Technical Director of the Centre, Dr V. Djukanović addressed the meeting, and spoke of the pleasure his Government had in acting as host country to the Centre, and considered it an obligation on the part of technically developed countries to assist others who were at present not so fortunate.

He referred to the efforts so far made in Yugoslavia to attain eradication of malaria and to the marked success they had thus far achieved; he felt the siting of the school in his country was opportune as the students would not only receive theoretical training but also the practical application of modern scientific methods.

Dr Kraus, Under-Secretary of the Health Secretariat of the Federal Executive Council, also made a speech of welcome.

Dr Pampana, late Director of the Division of Malaria Eradication, WHO Headquarters at Geneva, speaking on behalf of the Director of the WHO Regional Office for Europe, thanked the Government of the People's Republic of Yugoslavia for the hospitality offered to the Centre and for their kind co-operation. He referred to the days of the League of Nations when the Malaria Commission used to send a large proportion of the fellowship holders to Yugoslavia for the practical part of their courses, and paid tribute to the tutors of those days, two of whom were present at the opening ceremony - Professor Simić who was a consultant lecturer on the present course, and Dr Grujić, the Director of the Centre. Professor Simić replied on behalf of the lecturers of the course.

This official opening of the centre was attended by members of the press, radio and television broadcasting and received full publicity.

5. FRONTIER CO-OPERATION V

It is worth quoting still another example of arrangements made for ensuring close co-operation between neighbouring countries,¹ as neither the vector mosquito nor the infecting parasite recognize these political frontiers and full co-operation between neighbouring countries is absolutely essential throughout all phases of a malaria eradication programme.

¹ Previous notes have appeared in Mal/Inform/35 of 1 September 1958, 39 of 15 December 1958, 43 of 1 April 1959, 61 of 1 August 1960 and 66 of 15 December 1960.

PLAN OF CO-ORDINATION BETWEEN THE NATIONAL MALARIA
ERADICATION COMMITTEE OF MEXICO AND THE
NATIONAL MALARIA ERADICATION SERVICE OF GUATEMALA¹

Background

At the first meeting of the Mexico-Guatemala Public Health Association held on 13 and 14 January 1961 in Tapachula, Chiapas-Mexico, it was recommended that a plan be prepared for co-ordinating the work of malaria eradication in the frontier zones. Pursuant to this recommendation, the directors of the respective services, together with a representative of the Pan American Sanitary Bureau, met on 17 and 18 January 1961, at the headquarters of the Guatemala National Malaria Eradication Service and drew up the plan set out hereunder:

Plan of co-ordination

1. Delimitation of frontier zone

Since there are no natural features which form the frontier, it was agreed that the frontier zone should comprise all the communes adjacent to the boundary.

2. Basic information

It was considered necessary to have certain basic information and it was agreed that each country would prepare a document giving:

- (a) The number of localities, houses, inhabitants and square kilometres per commune;
- (b) the history of the spraying operations;
- (c) general epidemiological information.

3. Exchange of information

It was decided that an exchange of the following information would be essential in order to evaluate the progress of the operations and the results obtained:

- (a) Details of the spraying operations plan, by cycle;
- (b) a monthly report on houses per locality, commune, department or state;

¹ The Spanish text was translated into English and French at WHO headquarters.

- (c) notification of any change in the established plans;
- (d) due notification of the presence of any focus;
- (e) immediate notification of the discovery of resistance of vectors to the insecticides in use.

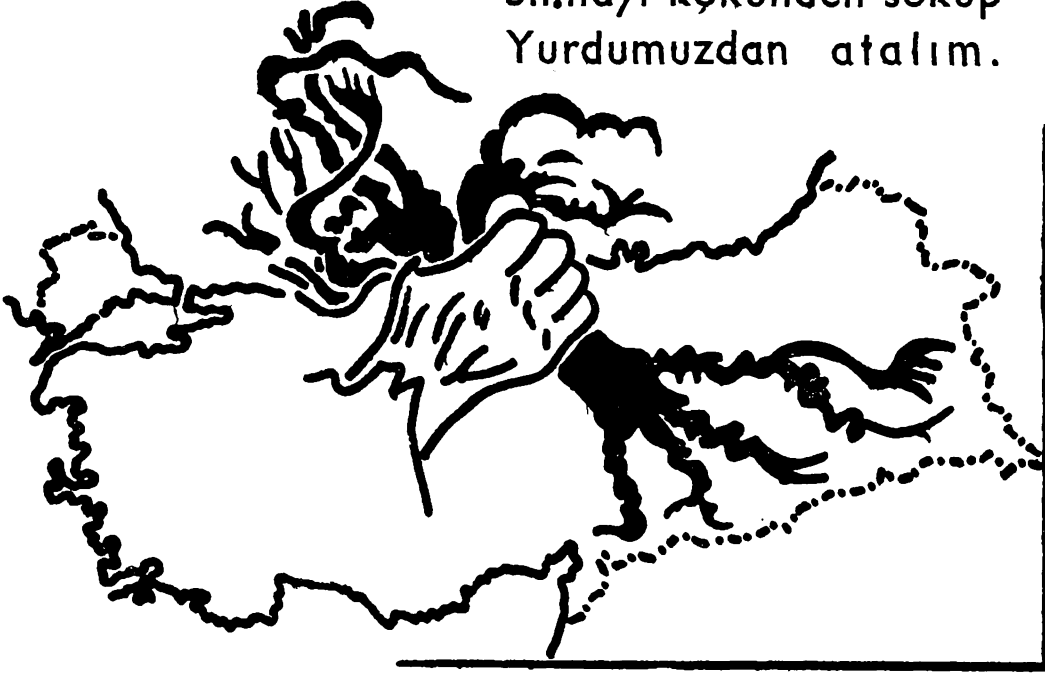
4. Recommendations

- (a) It was recommended that the necessary readjustments be made for the purpose of synchronizing the spraying operations on both sides of the frontier.
- (b) Since population migration is the chief problem, it was recommended that a complete study on migration be made for the purpose of establishing methods of control.
- (c) It was recommended that the agenda of each meeting of the Mexico-Guatemala Public Health Association should include an item permitting discussion of malaria problems in the frontier zones.
- (d) It was recommended that the Directors of the Malaria Eradication Services of the two countries be empowered to implement this present agreement either directly or through the Association's Secretariat, and the Zone II and Zone III representatives of the Pan American Sanitary Bureau.

6. MALARIA ERADICATION PUBLICITY IN TURKEY

Lutfen bize yardım edin ;

Sıtmayı kökünden söküp
Yurdumuzdan atalım.



The graphic representation illustrated above is used on posters and explanatory leaflets issued by the Malaria Eradication Programme in the Izmir Region of Turkey, and will probably be used generally throughout Turkey in the near future.

The symbolic uprooting of a dangerous weed is particularly apt for use in an agricultural country.

Lutfen bize yardım edin; Sıtmayı kökünden söküp
Please help us; let us eradicate malaria
Yurdumuzdan atalım.
together from our country.