



WHO/CDS/CSR/EPH/2002.8

STRATEGIES FOR THE CONTROL AND ELIMINATION OF RABIES IN ASIA

Report of a WHO Interregional Consultation

Geneva, Switzerland
17-21 July 2001

World Health Organization
Department of Communicable Disease
Surveillance and Response

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1. Introduction

The Consultation was opened by Dr David Heymann, Executive Director, Communicable Diseases. He stated that rabies still represents an important public health problem in certain parts of the world, especially in Asia. Nevertheless, in the field of Communicable Diseases, rabies ranks far behind the current and future priorities of WHO when considering their public health impact expressed in terms of mortality, morbidity and disability adjusted life years (DALYS). Rabies is perceived by many high ranking/decision making public health and animal health officers in developing countries as a "rare disease of humans" resulting from the bite of a non-economical animal, (the dog) and falls "in between 2 stools". For all of these reasons rabies is a neglected disease yet has many of the characteristics of a disease on which we could have a significant and rapid impact.

Rabies is:

- a vaccine preventable disease (in both humans and animals);
- a disease of poverty affecting very vulnerable often remote/isolated rural populations;
- a disease of young people (mostly affecting the age class 5-15 years);
- today more people die from rabies than from yellow fever, dengue and Japanese encephalitis combined.

Dr Heymann reminded participants that to date, WHO has organized a number of WHO Expert Meetings dealing with the feasibility of rabies elimination. These meetings dealt mostly with the scientific and technical aspects of the problem but the present meeting was of a different nature particularly because many groups and organizations likely to be interested and involved in a new initiative had been invited to contribute to the outcome. The following organizations were mentioned and thanked: Organization International des Epizooties (OIE), the International Federation of Pharmaceutical Manufacturers (IFPMA), the Rockefeller Foundation, the Mérieux Foundation, the World Veterinary Association, (WVA) and representatives from pharmaceutical companies (international and national) producing rabies biologicals.

Finally, Dr. Heymann stressed that a number of advances in rabies control had been reported recently in certain Asian countries and that more and more governments, often under general public pressure, were becoming interested in improving the situation vis-a-vis rabies. Therefore WHO considered that the time has come to assess the interest of various groups, organizations, and institutions to establish a partnership and agree on a common strategy for rabies control and elimination in certain countries.

Dr Elizabeth Miranda, Rabies Research Programme Leader and Head of the Veterinary Research Department, Research Institute for Tropical Medicine, Alabang, Philippines and Dr Rattan Ichhpujani, Head Zoonoses Division, NICD, New Delhi, were nominated and accepted to serve as Chair and Co-Chair of the Consultation respectively. Dr Naseem Salahuddin, Department of Infectious Diseases, Liaquat National Hospital, Karachi, Pakistan and Dr Ziauddin Ahmad, Rabies Control

Programme Manager, Dhaka, Bangladesh accepted the nomination of rapporteur and co-rapporteur respectively.

The Consultation was expected to:

- assess the current situation and identify the strengths, weaknesses opportunities and challenges which Asian countries possessed or faced in relation to rabies control;
- identify the tools and mechanisms available to ensure availability and affordability of human and animal vaccines as well as rabies immunoglobulin and alternative rabies biologicals in the short and long term;
- if considered feasible, to propose new strategies and identify partnerships required for the control and eventual elimination of rabies in Asia in humans and animals.

2. Assessment of the current situation and future needs

2.1 Overview

Centralized well-equipped laboratories with trained staff exist in many Asian countries, but the lack of awareness from both health professionals and the public, as well as communication difficulties, prevent collection of complete information on the real number of human rabies cases within a country, particularly in rural areas, thereby affecting some countries disproportionately. Even in Thailand, which has excellent laboratory diagnostic facilities and well-trained health professionals, the number of human cases diagnosed by clinical observation able to be confirmed as actual cases by laboratory analysis is quite low (27%). The highest estimates of the number of human rabies fatalities are from countries with the largest human populations, and very limited rabies prevention and control activities such as Bangladesh, India and Pakistan, where it is estimated that a total of 40,000 deaths occur each year. In addition, these countries have weak surveillance systems, so that the true numbers can be expected to be even higher.

Some countries providing reliable rabies mortality data (at least in parts of their territory) have reported significant decreases in the number of rabies deaths over the past decades. In Thailand, the number of deaths due to rabies decreased steadily, from 370 in 1980 (0.78 per 100,000) to 185 in 1990 (0.33 per 100,000) and 57 in 1998 (0.1 per 100,000). In Vietnam, the number of treated patients increased by 63% during the last 10 years while the number of rabies deaths decreased by 76% from 500 deaths/year (0.6 deaths/100,000 inhabitants) in the early 90's to less than 50 deaths (<0.1/100,000 inhabitants) in 1999-2000. Conversely the Philippines has observed a 20% increase in human deaths from rabies during the past 5 years. These increases may reflect real trends and/or increasingly effective surveillance of rabies cases.

The main route of transmission is through the bite of rabid dogs. In the Philippines, Thailand and Vietnam, where the animal species responsible for fatal human cases are recorded reliably, dogs are responsible for 94-98% of deaths.

Optimal conditions for surveillance of rabies in animal species are met in only a few countries. In countries with one or several diagnostic laboratories, the rabies status in animals of large areas remains unknown often because of their remoteness, or lack of appropriate and sustainable systems for sample collection, preservation and shipping. Nevertheless, several Asian countries have made real progress in animal rabies surveillance during the last five years. In other countries in this part of the world, despite the availability of basic laboratory facilities, equipment and training, the number of rabies cases reported in animals is inadequate to be used as a basis for the design and initiation of a rabies control programme. These countries include Bangladesh, Cambodia, India, the Lao People's Democratic Republic, Mongolia, Nepal and Pakistan. In most countries, Ministries of Agriculture give priority to livestock production and information on the dog population is usually poor. The dog population in these countries can be categorized into three groups: owned dogs; community dogs (living in public areas and fed by the population) which can be reached by control measures under certain conditions; and ownerless strays which usually escape control programmes. According to a dog population survey carried out in 1999 in Bangkok, Thailand, there were approximately 650,000 dogs living in the area, 20% of which were ownerless. The total estimated dog population was 6.7 million in Thailand in 1995, 13-16 million in Vietnam (80% in rural areas, 20% in cities), 1 million in Cambodia, and over 24 million in India.

Most patients who die from rabies are either not treated or do not receive timely and appropriate post-exposure treatment. In children, many dog bites are not reported and may go completely unrecognized or be discovered late by both parents and health care providers. Consequently, exposed children often do not receive post-exposure treatment at all or receive untimely or incomplete post-exposure treatment.

Modern rabies vaccines produced on cell cultures or embryonating eggs are safe and effective. Some Asian countries have moved towards modern rabies vaccine usage, either through imports or local production. In Thailand, discontinuation of sheep brain vaccine (Semple vaccine) production in 1989 and of suckling mouse brain (Fuenzalida) vaccine in 1993 and importation of increasing quantities of modern vaccines have played a major role in the drastic reduction in the number of cases of human rabies in this country.

Similar decisions were taken in Sri Lanka and the Philippines in 1995 and 1997, respectively. In Indonesia, during the past 10 years, post-exposure treatment has been carried out mostly using imported modern cell-culture vaccines.

However some Asian countries where canine rabies is endemic still produce and use vaccines produced on nervous tissue. Sheep brain vaccine (Semple vaccine) represents most of the rabies vaccine used in Pakistan, an estimated 70% of rabies vaccine doses used in Bangladesh, and 45% of those used in India today. In Vietnam, vaccine based on suckling mouse brain (SMB vaccine) is predominantly used.

These vaccines, which are provided usually free of charge in these countries, are mainly administered to the poorer segment of the population. With the increasing public awareness about rabies and knowledge that modern vaccines provide better protection and safety, health staff in major public and private hospitals or rabies vaccination centres have to face an increasing demand for better vaccines from all

layers of the society, including the most vulnerable groups. In Bangladesh, where nervous tissue vaccines are still used, the number of doses of brain tissue vaccine used has increased less rapidly than those of modern vaccine during the last 5 years. In India, brain tissue vaccines represented about 90% of all vaccine doses used in the mid 80s, 50% in 1995 and about 45% today, whereas the total number of brain tissue vaccine doses used remained stable.

Although the main reason for using brain tissue vaccines is their lower production cost, it was shown that their real cost and their storage and administration costs are underestimated. On the other hand, the cost of modern vaccines has been continuously decreasing, due to an increase in production and escalating demand.

Moreover, most patients in Asia who have received single or multiple transdermal bites do not receive the necessary rabies immunoglobulin, because of a permanent global shortage and its high price, which makes it unaffordable to most patients in countries where canine rabies is endemic.

Systematic vaccination of infants and children could be a solution to these problems in countries or areas where canine rabies is still endemic and has not been controlled by conventional methods.

Rabies control in dogs remains the only long-term, cost-effective means of eliminating or preventing most human cases. Human public health preventive measures should be paralleled by programmes for dog rabies control.

Strategies for dog population management and control have to be adapted to the cultural and social aspects of each country or area. In Asia, as in many other parts of the world, dog population reduction policies are extremely unpopular. Several countries, including Indonesia, Malaysia, the Philippines, Sri Lanka, and Vietnam, have ongoing dog control activities, all over their territory or in localized areas. Elimination of ownerless dogs is rarely practised on a large scale in these countries, and usually affects an insignificant proportion of the entire dog population. The conventional approach consists in mass parenteral vaccination of dogs, with efforts to improve vaccination coverage each year. In Malaysia, dog vaccination is carried out within an 'immunity belt' along national borders. In the Philippines, a pilot rabies elimination programme is currently being conducted in the Visayas. In Vietnam, the programme is focusing on the most heavily populated urban areas (such as Hanoi, Ho Chi Minh City and the Mekong Delta region). In these countries and areas, dog vaccination coverage is estimated to range from 10% to 94%. This wide range illustrates the need to enhance both the efficacy of mass vaccination campaigns and use of reliable methods for evaluating the coverage.

2.2 Analysis of weaknesses and opportunities for rabies control in Asia

Canine rabies is almost entirely limited to the developing world. In order to realize the eventual goal of rabies prevention and control, we must first outline the present weaknesses associated with developing a rabies control programme in Asia and focus on the opportunities available to overcome them.

2.2.1 Weaknesses

-Insufficient surveillance systems

Rabies is not a notifiable disease in humans and animals in most developing countries of the region and therefore accurate mortality data are unknown. Due to this fact, rabies is ranked low on the priority list for disease control programmes. Additionally, the number of rabies diagnostic laboratories is limited, most are poorly equipped and lack essential quality assurance programmes. Thus the reliability of current epidemiologic data is questionable.

-Limited accessibility of modern rabies vaccine and supply problems

Due to the high cost of modern cell culture rabies vaccines, outdated nerve tissue origin rabies (NTO) vaccines are still administered to most socioeconomically disadvantaged people who are at an increased risk of exposure. Additionally, most modern cell culture rabies vaccines are imported into developing countries and because many countries impose a "luxury" importation tax to them, the cost of treatment is increased.

The continuous supply of rabies vaccine is unpredictable in major urban health care facilities and worse in rural health centres. At least 55% of a community's budget for their canine rabies control programme is usually spent on vaccine procurement. The continuous and rapid dog population turnover and limited parenteral vaccination coverage prevents total protection.

-Lack of public awareness

The lack of effective health education programmes results in a low degree of awareness of the disease burden and the methods necessary to prevent and control rabies. Low awareness also causes poor community participation in local rabies control programmes. Any and all effective public education programmes must consider cultural, religious, and political factors.

-Insufficient political commitment

In developing countries, rabies control programmes are a low priority when compared to economic development. Generally there is no clear responsibility and budgetary allocations for rabies programmes in either Ministries of Health or Agriculture. Additionally, the costs of rabies elimination campaigns fall short of similar cost/benefit programmes when compared to food production and human health programmes like TB, malaria, HIV/AIDS and EPI. Finally, prevailing political and economic situations in countries where rabies poses a significant health problem conditions usually interfere negatively with rabies control programmes.

2.2.2 Opportunities

-Utilize models of successful rabies control programmes

Rabies prevention and control programmes have already eliminated rabies in several countries and areas, including Japan, Taiwan and peninsular Malaysia. The operational strategies and cost/benefit analysis made for these programmes should be used as a model for developing countries where canine rabies continues to be endemic.

-Utilize current safe and efficacious vaccines

There is no immediate need for a new animal or human rabies vaccine since the currently available vaccines have a long track record of proven safety and efficacy.

-Increase the number of patients receiving modern cell culture vaccines

The use of intradermal (ID) regimens in large anti-rabies clinics has dramatically reduced the cost of post-exposure treatment (PET) and enabled some developing countries to stop the use of neural tissue origin (NTO) vaccines.

-Mobilize the support of the civil society, private sector and government sponsored initiatives

Increasing the coverage of public education can be achieved by using commercially available media (radio, TV, printed material). Additionally, public and /or private initiatives for the transfer/acquisition of technology for local production of human and animal rabies biologicals through joint ventures between private companies or private and public enterprises should be supported.

-Secure existing expertise on rabies

Rabies experts have already developed innovative technologies and have the expertise to develop strategic plans to control rabies in Asia.

2.3 Review of existing tools/methods for human and dog rabies control

In order to control and prevent human rabies in canine rabies endemic countries in Asia, there are at least five requirements that need to be fulfilled including:

- consistent availability of modern effective cell culture rabies vaccines for humans and for animals;
- an increased awareness in the public, and in the medical profession of rabies and effective methods of control and prevention;

- implementation of dog control programmes and elimination of canine rabies;
- eliciting of political support;
- improved surveillance.

In fact all of the tools and methods necessary to fulfil the above requirements for rabies prevention are currently available.

-Promoting human rabies prevention with modern vaccine

It is clear that human rabies can be successfully prevented through the use of modern highly potent cell culture rabies vaccines. These vaccines were developed over two decades ago and yet NTO vaccines are still used in well over a million people every year in Asia and most human rabies deaths occur as a result of the lack of receiving any post exposure treatment (PET). The cost of PET with highly purified cell culture vaccines has been dramatically reduced through the use of intradermal regimens, proven to be highly efficacious. Although some countries have replaced NTO vaccines with low cost intradermal regimens, more lives could be saved if the use of these regimens was expanded. NTO vaccines are still the mainstay of post-exposure treatment for low-income people in the public sector of most Asian countries and are administered to well over one million patients annually. The cost of grading current NTO vaccine production facilities in order to produce cell culture rabies vaccines is beyond the financial budget of most governments. 'Banning' the use of NTO vaccines alone should not solve the problem as this would remove access to the only PET available to many patients unable to afford cell culture vaccines. A more realistic approach will be to phase out the use of NTO vaccines through advocacy and by a gradual replacement within a given period of time with lower cost, reduced volume regimens of cell culture vaccines. Additionally, anti-rabies clinics need to be remodelled and/ or restructured and staff re-trained in order to replace administration of NTO vaccines with cell culture vaccines.

-Changing public and health care workers perception through education

One of the most important points in rabies prevention concerns the level of awareness in both the medical profession and the general public. Programmes that use imaginative 'information highways' like schools, religious and other local organizations and meetings have had some impact in increasing awareness. However, more emphasis is needed on the development and implementation of national guidelines for rabies prevention to meet each country's needs. These types of documents can be secured from countries with similar guidelines in place as well as from WHO. Other methods to increase rabies awareness should include specific rabies information given to medical students, long distance learning through various international internet sites, the utilization of currently existing 'mother and infant' programmes, and public media spotlights. The most important points are that the means by which to convey the message of awareness are already in place, and it is the motivation to do so that needs most to be encouraged.

In India beginning in 1985, a major educational campaign has provided educational awareness regarding rabies prevention to physicians and the general public. Through this programme, physicians have become more confident in providing appropriate PET at private clinics instead of sending patients long distances to anti-rabies clinics. In addition, the campaign has had a significant impact on replacing dangerous and ineffective "folk treatments" with modern cell culture rabies vaccines. As a result of the educational campaign, the percent of patients in India that receive NTO vaccines has declined from almost 100% to approximately 50%. This programme was mainly sponsored through industry and is an example of how partnerships between industry, governmental agencies and medical officials can provide critical financial and educational support to reduce the number of human rabies fatalities in developing countries.

-Increasing activities for dog rabies prevention

Dog vaccination and control programmes may be a difficult undertaking but should not be regarded as an impossible task. Parenteral and oral vaccines and programmes can protect dogs against rabies and consequently reduce human rabies deaths. The expertise to formulate a strategy to successfully eliminate the cycle of rabies in dogs already exists within the rabies community. One very successful example of an ongoing parenteral vaccination programme is in Latin America where the continuing reduction of canine rabies has significantly reduced the number of human deaths and eliminated the disease in humans in many urban centres. Additionally, Sri Lanka has recently initiated a canine oral vaccination programme. There are numerous documents available from WHO and other sources that outline the essential components of a successful canine vaccination and control programme.

These successful programmes were dependent upon:

- Sustained political commitment and financial support to dog rabies control programmes
- Strengthened surveillance data
- Implementation of new diagnostic technologies
- Understanding dog dynamics, and
- Strengthened intersectoral coordination.

In order for a similar programme to be implemented in Asia, it will be important to have a better understanding of the structure of the dog population.

-Eliciting political support

Eliciting political support must come from within individual countries accompanied by continuing pressure from WHO. However, the most important influence for political change will have to originate from private citizens, medical professionals, and agricultural and health ministers within each country.

-Strengthening rabies surveillance and evaluating the rabies burden

Currently the number of human rabies fatalities is underreported for many reasons including:

- Cases of paralytic rabies may not readily identified by medical staff;
- Patients die at home and rabies deaths are not reported;
- Cases are not recorded at a local, national; and/or international level;
- Patients do not seek treatment or seek treatment from local folk healers.

Data on surveillance of human rabies deaths need to be collected for distribution to support advocacy for rabies prevention on a global scale. Thus rabies needs to be a notifiable disease in all countries.

Due to these facts, the true economic impact of human rabies is unknown. Disability-adjusted life years (DALYs) is a standardized method that permits comparison between different diseases and populations. DALY's is a method to assess the cost of a disease in terms of cost per DALYs lost. In addition, DALYs can account for both disability and death, and measure the age-specific burden of death. DALYs have been used to analyse the impact of a number of diseases and recently have been used to assess the impact of rabies in Tanzania. The result of the DALYs analysis conducted in Tanzania revealed that the annual incidence of rabies may be equivalent to as many as 4.7 human deaths per 100,000 whereas the incidence reported by the Ministry of Health as 0.04 per 100,000. Expanding the use of DALYs into Asian countries should be considered a viable method to increase the global awareness of rabies.

-Strengthening research and development on rabies biologicals

Most human rabies cases occur because no PET of any kind is used; rabies immune globulin is unavailable or unaffordable; local vaccines are less than ideal; treatment is significantly delayed or inappropriate; or acute illness, malnutrition, or other underlying conditions compromise appropriate immune responses.

Compounding this dilemma is a regulatory focus on the safety of modern biologicals and human serum products. Methods intended to maximize immune globulin safety through purification by the removal of extraneous substances, or the inactivation of contaminants, may have an untoward effect, even when testing shows little or no effect upon absolute antibody concentration, *in vitro* virus neutralization, nor adverse health effects when administered to healthy humans. With the continued maintenance of endemic dog rabies, discovery of new lyssaviruses, recurrent mass exposure events, and the realities of disease control in a developing world, public health demands will continue to challenge the immune globulin market.

Given these issues, immediate additional focus is necessary to address basic health concerns, to promote the local production of equine immune globulin, and to develop future pure, potent, safe, and efficacious alternatives to current rabies

immune globulins, so that any new paradigm shifts may be made more widely available and economically realistic.

3. Working Groups

3.1 Terms of reference of the Working Groups

Each group was assigned one of the following four subjects to discuss:

- Improving the access to human and animal rabies biologicals: availability of biologicals; the shortage of rabies immunoglobulin (RIG); affordability of biologicals (direct and indirect costs - route of administration, etc.); quality of biologicals (production - application).
- Improving the delivery of rabies biologicals to humans and animals: the role of health care providers' and veterinary assistants' and their availability and training; density of anti-rabies treatment centres (primary health care level or higher and dog vaccination centres; contribution of the private sector, types of vaccines and regimens).
- Changing public perception to rabies control and prevention: public awareness; target populations and socioeconomic classes vis-a-vis PET; preventive immunization oral vaccination and dog rabies control including dog population management (including destruction).
- Eliciting support and political commitment by discussing prerequisites: development of a convincing proposal (defining the contents); other advocacy documents; the means available (e.g. ministerial conference, regional resolution, World Health Assembly resolution); potential funding agencies (foundations and governments) to approach; other partners to include

Each group was asked to identify and prioritize rabies strategy sub-components .

3.2 Summary of reports from Working Groups

3.2.1 Promote human rabies prevention:

-Increasing availability of modern rabies biologicals for human use

The objectives are to improve access and effective delivery of PET to those who require it most. To this goal vaccines need to be affordable to the population most at risk, generally people having very low annual income.

To increase modern rabies biologicals availability strong consideration should be given to commercial vaccine bulk transfers, grouped regional purchases, and tariff reduction for the direct acquisition of these products; In parallel existing NTO vaccines should be discontinued and as they are gradually phased out, they

should be replaced by either the purchase of commercial products on the world market or via local production of modern biologicals.

The use of less expensive intradermal regimens is strongly encouraged. In order to facilitate the use of intradermal vaccine schedules, the current WHO vaccine regimens should be simplified. In addition, WHO should encourage the transfer of ID technology to developing countries.

Current WHO policy regarding their Expanded Programme on Immunization (EPI) vaccines requires that open multi-use vials used in immunization be kept for a maximum of 6 hours. Considering that rabies vaccine is not currently a part of the EPI list of vaccines, national health authorities may consider using reconstituted vaccine vials at 2 - 8° Centigrade for no more than 7 days provided that studies have demonstrated the safety of the procedure under local conditions and that these conditions can be maintained in a sustainable manner.

Combined with local wound care, and modern vaccines, the administration of RIG is an essential component of PET. The cost of human RIG diminishes its utility in most developing countries. Heterologous products, such as equine RIG (ERIG), have been demonstrated to be safe, effective and more affordable biologicals. However, severe commercial shortage of ERIG is anticipated, and current supply are projected to last for only 1-2 years. Today only few Asian countries can produce RIG to meet projected demands. Local production of RIG should immediately be strongly encouraged to compensate for impending shortages.

-Improving delivery of modern human rabies biologicals

There should be an effort to decentralize and expand human and animal rabies clinics. In order to allow patients with low incomes to have access to rabies vaccines, modern rabies vaccines should be administered free of charge or at the least possible cost. The cold chain system should be maintained at all facilities.

Due to the fact that intradermal vaccination is cost effective, extending its use into smaller hospital centres should be considered. In addition to the above extending the length of time that a vaccine can be stored after reconstruction requires that a physician is responsible for ensuring that the sterility of the vaccine is guaranteed by maintaining the consistent use of sterile techniques and adequate refrigeration conditions. The logistics of vaccine delivery should be rationalized in order to increase availability.

The number of vaccine vials used and ID doses applied should be recorded in order to increase surveillance data. The data collected at the local level and analysed at the national level should be provided back to local level for readjustment of rabies strategies.

-Supporting preventive immunization of certain age groups

Due to the fact that between 40 to 60% of rabies victims are children under the age of 15, this age group should be considered a top priority. In case of other individuals or groups at risk, pre-exposure immunization should also be considered.

-Changing current public perception regarding rabies prevention and control

Key activities for public education should include increasing rabies awareness through media activities, fund raising, and education programmes. Examples of media activities could include TV, radio, printed materials, movies, press releases, celebrity endorsements and commercial sponsorship. Fund raising activities could be coordinated through nongovernmental organizations (NGOs), as well as through the private sector. Public awareness activities should prioritize those most at risk of exposure including: the underprivileged segments of society, school children, animal control workers and veterinarians. In addition, rabies education should extend to medical and veterinary students and professionals, health care providers, and politicians. Country specific and language specific messages regarding responsible dog ownership and appropriate PET are essential.

3.2.2 Promote dog rabies control and elimination:

-Increasing dog vaccination coverage

In order for successful programmes to be implemented in Asia, it will be important to have a better understanding of the structure of the dog populations. Different strategies can be used for launching dog mass immunization campaigns such as:

- Expansion: Vaccinate dogs in a limited area and then slowly expand to cover larger areas.
- Global: Vaccination covers a large part or even the entire country immediately.
- Hot spots: Vaccination is initiated in geographically separated areas characterised by a high incidence of rabies in animals and humans. The areas are then extended.

The purity, potency, safety, efficacy and cost of existing modern rabies vaccines appear adequate to meet the projected needs for programmes directed toward mass immunization of dogs.

Although the preferential vaccine for dog immunization should be parenteral inactivated tissue culture (given by intramuscular (IM) route), oral vaccination should be used whenever there is a high population of inaccessible dogs. Further field studies are encouraged to assess safety, efficacy and economics of oral vaccination in dog-rabies endemic countries throughout Asia. In addition WHO should continue to endorse oral immunization for dogs.

The private sector should be involved in dog rabies control programmes. Any and all human rabies deaths should be investigated. As part of rabies outbreak follow-up, all neighbourhood dogs if not directly exposed should be vaccinated and there should be an investigation as to the reason for the human death in order to increase public awareness. There should be regular meetings of the local rabies control programme authorities which should include veterinarians, physicians, and others in order to facilitate continuous cooperation and in-service learning.

Dog vaccines should be administered free of charge. In addition the 'import' tax on rabies vaccines should be eliminated where it exists.

-Managing dog populations

WHO has expressed its strategy regarding dog population management in Annex 4 of the eighth report of the WHO Expert Committee on Rabies (WHO, Technical Report Series 824, 1992). There are 3 recognized practical methods for dog population management: movement restriction, habitat control and reproduction control. Capture and removal of dogs are no longer considered effective direct control measures. Indirect benefits may be obtained by selective elimination of unvaccinated dogs that are not in compliance with control regulations and may accumulate around markets, abattoirs and food industries. The World Society for the Protection of Animals (WSPA) and the International Association of Human-Animal Interaction Organizations (IAHAIO) have developed strategies, training methodologies and dedicated resources to promote in collaboration with WHO, dog population management and responsible dog ownership activities as an integral part of national rabies control and elimination programmes.

3.2.3 Strengthen rabies surveillance

The first priority is to have strong advocacy for global awareness of rabies. As part of the advocacy process, there is a need to increase rabies surveillance. Therefore rabies should be a notifiable disease and be included in the integrated communicable disease surveillance system. In addition WHO should provide technical assistance to strengthen the surveillance system for rabies.

The surveillance data should include both human and animal rabies cases plus data on rabies exposures and human post-exposure treatments.

There is a need for regional and national laboratory networking and quality assurance programmes to ensure collection of more reliable data

3.2.4 Promote research on human rabies biologicals

Additional basic and applied research approaches are necessary to develop and evaluate new human vaccine candidates, practical alternatives to existing veterinary biologicals, and additional methods of product delivery. These include, but are not limited to, monoclonal antibodies, DNA vaccines, novel expression vectors, immune potentiators, needleless applications, etc.

For example, one of the most promising practical existing alternatives to RIG production is monoclonal antibody technology. Immediate and committed focus is crucial to evaluate the feasibility of such an approach. The creation of a specialized working group consisting of qualified WHO Collaborating Centres and other relevant parties with the possession of monoclonal antibodies against lyssavirus, tasked with the creation of a well-characterized international cocktail of monoclonal antibodies equivalent, if not superior, to current RIG, products is recommended.

Any new RIG products or alternatives should receive increased scrutiny. Any equivocal results obtained between laboratories should be reviewed objectively, and, if necessary, experiments repeated by a qualified WHO-confirmed third party.

Cost-effective technology transfer of local RIG production is critical, as is the utilization of modern methods directed to rabies vaccine manufacturing, such as micro-carrier and perfusion-based systems. Qualified WHO Collaborating Centres, NGOs and Foundations should support these efforts, particularly in those Asian countries where the needs are greatest and the necessary infrastructure and political exist. Concomitantly, potential commercial partners need to be solicited with the assistance of WHO, to produce the monoclonal cocktail at an affordable price.

Additionally, requests for direct country participation should be elicited for the design and conduct of relevant clinical trials as product development ensues.

4. Strategy

Prevention of rabies can only be achieved by:

- Securing political and financial support for effective rabies control programmes in countries that do not currently have a strong programme in place.
- Initiating a successful advocacy programme to increase global awareness on the burden of rabies in humans and animals.
- Developing/refining new tools (e.g. post-exposure regimens and biologicals) particularly for human treatment, oral vaccines for dogs and techniques for effective and humane dog population control.
- Developing and implementing in each country a national plan for the prevention of rabies in humans and animals.

Implementation of this strategy will require that certain preliminary steps are taken.

These are:

4.1 Establishing a coordinating structure at international, regional and national levels

A structure was set up at the international and regional levels, under the WHO, to take responsibility for developing an interregional programme for rabies control and elimination (see diagram attached as Annex 3).

This structure would spearhead rabies control initiatives, which include the development of a proposal for submission to funding agencies, obtaining mandates from governments of countries within the Regions, and the preparation of a technical paper for submission to the Executive Board of the WHO. The structure should comprise one or more rabies specialists based at WHO Headquarters, Geneva, Regional WHO representatives, at least a member from each of the designated countries in the programme and other interested partners. A key element of the first phase would be the completion and analysis of available data on human and animal mortality and computing the disease burden of rabies in the relevant countries.

At the national level each participating country is strongly encouraged to take steps which should include, but not be limited to:

- the appointment of (a) person(s) in the department of the Ministry of Health (and Agriculture) responsible for rabies;
- the establishment of an effective interministerial committee for rabies control;
- the development of a national rabies surveillance system;
- compulsory domestic dog vaccination and stray dog control (and immunization if feasible);
- the discontinuation of the production and use of Nerve Tissue Origin (NTO) vaccines; and
- the implementation of public and health care workers education programmes.

4.2 Soliciting political global support

Emphasis should be placed on:

- Rabies as a horrifying, incurable, fatal disease, incomparable with other diseases addressed by WHO, and with the disease burden falling most heavily on children.
- The availability of tools to eliminate the disease. Rabies is an entirely preventable disease.
- Available surveillance data that underestimates the true number of deaths.
- A comparison of the estimate of the rabies death toll and disease burden with other diseases should be provided together with an estimation of the global figure for human rabies deaths with a breakdown by region.
- A study to estimate of the economic burden of rabies, with results of economic analyses, including cost-benefit and cost-effectiveness analysis of control strategies, should be carried out by an economic consultant.

4.3 Developing national plans for rabies control

National plans should include the following components:

- Access to modern human vaccines and application of new economical post-exposure treatments.
- Rabies surveillance and the collection and processing of data at the national, regional and global levels.
- Intersectoral collaborative efforts for the control of rabies in dogs at the national and regional levels.
- Plan to increase public and health care workers awareness regarding rabies control and prevention.
- A detailed budget covering a 3 to 5 year period.
- A time frame and targets for each year.

Political commitment and leadership for the national plan should be through the Ministry of Health, with additional partnerships that are appropriate to implement the programme within each country. The participation of the Ministry of Agriculture is especially required as well as the Ministries of Local Government, Finance, Law, and Environment. Relevant national and international NGOs and other agencies should also be invited to contribute.

4.4 Building partnership and mobilizing resources at the global level

- A partnership should be forged with relevant pharmaceutical companies.
- The partnership should be expanded with a closer collaboration established between animal and human health organizations, with attendance of WHO representatives at the Office International des Epizooties (OIE) and the Food and Agriculture Organization of the United Nations (FAO) meetings and vice-versa.
- Once the proposal is developed, an advocacy specialist should be consulted for the best way to present the proposal to funding agencies and other potential partners such as: Global Alliance for Vaccines and Immunization (GAVI) Fund, the Gates Foundation, the World Bank, The Asian Development Bank (ADB), the European Union, Government aid programmes from Australia, France, Japan and the United Kingdom, other charities – e.g. International Federation of the Red Cross and Red Crescent Societies, Oxfam, Save the Children Fund, World Society for the Protection of Animals (WSPA).

5. Conclusions and recommendations

5.1 Conclusions

The Consultation established four task forces. The four Task Forces (see Appendix 4) are dealing with the following subjects:

- Surveillance, data collection, processing of evidence and training.
- National and regional collaboration.
- Research and Development.
- Advocacy/funding and political support .

On the diagram the boxes at the bottom provide an indication of what their respective role may be.

Participants in the meeting volunteered for one or more of the Task Forces, according to their interest and/or expertise (see attached list). The list is not limited to the participants to this Consultation. All those experienced in rabies research, prevention and control interested at national (targeted Asian countries) and international level are welcome to contribute.

Each Task Force was invited to designate a Leader and a co-Leader. Some were nominated at the occasion of the meeting and some later through email discussion (see attached list). Leaders and co-Leaders will work with their members and in close collaboration with the Secretariat in WHO/HQ.

Each of the Task Force leaders defines, in collaboration with its members, the tasks to be achieved and the deadlines for their execution. These will be sent to the WHO Secretariat for review and endorsement. The Consultation identified probable major tasks for the Task Force on “National and Regional Collaboration”. These are for example to assure that:

- Rabies in humans and animals becomes a notifiable disease in all countries involved in the programme.
- A national intersectoral coordinating committee is being or has been established and is effective.
- A focal point or 2 (maximum) contact persons, one in the Ministry of Health, one in the Ministry of Agriculture/Veterinary Services are identified in each country. The focal point or the contact persons will liaise with the Task Force leader.
- A national rabies control plan exists or is being developed.

5.2 Recommendations

-To participating countries

- Asian countries where rabies poses a significant problem other than those that participated in this consultation should be invited to join the Consortium.

- National Rabies Control programme managers should investigate mechanisms for cost reduction and tax exemption (for this latter where an import tax is present)

-To WHO

- A summary proposal including all major components of rabies control and elimination prepared by the Secretariat with input from all Task Forces should be submitted through WHO channels to possible funding agencies including GAVI.
- Dedicated staff for zoonotic diseases especially rabies should be posted in the WHO Regional Offices of Cairo (EMRO), Manila (WPRO) and/or New Delhi (SEARO) to assist their Communicable Disease Departments in the implementation and follow-up of activities of the Consortium within the Regions.
- WHO to investigate with vaccine manufacturers any mechanisms to ensure continuous supply of safe and efficacious rabies biologicals and tariff reduction.
- WHO should continue to collaborate very closely on dog population management issues with the most relevant international NGOs such as WSPA and IAHAIO. These Organizations should be contacted concerning existing opportunities for advice, training and technology transfer.

-Future research needs

Priority should be given to applied research themes. The themes that were identified are (by decreasing order of priority):

- Studies on socioeconomics of PET recipients and economics of rabies control are required for advocacy purposes.
- Improved PET and pre-exposure regimens are of paramount importance. It is important to assess the efficacy of multisite ID application in the absence of RIG by following-up category 3 exposure patients treated with vaccine alone.
- Feasibility of rabies elimination in a pilot area should be studied. Inclusion/exclusion criteria for selection of the area should be developed.
- Safer rabies immunoglobulin production in Asian countries and alternatives for RIG are required. Owing to their defined antigenic specificity and expected yields in bulk culture, monoclonal antibodies have been suggested as one possible solution, which could reduce some problems associated with current rabies immune globulins and offer several theoretical advantages over existing products. In this connection a specialized working group should be established with the task of creating a well-characterized international cocktail of monoclonal antibodies equivalent if not superior to current RIG products. This task force should consist of qualified WHO Collaborating Centres and other relevant parties with the possession of monoclonal antibodies against lyssavirus.

- New vaccine candidates for humans and animals especially oral vaccines for dogs should be developed.

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* Invited but unable to attend

Annex 2. Agenda**Tuesday 17 July 2001**

08.30-09.00	Registration	
09.00-09.15	1. Opening	Dr D.L. Heymann
09.15-09.45	2. The current situation of rabies in Asia: an overview	Dr F.-X. Meslin
09.45-10.30	3. Analysis of weaknesses and opportunities for rabies control in Asia	Dr E. Miranda
<i>10.30-11.00</i>	<i>Coffee/Tea</i>	
11.00-11.30	4. Review of existing tools/methods for human and dog rabies control	Dr D. Briggs
11.30-12.30	5. Special issues for strategy development: 5.1 Access to rabies biologicals 5.1.1 Vaccines (for human and/or animals) Current situation regarding human rabies vaccines Availability and affordability in Asia Technology transfer for rabies vaccine production Increasing access	Dr F.-X. Meslin Dr E. Aycardi Overall Discussion
<i>12.30-13.30</i>	<i>Lunch</i>	
13.30-14.30	5.1.2 Immunoglobulin Current global shortage R&D for alternative rabies biological production Increasing access	Dr H. Wilde Dr M-P. Kieny, C. Rupprecht C. Tuffereau Overall Discussion
14.30-15.00	5.1.3 Discontinuation of Semple vaccine production and use	Dr N. Salahuddin Dr R. Ichhpujani
15.00-15.30	5.2 Access to vaccine recipients (human and animals) 5.2.1 Current and new practices in post-exposure treatment	Dr O. Wimalaratne
<i>15.30-16.00</i>	<i>Coffee/Tea</i>	
16.00-17.00	5.2.2 Preventive immunization of children A new paradigm in rabies prevention Comments	Dr D. Briggs, Dr V. Delore Dr Dinh K.X

17.00-17.30 5.2.3 Mass immunization of dogs

A successful regional programme
- Latin America Dr A. Belotto
Comments by participating country representatives

18.30-20.00 *Cocktail party - WHO cafeteria*

Wednesday 18 July 2001

09.00-09.45 5.3 What coverage can be achieved in Asia? Dr H.Matter
Comments by participating country representatives

09.45-10.30 5.4 Increasing awareness – changing perceptions on rabies
prevention
Changing health care providers and general public
perception on rabies: India as an example Dr M. Alam

10.30-11.00 *Coffee/Tea*

11.00-12.30 5.5 Commitment to rabies control
Eliciting support, estimating burden of rabies in developing
countries Dr S. Cleaveland
Study of canine rabies in N'Djamena, Chad Dr U. Kayali
Political commitment: current status and foreseeable trends
Comments by WHO representatives/country representatives

12.30-13.30 *Lunch*

13.30-14.00 5.6 Global Initiative on Vaccines and Immunization (GAVI)
Current and Future Priorities Dr M. Zaffran

14.00-15.30 6. Strategy identification for Asian countries
6.1 What's necessary Plenary discussion

15.30-16.00 *Coffee/Tea*

16.00-18.00 6.2 Working groups on suggested themes:
improving access to biologicals
improving delivery to vaccine recipients
changing public perceptions to rabies control and prevention
eliciting support and political commitment

Thursday 19 July 2001

09.00-10.30 6.2 Working groups (continued)

10.30-11.00 *Coffee/Tea*

11.00-12.30 7. Role of the Partners including the pharmaceutical
industry in strategy implementation:

	7.1	Pharmaceutical industry	IFPM and individual companies
	7.2	NGOs	WVA, VSF (Italy)
	7.3	Foundations	Merieux fondation
	7.4	International organizations and UN organizations	OIE,
12.30-13.30		<i>Lunch</i>	
13.30-15.30	7.	Role of the Partners including the pharmaceutical industry in strategy implementation (continued)	
15.30-16.00		<i>Coffee/Tea</i>	
16.00-17.30	7.	Role of the Partners including the pharmaceutical industry in strategy implementation (continued)	

Friday 20 July 2001

08.30-10.30	8.	Conclusions and recommendations	
10.30-11.00		<i>Coffee/Tea</i>	
11.00-11.45	8.	Conclusions and recommendations	
11.45-12.00	9.	Closure of the meeting	

Annex 3. List of Task Force (TF) members

TF on Advocacy and funding

Dr Ziauddin Ahmad, Dr Albino Belotto, Dr Deborah J. Briggs, Dr Betty Dodet, Dr François-Xavier Meslin, Dr A.B. Negi, Dr C.E. Rupprecht, Dr Noel Tordo, Dr Carolin Schumacher, Dr Thomas Suroso.

TF on Surveillance

Dr Albino Belotto, Dr Sarah Cleaveland, Dr Florence Cliquet, Dr F. M. Cancellotti, Dr P.A.L. Harischandra, Dr R.L. Ichhpujani, Dr Thavatchai Kamoltham, Dr A. King, Dr Rossella Lelli, Dr H.S. Lutra, Dr Mary Elizabeth G. Miranda, Dr Yolande Rotivel, Dr C.K. Singh, Dr Mary Warrell.

TF on Research and Development

Dr Cong Vien Nguyen, *Dr Anthony Fooks, Dr Thiravat Hemachudha, Dr Ursula Kayali, Mrs Pakamat Khawplod, Dr S.N. Madhusudana, Dr Yolande Rotivel, Dr C.E. Rupprecht, Dr Arunee Sabcharoen, Dr Carolin Schumacher, Dr Chantra Singhchai, Dr Noel Tordo, Dr Christine Tuffereau, Dr Mary Warrell, Dr Henry Wilde, Dr Omala Wimalaratna, Dr Cicilia Windiyaningsih.

TF on National and Regional Collaboration

Dr Ziauddin Ahmad, Dr Albino Belotto, *Dr Bui Quang Anh, Dr G.S. Chahal, Pr Dinh Kim Xuyen, Dr Ahmad Fayaz, Dr P.A.L. Harischandra, Dr R.L. Ichhpujani, Dr Thavatchai Kamoltham, Dr Mary Elizabeth G. Miranda, Dr Mohammed Sultan Mohiuddin, Dr A.B. Negi, Dr Naseem Salahuddin, Dr Omala Wimalaratna, Dr Cicilia Windiyaningsih.

Annex 4. Organigram: Consortium/Organization for Rabies Control and Elimination



