Some major trends in vector Biology and control.

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At the seventh International Congress of Parasitology, ICOPA VII held in Paris last August we tried to identify, the new findings in medical entomology and vector control (1). The purpose here is not to rewrite a similar paper but to highlight what we think are the dominant trends in Vector Biology and Control :

- the input of high technologies in entomology and parasitology;
- the impact of environmental changes on vector ecology and the epidemiology of vector borne diseases ;
- the difficulties in malaria control.

1. The input of high technologies.

High technologies generate tremendous advances in vector and parasite taxonomy allowing for a better understanding of their ecology, of the vector/parasite relationships and of the epidemiology of vector borne diseases.

1.1. Taxonomy.

Morphology is still the basis for vector identification at the species level. In some groups of mosquitos and sandflies, computer assisted keys are available; they also integrate some biological and ecological data (2).

Important progresses in the knowledge of species complexes e.g. *Anopheles gambiae, Anopheles dirus, Simulium damnosum,* have been achieved by cytogenetical technics during the last 20 years (3, 4, 5).

Isoenzyme electrophoresis and DNA probes have also proved to be useful for the investigation of the complexes. Moreover they have helped the morphotaxonomists in confirming the status of some questionnable species (6, 7, 8, 9, 10, 11).

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Cuticular hydrocarbon analysis remains a laboratory technic.The pheromone analysis has been tried for studying *Lutzomyia longipalpis* in Brazil but the results were not in agreement with the morphology (12, 13).

1.2. Vector/parasites relantionships.

Circumsporozoite monoclonal antibodies revealed by ELISA made possible the identification of the *Plasmodium* species within the anophelines. The percentage of infected anophelines can be established on dried specimen without tedious dissection. However a non-neglectible percentage of false positive results has been recorded by several laboratories (14, 15, 16).

Monoclonal antibodies are available for the direct identification by IFAT on the dissection slide of several species of *Leishmania*. The sensibility and specificity of the method are very high (17). Specific identification of african Trypanosomes in tsetse flies and of *T. cruzi* in bug feces by DNA is now possible (18, 19).

DNA amplification by PCR has been applied to the identification of *Onchocerca volvulus* larvae (20).

In the area of genetic manipulations a bacterial gene was integrated in the genome of *Anopheles gambiae* (21). Moreover a strain of this anopheline refractory to *Plasmodium falciparum* has been selected in the laboratory (22).

1.3. High technologies in Ecology, Epidemiology and Control.

Isoenzymatic studies of *Triatoma infestans* have shown that specimens found in wild guineapig burrows are derived from domestic populations (86). The same method has brought some clarification on the identity of species invading the domestic environment when made free from domestics species by insecticide treatment (23).

The progress in the specific identification of *Leishmania* in sandflies has considerably clarified the cycles of the different parasite species. It is now possible to pair each parasite to a limited number of sandflies species belonging to one or two subgenus (24). These findings have open the way for a better ecological mapping of the disease (25).

The aim of enzymatic studies on insecticide resistance is to elucidate the enzymatic mechanisms involved and also to produce simple tests for an early detection of the phenomenon and if possible to predict its apparition (26).

The recognition of the different forms in the complex *Simulium damnosum* by cytotaxonomy was of paramount importance for the planification of the onchocerciasis control programmes (27). In West Africa the limits of OCP were first drawn according to the mapping of savana species of flies bearing blinding forms of the disease. The areas where forest forms were dominant were left out of the programme area because the disease was far less severe. When OCP grew out the primitive area the association of the disease with particular species of flies appeared more complicated. At the present time there is an urgent need for techniques to identify *Onchocerca volvulus L3* larvae from different origins.

2. Impact of environmental changes on vector borne diseases

2.1. Changes in the world environment.

Present fauna and flora result from an evolutionary process following tectonic movements and climatic variations. Man himself, the last to arrived, was the passive witness of two glaciation ages in temperate areas and of the alternance of heavy rainy periods and droughts in the tropics e.g. the Sahara desertification. The level of the oceans has been subject to variation which bridged Asia to North America, most of South East Asia islands with the continent, and made possible human migrations through the emerged lands.

Since the neolithic revolution, 10.000 to 15.000 years ago, man began to change the order of nature. The process was very slow for several thousands of years but bolted at the XXe century following the demographic boom and technological progress. Far from slowing down this process is expected to speed up in the near future because the world population which is now 6 billion will reach more than 10 billion by 2050. Moreover every inhabitant is asking for higher standard of living involving an increased industrial production.

For the first time it seems that man has a direct influence over the world climate. The combustion of fossil hydrocarbons, mainly oil, has brought about an increase of carbon dioxide in the atmosphere which is the origin of the green-house effect. The mean world temperature could increase by 0,5 to 2 Celsius degrees depending on the authors. Different predictive scenarii sometimes opposing have been proposed. The subject is highly controversial and a better knowledge of the role of the oceans, the main carbon reserve (in carbonate) is necessary to consolidate any prediction (28). Modifications of the ozone layer due to the use of CFC is also claimed to be a possible source of climatic disturbance by the ecologists but there is no consensus among the scientists.

Environment is changing very fast, mainly in tropical areas where demographic growth is in mean nearly 3% per year.Virgin lands are retreating before cultivation and large cities are rising in a few years. Repartition and ecology of vectors are changing because they are highly dependent on the environment. For the same reason their behaviour toward man is also changing. These changes can be detrimental or beneficial to public health.

The main aspects of world environment changes that concern vectors are :

- Clearing of vegetal coverage
- Manipulations of surface water networks
- Changes in cropping techniques
- Urbanization
- Environmental pollution
- International exchanges development
- World climatic changes

2.2. <u>Clearing of vegetal coverage</u>.

Forest clearing and burning was associated to the shifting cultivation for centuries. In the last 30 years there was an attack against the rain forest which is endengered to disappear in the next century. The clearing eliminates ombrophilic species like *Chrysops silacea* and *C. dimidiata* the loa loa vectors in Central Africa, the *Aedes* of the *africanus* group and *Haemagogus* vectors of sylvatic yellow fever, respectively in Africa and South Africa, the forest sandflies (*Psychodogygus, Nyssomia*) vectors of tegumentar *Leishmaniasis* in South America, some malaria vectors like *Anopheles dirus* in South East Asia (29, 30, 31, 32).

Woodcutters enter in contact with the natural foci of zoonosis and are at high risk of contamination by *Leishmaniasis* (33), yellow fever (34) etc.

The deforestation allows heliophilic species to become established. *Anopheles gambiae* and malaria in the South Cameroon forest were linked to man made clearing to settle villages, to build roads and to cultivate crops (35, 36). In Cote d'Ivoire, *Bulinus forskalli*, later *B. globosus* and finally *G. truncatus* followed the regression of the rain forest. As a consequence urinary schistosomiasis is now firmly established (37).

The clearing of forest galleries followed by land reclamation was an excellent control method of tsetseflies but it is no larger acceptable since the safeguard of these galleries is an ecological priority in Africa.

In the semi desertic areas of Africa (Sahel, Botswana) the overgrazing, followed by the trampling of cattle around wells made the soil impervious. When heavy rains fell, the cattle foot prints create innumerable breedings groots for *An. arabiensis* (30).

2.3. Manipulations of surface water networks.

Cisterns are often the only suitable places for vector breeding e.g. for *Anopheles gambiae* in Grande Comore Island (38), and for *An. arabiensis* (39) in Somalia. They harbour large populations of *An. stephensi* in South Indian towns.

Pipped water has improved health conditions and leads in India (40) and West Africa (41) to the elimination of guineaworm. But even when pipped water is available some people keep water reserves in jars and containers where *Aedes aegypti* breeds. These domestic mosquitoes are present at the start of dengue epidemics.

To answer the increased demand for food production and energy, a number of large and small dams have been built or are being built everywhere in the tropics and irrigated cultures tend to replace pluvial ones. A lot of redundant papers have been written on the impact of these water management projects on vectors, mainly in the increase in mosquitoes, snails, and sometimes blackfly populations and the establishment of new species, (30, 31, 42, 43). What should be kept in mind is that an increase in vector population is not directly correlated to an increase of the disease incidence. For example in the highlands of the Burundi, where malaria was rare or inexistent, rice fields provided suitable breeding places for *Anopheles arabiensis* and malaria became prevalent (44). In a region of Burkina Faso where malaria was holoendemic, the scenario was completely different. In the rice growing area the number of *An. gambiae* increased by seven times but nevertheless the parasite transmission decreased by four times because the sporozoite index of the anophelines was very low as compared with the areas outside rice farming project (46). This could be due to a reduced longevity of vectors depending on larval density or to the use of bednets by the farmers families. These two examples show the difficulty of predictive statements in development projects areas. It is clear that the evaluation of the vector population alone is not sufficient for epidemiological predictings.

We should also consider that the detrimental effects of development projects due to vector increase are overcome by an improvement in food supplies and in the income of farmers used for better health care facilities.

2.3. Urbanization and habitat.

When the income increases traditional housing is replaced by better houses unsuitable for Triatomids bugs (47). Modern houses are also unattractive for the resting of anophelines which become exophilic and have a reduced vectorial capacity.

Urban population is increasing at the rate of 6% per year in developping countries where more than 50% of the inhabitants will live in towns of more than 5000 people by the year 2000. This uncontrolled urban explosion makes almost impossible to build appropriate infrastructures to house the migrants. They live without water, proper housing and health facilities and are sometimes detached from the social communities. As far as vectors are concerned it should be pointed that :

- inside the cities, land is occupied by houses and infrastructure leaving little space free for anophelines breeding places.

- surface waters are polluted with organic matters and detergents which are detrimental for most of the mosquitoe larvae except *Culex quinquefasciatus* . This last species has no competitors (65) and few predators. Therefore it has become a pest in most of the tropical cities all around the world.

Generally malaria transmission decreases from the outskirts of towns to their center as illustrated in Bobo-Dioulasso, in Burkina Faso (48) and Brazzaville in the Congo (49). The notable exception is the urban malaria transmitted by *Anopheles stephensi* breeding in the domestic water tanks in the Indian subcontinent. The nearby rural areas are free of the disease.

Bancroftian filariasis transmitted by *Culex quinquefasciatus* occurs all around the Indian Ocean and in the Carribean. Its adaptation to urban environment has been well studied in Rangoon, Burma (50) and Pondicherry, India (51).

Water storage in the domestic environment depends on the traditional habits (52) and on the availability and reliability of piped water. The main mosquito found in domestic water supplies is *Aedes aegypti* at the origin of dengue epidemics.

Reduvids *Triatoma infestans* and *Panstrongylus megistus* are now established at a low level in the outskirts of a number of South American cities.

In Barquisimeto, Venezuela, a true urban leishmaniasis due to *Leishmania venezuelensis* occurs. The vector as well as the reservoir(s) are unknown. In the Eastern Mediterranean Region the outskirts of growing cities reach areas of zoonotic cutaneous leishmaniasis which is said to become urban, a questionnable statement (53).

2.5. Changes in cropping practices.

Tractors tend to replace animals for farming activities. The mosquitoes mainly fed on cattle and rarely on man in the past had to reverse their behaviour being forced to be more anthropophilic. It has increased their vectorial capacity and they became effective vectors in places where they were not so previously. This is illustrated by the well documenters case of *Anopheles aquasalis* in Guiana (54). In the near future such problems can arise in the Far East where the modernisation of agriculture implies its motorization.

The wet irrigation has been considered as a method to limit mosquito populations in rice fields. This practice is traditional in certains regions of China where they use human fertilizers but it can hardly be generalised (55).

In Cote d'Ivoire new coffee plantations have been settled far from villages after cutting patches of the primary forest. Farmers increase their contacts with tsetseflies alongside the ecotone of the forest edge and became infected with gambian sleeping sickness (56).

2.6. Environmental pollution.

Uncontrolled use of pesticide in agriculture mainly for cotton and rice crops, has selected insecticide resistance in many species of anophelines, some culicines (*Culex tritaeniorhynchus*) and even blackflies (*Simulium damnosum*) (57).

Health activities accounting for less than 5% of the insecticides used in the world have a very limited effect on the environment pollution. Insecticide used for house spraying is locked up in the wall mud. In the onchocerciasis control Programme where rivers are treated every week with Abate® and/or *Bacillus thuringiensis* , a special surveillance team of hydrobiologists concluded that after 10 years of treatment the fish stock had not been changed and that invertebrate biomass was only reduced by 20%. But the balance between species had changed (27).

The increasing use of pesticides and other polluting agents can lead to deep modifications of the ecosystems and nobody can predict what will be the effect on vectors. In France, the organic pollution of a small mountain river bring about multiplication of the blackfly, *Simulium ornatum* which killed cattle by its toxic bites alone (58). The same thing happened in several other places in Western Europe.

2.7. Traffic development.

Man has transported vectors, sometimes harbouring pathogenic agents, from one continent to an other for ages. It is the case of *Aedes aegypti* , *Xenopsylla cheopis* which have colonized the whole tropical world. *Anopheles gambiae* has established in Brazil, Mauritius, La Reunion.

With the development of air transport, the increase road and maritime traffic, no country of the world is safe from the importation of vectors and/or pathogenic agents whatever was the protective measures taken (59).

These imported vectors can establish themselves or vanish. It depends on their capacity to adapt to new ecological conditions, to competitors and predators. Recently *Aedes albopictus* established in USA (60) and the screw-worn, *Cochliomyia hominivorax* in Libya. *Anopheles gambiae* s.l. became established in the islands of Mauritius, La Reunion, Grande Comores in the last century (62). When the same anophelines were imported in the nearby Seychelles Islands they spontaneously disappeared (61). The African anophelines recently introduced in European airport also vanished without offsprings.

Experimental introduction of *Aedes albopictus* in an atoll of Polynesia was unsuccessfull in the presence of the local species *Aedes polynesiensis* (63).

Little is known about the risk of a new vector species to become established in a given area and no predictions can be made.

2.8. Climatic changes.

Scientists are very cautious in their predictions on the climatic changes due to the increase of the CO_2 content in atmosphere (28), the destruction of the ozone layer and a possible increase of world temperature. There is no doubt that the species distribution would be modified by temperature variations. Moreover parasite transmission could occur in places where the vectors are already present but where sporogonic cycle cannot be achieved because the temperature is too low.

The problem is becoming emotional. In the present state of knowledge it is not possible to make any reasonable predictions.

3. Difficulties in malaria control.

3.1. World malaria situation.

Malaria considerably regressed during the Global Malaria Eradiction Programme from 1955 to 1970. Of course its ambitious goal had not been fully reached but the disease had been eliminated from half of its distribution area. At the beginning of the seventies when it appeared that eradication was not attainable everywhere in the world the MEP was changed in the more flexible malaria control Programme. Each country had to define its own strategy. Some continued on the line of eradication, others reduced their activities to case treatment. Many took intermediate position.

Since 1972 malaria has spead across some of the lands which were freed by MEP. Epidemics occured in areas free of the disease for some ten to thirty years e.g. Sri Lanka, Swaziland, Plateaux of Madagascar etc. Moreover the case treatment became more difficult in many areas because of the development of drug resistance in *P. falciparum* : The long term drug prophylaxis is now almost impossible in most of the malarious areas. Travellers and technical assistants from industrialized countries are at risk to return home with severe forms of the disease.

The increase of the cases among tourists and technical assistants following drug resistance gave the impression that the disease was exploding. Moreover the medias have reported epidemics, with some exaggeration. WHO statistics were exentensively published.

So malaria is becoming a concern of international dimension calling for international solidarity. It is difficult to accept that some 2 million people (WHO estimation) die every year from a disease which could be cured so easily by available therapy and in many areas could be prevented through mass campaigns.

Even if individual treatments are easy, malaria control at the world wide level is a very difficult task because :

- the size of the problem ; more than 2 billion people at risk, 400 million parasite carriers, around 100 million cases per year with 90 million for Africa only (64).

- the epidemiological heterogeneity of the disease which does no allow a unique world wide strategy (66).

- the lack of alternative technical tools for vector control.

- the economic status of endemic countries ; some of the most affected are among the poorest of the world.

- the difficulties in getting international funding because in most cases the operations are not time limited.

- the lack of appropriate structures to implement the control measures and of motivated trained personnel to carry them out.

- the lack in many countries of the needed political willingness ; the trumpetted declarations in international assemblies are not always followed by implementation.

3.2. Tools for malarial control.

In the 1970's when MEP was cancelled, it was difficult to find an alternative strategy. A call for help was sent out to advanced laboratories. With the development of immunology, molecular biology and genetic engineering, it seemed reasonnable to consider the production of vaccine(s) and other advanced control tools.

Twenty years later this enormous amount of "high level research" has not yet produce anything that could now be used for malaria control. No vaccine is yet available and nobody wants to predict at what time it could be ready. Genetic manipulations of vectors have produced refractory strains (21, 22). But they remain laboratory curiosities until it is known how to release them in the field in competitive fashion to replace indigenous strains. This problem is far from being solved.

More progress has been achieved in drug development throught conventionnal methods e.g. Fansidar®, Mefloquine®, Halofantrine. But none of these drugs allow long term chemoprophylaxis (67). Industry should be stimulated in this field of research by outside funding. Because of the poor market outlook, the profit could not cover the heavy investment required. Furthermore new discoveries are not always protected by patents.

In vector control house spraying remains a useful basic technique in many countries, mainly in those where malaria is unstable . To replace DDT in resistant areas, O.P. (Malathion, Fenitrothion) Carbamates (bendiocarb, propoxur) and Pyrethroids (permethrine, deltamethrine, lambdacyhalothrine, cyfluthrine) are available. The prices of these compounds are higher than DDT (2 to 8 times) but the total cost of the treatment can be reduced by a rationalisation of the spraying taking in account the vector bionomics (68).

Impregnated mosquito nets are very promising for self protection (69). When they are used by all community members at large, they prevent disease transmission in the community (70). Excellent results have been achieved in China with deltamethrine impregnated bed nets (71). The cost of impregnation is low (less than 1 US $ per year) and can be afforded by most community members. If impregnated bed nets could become familiar equipment they would insure a long term protection of the users. The main limitations are the cost of the net itself and its social acceptability. In areas where the mosquito bites are scarce, most of the people are reluctant to sleep under a net even when malaria endemicity is high. Middle or long term pyrethroid resistance could appear and therefore other insecticides belonging to different chemical classes should be researched for impregnation.

Larval control can only be efficient against malaria in a very limited number of situations. Microbial preparations of *Bacillus thuringiensis* which are larvicidal have little future for malaria control. Because available formulations have no residual effect and breeding site treatment should be renewed every week. Integrated control, an addition of chemical and biological agents together with environmental management is mainly a larval control. It will remain speculative until serious experiments will have been carried out to evaluate its potentiality in terms of malaria control and its feasibility by health services or communities.

For the then next 10 years, no revolutionary new tool can be reasonably expected. Consequently available drugs and vector control methods should be properly utilized to alleviate the inacceptable load of malaria.

3.3. What can be done.

Facing the epidemiological polymorphism of malaria it is necessary to adapt the strategies to local conditions and to select the control methods which are likely to give the best results. It is not possible to have a single worldwide strategy. Each country should develop its own strategy, sometimes several strategies for different regions.

This preliminary but essential task can only be done through a sound knowledge of disease epidemiology, transmission patterns, vector ecology, susceptibility of parasites to drugs and vectors to insecticides, financial capabilities and operational structures etc. The procedures of stratification have been described by WHO (72), often in a too complicated and discouraging manner.

After selection a method for vector control has to be field tested in the area where it will be employed to evaluate its efficacy according to local ecological conditions. Such field experiments or pilot projects are not very popular but it is the only way to ensure that the selected method is the most appropriate for any particular area.

The implementation of a control programme needs structures able to carry out the selected control methods. Of course they are not the same for case treatment and for vector control. The dialectic quarrels between vertical and horizontal strategies should be overcome. Without adequate structures there is no hope to obtain any results.

It is not needed to further stress the importance of competent and motivated personnel. Training facilities should be established at all levels.

Financial problems should be resolved at the planning stage but successful results during the operations can attract more money to the programme from the governement or from external sources.

3.4. What can be expected from a malaria control programme ?

It will depend from the strategy chosen, the methods applied and from the epidemiological context (in a broad sense).

a) Case treatment for cutting down malaria mortality is the first priority ; it can be adapted to places without diagnostic falicities through the presumptive treatment of all febrile cases. Drug resistance has made the case treatment more difficult in several areas of the world but it remains possible in all health centers provided there are enough drug provisions for treatment. Case treatment also decreases the morbidity because treated patients recover rapidly.

b) The prevention of morbidity relies in chemoprophylaxis (recommended only for pregnant women) and in vector control. The result of house-spraying is different from an area to another according to vector biology. Moreover many countries cannot afford the insecticide treatments. Impregnated mosquito-nets offer an alternative for both people protection and vector control. We have discussed ealier their limitations.

c) The elimination of the parasite through vector control was the goal of MEP. In places where it has been obtained, a surveillance should be establish to avoid the resurgence of the disease.

Equivalent results cannot be expected from all the malaria control programmes whatever was the technical input. At the very beginning of a programme, an estimate should be made of the degree of control that could be expected. Different scenari can be imagined and their cost/effectiveness evaluated.

3.4. Research needs.

New tools are urgently needed for malaria control and I would not give another list of research priorities which have been repeatedly published. I wish only to draw the attention on three points.

a) The necessity of encouraging industry for the development of new drugs for case treatment, the highest priority.

b) The establishment of a double flow between the advanced laboratories and field workers on the basis of the equality of partnership to fight against the tendency of segregation which is developing between the two categories of scientits. Field workers are too often nothing more than collectors of biological material for laboratories.This attitute is also detrimental for advanced laboratories which are often suffering from a lack of expertise on the epidemiology of the disease.

c) The need of high level epidemiological research. Under this wording we place transmission pattern, vector ecology, human behaviour as it was at the beginning of the century. It is the *sine qua non* basis to develop rational programmes in the present and to adapt laboratory discoveries to field constraints.

4. Conclusions.

Malaria is highly representative of the problems of development. Of course the actual arsenal is not satisfactory but the available tools could avoid the mortality. They are not fully used because many countries cannot afford them or have no appropriate structures to implement control programmes.

Malaria with its 2 million death per year is becoming highly interpelative for rich countries. Help can be expected through international solidarity. However the lack of limit in time of the projected actions is discouraging for some donors.

Malaria allows us to compare the tremendous achievements in hightechs and the difficulties to solve minor problems. This is food for reflection. On one part the great scientifie discoveries and on the other the world population need. This is clearly illustrated by the technological distances between the bright laboratories and the field where patients cannot obtain the few tablets of drugs required to ease their suffering.

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