CHAPTER 2
LITERATURE REVIEW

2.1 Clinical Concept

2.1.1 Canine Rabies [22]

Rabies is a virus-induced neurologic disease of warm-blooded animals that, with rare exceptions, is fatal. Except for selected island countries and states, rabies occurs worldwide.

Rabies is regarded as a fatal disease although survivors of rabies have been documented, including dogs and humans. As a fatal disease, rabies is generally regarded as not treatable, but it is preventable by immunization of domestic animals and humans in groups at high risk of exposure and by postexposure treatment of humans with known exposure to rabies virus.

Etiology

Rabies virus is classified in the Rhabdoviridae family is a member of the genus *Lyssavirus*. Rhabdo means rod; members of the Rhabdoviridae family are rod-shaped, with one flat end and one rounded end, giving a bullet-shaped appearance. Rabies virus is about 75 X 180 nm in size; it possesses a lipid envelope and a genome of RNA. Rabies virus is a labile virus that does not persist in the environment. Sunlight, warm temperatures, drying, heat, and common disinfectants all destroy the infectivity of rabies virus.

Epizootiology

All species of warm-blooded animals are susceptible to infection with rabies virus, although there are differences in susceptibility. Opossums and birds are among the most resistant species; skunk, wild canids, raccoons, bats, and cattle are among the most susceptible species. Dogs, cats, horses, sheep, goats, nonhuman primates, and humans are intermediate in susceptibility to rabies. Wild animals are the primary reservoirs for rabies in many parts of the world, but domestic animal pets are the principal source for transmission of rabies to humans. When rabies in dogs and cats is controlled, the occurrence of rabies in humans is reduced to a very low level. Vaccination of at least 70 per cent of the dog population controls epizootics of dog rabies and provides a barrier that reduces the risk of human exposure to rabies.

Rabies virus must contact nerve endings and enter nerve fibers before infection occurs that leads to the development of rabies. Infection occurs primarily by contact of infected saliva from a rabid animal with nerve endings or damaged nerve fibers as a result of a bite from a rabid animal.

The incubation period for rabies from the time of exposure to the onset of clinical disease is usually from 3 to 8 weeks, but it can vary from a time as short as a week to more than a year. The location of the bite or exposure and the amount of virus present at exposure are the two most important factors affecting the incubation period. Bites that occur on the face, head, and neck result in shorter incubation periods. After rabies virus reaches the brain and multiplies in neurons, it migrates centrifugally in nerve fibers from the central nervous system to the salivary glands, allowing for shedding of virus in the saliva and further transmission.

Clinical Signs

Three clinical stages of rabies have been defined: the prodromal, excitative, and paralytic stages of the disease. The prodromal stage of the disease is characterized by change in behavior and is indicative that the rabies syndrome is to follow. Change in behavior is the basis for the expression, "mad dogs and friendly foxes." Wild animals lose their fear of humans, and they may be observed during the day in locations that are not normal, i.e., nocturnal animals are observed during the day in locations where they normally would be afraid to go. Friendly, affectionate pets become apprehensive, unusually alert to changes in their surroundings, and may hide out of fear, The prodromal stage of the disease may last for 1 to 3 days and is followed by the excitative or hyperreactive stage of the disease. Animals that manifest a prominent hyperreactivity to external stimuli or are easily excited may attempt to bite anything close by, including solid object such as wood, metal, and fences, and they may snap at imaginary objects. It is this stage of the disease that typifies the association of rabies with a "mad dog". If the manifestations of hyperreactivity are prominent, the animal is regarded as having "furious" rabies. Some animals with rabies may not manifest signs of hyperreactivity or it may be of short duration; they may be oblivious to their surroundings and appear to be in a state of stupor. Such animals are regarded as having "dumb" rabies. The excitative stage of the disease may be nonexistent, as in dumb rabies, or it may last as long as 3 to 4 days and be followed by the paralytic stage of the disease. Viral-induced damage to motor neurons results in paralysis, which is usually an ascending ataxia of the back legs. Incoordination is often one of the first signs of the paralytic stage of rabies. Animals with unexplained paralysis should be regarded as possibly rabid even though there may have been no antecedent signs suggestive of rabies. Paralysis of muscles of deglutition is responsible for drooling of saliva and inability to swallow. The paralytic stage of the disease may last for 1 to 2 days and is followed by death due to respiratory arrest. Death form rabies in domestic animals usually occurs within 2 to 7 days after the onset of clinical signs. Survival or recovery from rabies has been documented in dogs as well as in rare cases in human patients. Recovery from rabies in dogs has implications for possible exposure to rabies virus form dogs that appear to recover from lower motor neuron diseases that resemble polyradiculoneuritis. The lack of reliable methods for the antemortem diagnosis of rabies necessitates a cautious approach to minimize the risk of human exposure to rabies virus in cases that are misdiagnosed.

Diagnosis

Rabies should be suspected on the basis of clinical signs. Confirmation of the diagnosis depends on postmortem examination for rabies virus in portions of the brain and brain stem. The fluorescent antibody test is the primary method used in the postmortem diagnosis of rabies; it is more than 99 per cent accurate in diagnosing rabies based on correlations with mouse inoculation. If rabies virus is found in the brain, there is potential for the virus to be in salivary glands and saliva. If rabies virus is not found in the brain, it is concluded that there would be no virus in the salivary glands and saliva because rabies virus reached the salivary glands by migration through nerve fibers form the brain. If there has been possible human or animal exposure form an animal with clinical signs suggestive of rabies, mouse inoculation is usually done to verify negative fluorescent antibody results. A disadvantage of the mouse inoculation test is that a period of 2 to 3 weeks may be required to make final conclusions about the presence or absence of rabies virus in the brain. The presence of

intracytoplasmic inclusion bodies (Negri bodies) in neurons is pathognomonic for rabies in dogs, but Negri bodies are not always present and their absence does not rule out rabies.

Treatment and Prevention

Treatment is not recommended for animals with rabies because of the risk of human exposure. Dogs that present clinical signs consistent with rabies should be placed in strict isolation to prevent possible exposure of animals or humans, or they should undergo euthanasia and the brain should be examined for rabies virus. Rabies is preventable by immunization of dogs and cats and by control of stray animals. Vaccination of dogs on a widespread basis has been one of the most effective programmes in decreasing the occurrence of human rabies.

It is recommended that dogs and cats be vaccinated at 3 to 4 months of age, again one year later, and either annually or triennially thereafter, depending upon whether a 1-year or 3-year rabies vaccine is used. It is recommended that 3-year vaccines be used, since they are more effective in increasing the percent-age of immunized dogs and cats.

Management of Dogs and Cats That Have Bitten a Human

A dog showing signs of neurologic disease at the time it bites a human and an unwanted or stray dog or cat that has bitten a person should undergo euthanasia immediately and its brain examined for rabies virus to determine whether the bitten person was possibly exposed to rabies. Healthy dogs or cats that are owned pets should be confined for 10 days after the bite and observed for signs of rabies. The purpose of the 10-day observation is to determine whether the bitten person was exposed to rabies. This determination is based on the knowledge that dogs and cats do not shed rabies virus in their saliva for more than a few days before the onset of rabies. Six days before the onset of clinical signs of rabies is the earliest that rabies virus has been detected in the saliva of either dogs or cats. Therefore, if the dog or cat remains healthy for 10 days after the bite, the person was not exposed to rabies.

Management of Dogs and Cats Exposed to Rabies

Dogs or cats that are currently immunized against rabies according to recommendations for rabies vaccination and are bitten by a proven rabid animal or by a wild animal in rabies endemic area should be revaccinated immediately and observed for 90 days. Unvaccinated dogs or cats that are known to have been exposed to rabies virus should undergo euthanasia or be confined in strict isolation for 6 months if the owner is unwilling to consent to euthanasia. The dog or cat should be vaccinated at the fifth month of isolation and, if healthy at the end of 6 months, may be released to the owner.

2.1.2 Human Rabies [23]

Epidemiology

Rabies is found in animals in all region of the world except Australia and Antarctica. Rabies exists in 2 epidemiological forms: *urban,* propagated chiefly by nonimmunized domestic dogs and cats, and *sylvatic* rabies, propagated by skunks, foxes, and raccoons. Infection in domestic animals usually represents a "spillover" from exposure to wild animals in locales where rabies is enzootic or epizootic. The worldwide incidence of rabies is estimated at more than 30,000 cases per year.

Southeast Asia, the Philippines, Africa, the Indian subcontinent, and tropical South America are areas where the disease is especially common. While focal epidemics of terrestrial rabies have occurred in USA and Europe, human rabies is uncommon, largely because of successful domestic-animal vaccination programmes. In most areas of the world, the dog is the important vector of rabies virus for human. However, the fox (in Eastern Europe and Arctic Regions), the mongoose (in South Africa and Caribbean), the fox (in Western Europe) and the vampire bat (in Latin Africa) also may be prominent vectors.

Pathogenesis

The first event in rabies is the introduction of live virus through the epidermis or onto a mucous membrane. Initial viral replication appears to occur within striated muscle cells at the site of inoculation. The peripheral nervous system is exposed at the neuromuscular and neurotendinous spindles of unmyelinated sensory nerve cell endings. The virus then spreads centripetal up the nerve to the ventral nervous system. Probable via peripheral nerve axoplasm, at the rate 3mm per hour. Viremia has been documented in experimental conditions but is thought not to play a role in naturally acquired disease. Once the virus reaches the CNS, it replicates almost exclusively within the gray matter and then passes centrifugal along autonomic nerves to other tissues. The incubation period o rabies is exceedingly variable, ranging form 7 days to 1 year. Host immune responses and viral strains also influence disease expression. The neuropathology of rabies resembles that of other viral diseases of the CNS. The most characteristic pathologic finding of rabies in the CNS is the formation of cytoplasmic inclusions called "*Negri bodies*" within neurons.

Clinical Manifestation

The clinical manifestation of rabies can be divided into 4 stages:

1. A non-specific prodrome
2. An acute encephalitis similar to other viral encephalitis
3. A profound dysfunction of brainstem centers that produced the classic features of rabies encephalitis
4. Death

The prodromal period usually lasts 1 to 4 days and is marked by fever, anorexia, headache, malaise, myalgias, increased fatigability, etc.

The encephalitic phases usually ushered in by period of excessive motor activity, excitation, and agitation. Confusion, hallucinations, combativeness, bizarre aberrations of thought, muscle spasms, meningismus, opisthotonic posturing, seizures and focal paralysis soon appear. Characteristically, the periods of mental aberration are interspersed with completely lucid period.

The manifestations of brainstem dysfunction begin shortly after the onset of the encephalitic phase. Cranial nerve involvement causes diplopia, facial palsies, optic neuritis, and the characteristic difficulty with deglutition. If the intensive respiratory support is used, a number of late complications may occur.

The difficulty of diagnosing rabies associated with ascending paralysis is illustrated by cased of person-to-person transmission of the virus by tissue transplantation.

Laboratory Finding

Early in the disease, hemoglobin values and routine blood chemistry results are normal. Abnormalities develop as hypothalamic dysfunction, gastrointestinal

bleeding, and other complication ensue. The peripheral white blood cell count is usually slightly elevated but may be normal or as high as 30,000/uL. The specific diagnosis of rabies depends on

1. Isolation of virus
2. The serologic demonstration of acute infection
3. The detection of viral antigen in infected tissue
4. The detection of viral nucleic acid by PCR

Prevention & Post-exposure Prophylaxis

Post-exposure prophylaxis of rabies includes

1. Wound cleaning and treatment
2. Passive immunization with anti-rabies antiserum of either equine of human origin
3. Active immunization with anti-rabies vaccine

In an area in which feline or canine rabies is not prevalent, a healthy biting dog or cat can be confined and observed for 10 days.

Pre-exposure prophylaxis: individual at high risk of contact with rabies virus should receive pre-exposure prophylaxis with rabies vaccine.

2.2 WHO Expert Committee on Rabies [1]

2.2.1 Prevention of Rabies in Humans

2.2.1.1 General Considerations

In view of the extremely high fatality rate of human rabies, the prevention of rabies infection after exposure is of the utmost importance. Major advances have been made in the safety and potency of rabies vaccines. The Committee reiterated, as stated in its 1983 report (1), its support for the trend to limit or abandon completely – where economically and technically possible – the production of encephalitogenic brain-tissue vaccines, and strongly advocated the production and use of inactivated cell-culture rabies vaccines in both developed and developing countries. After exposure, prevention of infection is virtually assured by immediate treatment of the wound and post-exposure prophylaxis with one of the recommended regimens of rabies immunoglobulin (RIG) and cell-culture vaccines. If cell-culture rabies vaccine is not available, brain-tissue vaccine (preferably suckling-mouse brain vaccine) of proper potency may be administered. There are as yet no inexpensive vaccines available for mass pre-exposure vaccination and individual pre-exposure immunization should therefore be considered for all persons at high risk of exposure.

2.2.1.2 Pre-exposure Immunization

Vaccines of cell-culture origin are preferable for pre-exposure immunization of humans, since they are safer and more effective than nerve-tissue vaccines.

Pre-exposure immunization should be offered to persons at high risk of exposure, such as laboratory staff working with rabies virus, veterinarians, animal handlers and wildlife officers, and other individuals who are living in or travelling to areas where rabies is endemic.

Such immunization should preferably consist of three full intramuscular doses of tissue-culture rabies vaccine of potency at least 2.5IU per dose given on days 0, 7 and 28. (A few days' variation is not important.) The presence of virus-neutralizing antibodies in vaccinated individuals should be ascertained, where

feasible, using serum samples collected 1-3 weeks after the last dose. For adults, the vaccine should always be administered in the deltoid area of the arm. For young children, the anterolateral area of the thigh is also acceptable. The gluteal area should never be used for vaccine injections, since administration in this area results in lower neutralizing antibody titres.

Tissue-culture or purified duck-embryo rabies vaccines of potency at least 2.5 IU per dose have been shown to induce adequate antibody titres when carefully administered intradermally in 0.1 ml volumes on days 0, 7 and 28. After reconstitution of the vaccine, the entire volume should be used as soon as possible. Separate syringes and needles must be used for each dose. Intradermal application of the vaccine is of special interest in areas where economic constraints limit vaccine availability. However, pre-exposure immunization with human diploid cell (HDC) vaccine administered intradermally should, whenever possible, be performed before starting antimalarial prophylaxis, since virus-neutralizing antibody titres have been shown to be lower in patients receiving chloroquine phosphate. When this is not feasible, HDC vaccine should be administered intramuscularly.

Periodic booster injections are recommended for persons at continuing risk of exposure to rabies. The following guidelines are recommended for determining when boosters should be administered.

All persons who work with live rabies virus in a diagnostic, research or vaccine production laboratory should have a serum sample tested for rabies virus-neutralizing antibodies every 6 months and a booster administered when the titre falls below 0.5 IU/ml. Responsible authorities should ensure that all staff are properly immunized.

All other persons at continuing risk of exposure to rabies should have a serum sample tested for rabies virus-neutralizing antibodies every year; a booster should be administered when the titre falls below 0.5IU/ml.

A rabies vaccination pre-exposure certificate should be filled in and given to the vaccinee, indicating the type of vaccine used, the manufacturer, lot number, schedule used, antibody titre (if tested), and any allergic reactions that may have occurred.

2.2.1.3 Post-exposure Treatment

2.2.1.3.1 General Considerations

The combination of local treatment of the wound, passive immunization with rabies immunoglobulins (RIG) and vaccination is recommended for all severe exposures (category III) to rabies. Prompt and thorough cleansing of the wound, and administration of purified equine or human rabies immunoglobulins (ERIG or HRIG) and cell-culture rabies vaccine immediately after exposure virtually guarantee complete protection, and the risk of post-exposure treatment complications is much lower than with brain-tissue vaccines. Pregnancy and infancy are never contraindications to post-exposure rabies vaccination. Since prolonged incubation periods have been noted, persons who present for evaluation and treatment even months after having been bitten should be dealt with I the same manner as if the contact occurred recently.

Factors that should be considered I deciding whether or not to initiate post-exposure treatment are:

- the nature of the contact;
- the presence of rabies in the area where the contact occurred or

from which the animal involved came;
- the species of the animal involves;
- the vaccination and clinical status of the animal involved, the type of vaccine used and the availability of the animal for observation;
- the results of laboratory testing of the animal for rabies, if available.

An apparently healthy dog or cat that bites a person may or may not justify the initiation of treatment, depending on the perceived risk. If the animal involved is a recognized rabies vector in the area where the contact occurred, initiation of treatment should never await the results of laboratory diagnosis. If the animal is suspected of being rabid, immediate euthanasia and laboratory examination of the brain should be performed. Wound treatment must be completed and serum and vaccine therapy instituted as soon as possible after any exposure. If the species involved is unlikely to be infected with rabies, treatment may be deferred pending the outcome of laboratory testing provided that diagnosis can be made within 48 hours. A report from a reliable laboratory indicating a negative result usually justifies cessation of treatment.

If the animal involved is a dog or cat, it should be kept under observation, preferably under veterinary supervision, for 10 days. Treatment may be discontinued if the dog or cat remains healthy during this period. The Committee suggested, however, that people in contact with animals other than cats and dogs that are suspected of being rabid should receive full post-exposure treatment unless the animal is available and can be killed humanely and examined for rabies in a reliable laboratory immediately.

2.2.1.3.2 Local Treatment of Wounds

The Committee emphasized the importance of prompt local treatment of all bite wounds and scratches that may be contaminated with rabies virus, even if the person presents after a prolonged period.

Recommended first-aid procedures are immediate thorough flushing and washing of the wound with soap and water, detergent or other substances of proven lethal effect on rabies virus. People who live in rabies-infected areas should be educated in simple local wound treatment and warned not to use procedures that may further contaminate the wounds. If possible, suturing of wounds should be avoided; however, if suturing is necessary, anti-rabies immunoglobulin should be infiltrated around the wound. Other treatments, such as administration of antibiotics or anti-tetanus procedures, when indicated, should follow the local treatment.

2.2.1.3.3 Administration of Rabies Immunoglobulin

Rabies immunoglobulin (RIG) should be given for all category III exposures, irrespective of the interval between exposure and beginning of treatment. Two kinds of rabies antibody preparations may be used: human rabies immunoglobulin (HRIG) and equine rabies immunoglobulin (ERIG). A skin test must be performed prior to the administration of ERIG. As much as possible of the recommended dose (20 IU/kg of body weight of HRIG or 40 IU/kg of body weight of ERIG) should be infiltrated around the wounds if anatomically feasible. The remainder should be administered intramuscularly (into the gluteal region) in a single dose and followed by a complete course of vaccine.

Rabies immunoglobulin of human origin (HRIG) is available in some countries; however, it is expensive and only limited amounts are available.

Rabies immunoglobulin of equine origin (ERIG) is available in many countries and is considerably cheaper than HRIG. Most of the currently available

preparations of ERIG are highly purified and quite safe; however, a skin test should always be carried out prior to its use.

2.2.1.3.4 Vaccine Administration

The vaccination schedule recommended in a given situation depends on the type and potency of the vaccine available.

Brain-tissue-derived vaccines

The Committee did not recommend any particular vaccination schedule. In countries where brain-tissue vaccines are used, the national authorities should recommend a schedule of immunization that has been shown to induce and adequate level of protection.

Tissue-culture rabies vaccines or purified duck-embryo vaccine

The company of these vaccines should be of at least 2.5 IU per single human dose. All these vaccines are considered equally safe and effective when used properly. They should be applied according to the following schedules:

Intramuscular schedules

One dose of vaccine should be administered on days 0, 3, 7, 14 and 30. All intramuscular injections must be given into the deltoid region or, in small children, into the anterolateral area of the thigh muscle. Vaccine should never be administered in the gluteal region.

In the abbreviated multisite schedule, the 2-1-1 regimen, one dose is given in the right arm and one dose in the left arm at day 0, and one dose applied intramuscularly in the deltoid region on days 7 and 21. The 2-1-1 schedule induces an early antibody response and may be particularly effective when post-exposure treatment does not include administration of rabies immunoglobulin.

Intradermal schedule

One dose (0.1 ml) should be given at each of two sites, either the forearm or the upper arm, on days 0, 3 and 7 and one dose at one site on days 30 and 90. This regimen considerably lowers the cost of vaccination against rabies, as the total volume of vaccine required is much less than that required for intramuscular regimens. Separate syringes and needles must be used for each dose. Intradermal injections should be administered only by staffs who have been trained in this technique. Vaccine vials should be stored between 4°C and 8°C after reconstitution and the total contents should be used as soon as possible.

2.2.2 National Programmes for the Control of Rabies in Dogs

2.2.2.1 Introduction

In over 80 countries, rabies is still prevalent in its most dangerous reservoir, the dog population. Each year approximately 4 million people in these areas receive treatment after exposure to rabies and over 30,000 people die after being bitten by rabid dogs. In more than 99% of all human rabies cases, the virus is transmitted form dogs, and over 90% of people who receive rabies post-exposure treatment live in areas of canine rabies.

Effective veterinary vaccines that provide a considerable duration of immunity have been developed; however, mechanisms to ensure their worldwide availability still need to be defined.

Up to the 1960s, an increasing number of countries reported the elimination of canine rabies reservoirs from their territories. With the exception of a few areas in Latin America, the Caribbean and Europe, this process, however, came to a standstill

until the 1980s, when a number of successful field projects were initiated or reactivated under the aegis of WHO.

Canine rabies is almost entirely limited to developing countries. Control measures such as confinement of dogs on owners' premises, capture and removal, and dog population control have widely failed to be adopted and maintained in these countries. Much of the problem has been in failure to understand the relationship of dogs to the society, and attempts to impose rabies control approaches that have been successful in many developed countries. However, dog population immunization programmes adapted to the social structure are now feasible and are being developed in several countries. In order to reach a high proportion of the dog population, such programme must be based on the local ecology of the dog population, on understanding of the local society, on coordination of the related sectors of society and on culturally adapted education for the control of rabies. Dog elimination programmes by themselves are not effective in rabies control.

Studies coordinated by WHO on dog populations have shown that, in parts of North Africa, Latin America and Asia, up to 75% of the total dog population is accessible to parenteral immunization. This is usually high enough to break the rabies transmission cycle.

The Committee recognized the significant reduction in the number of human deaths due to rabies achieved by the PAHO/AMRO coordinated programme for the elimination of urban rabies in the Americas since its inception in 1983, as well as by the AGFUND.WHO coordinated programme for the control of human and canine rabies in developing countries during the period 1985-1988. Rabies has been spreading through canine populations in wide areas of sub-Saharan Africa during the past two decades and is becoming more common in other continents with increasing urbanization, density and mobility of human populations. Control programmes are inadequate in the absence of comprehensive schemes aiming at the elimination of the disease. The number of persons requesting post-exposure rabies treatment is also increasing; in some countries it has almost doubled over the past 10 years. This increase in demand is mainly due to greater public awareness regarding the safety and potency of rabies vaccines and immunoglobulins, together with a lowering of the costs of these products.

The social and economic significance of post-exposure treatment is often overlooked by national authorities in areas where the number of human rabies deaths has become negligible, but where post-exposure treatments remain at a high level.

There are three basic elements to any programme for the control of rabies in dogs and other domesticated animals. Their priorities will depend on the social, cultural, and economic factors prevailing in each region, country or community. The basic elements are (a) epidemiological surveillance (section 9.2); (b) immunization (section 9.3); and (c) dog control (section 9.4). They will require community participation, managerial skills and legislation. Further technical and managerial information for planning, implementing and evaluating national programmes for the control of rabies in dogs in given in Annex 4.

2.2.2.2 Epidemiological Surveillance

Surveillance of rabies is the basis of any programme for rabies control. Epidemiological data should be collected, evaluated, processed and mapped whenever possible and disseminated rapidly. Such data are essential both to physicians in deciding whether to initiate post-exposure treatment and to veterinarians in deciding what measures to adopt towards the animal responsible for the contact.

This information is also required for planning, organizing and implementing rabies control programmes.

The surveillance of rabies has at present reached a satisfactory standard in only a few countries and this has a direct bearing on the treatment of exposed persons and on rabies control activities in animals. National authorities should be encouraged to collect more systematically the available data on rabies, including clinical records, and to ensure rapid exchange of information, after collation and processing, between different administrative sectors and levels. This would permit them to analyze the epidemiology of rabies in their area, to plan appropriate control procedures and to pass the appropriate information to authorities in other countries. National authorities should be aware that, even in areas where laboratory support is inadequate or lacking, valuable information can still be obtained from clinical observations. Countries are urged to adopt or establish regional and international systems of rabies reporting (see section 12.1). International collaboration in surveillance is particularly important, especially for the investigation of rabies outbreaks and identification of the rabies virus strains involved, in view of increased international travel and transfer of animals.

2.2.2.3 Mass Parenteral Vaccination Campaigns

Mass canine vaccination campaigns have been the most important measure applied for controlling rabies in developing countries. At least 75% of the dog population in each community should be vaccinated within a month. In areas where the dog population turnover is rabid, it may be necessary to carry out a mass vaccination campaign each year. However, if the effective immune period of the vaccine is longer and the system for identifying vaccinated dogs can be trusted to last more than one year, the advantage of vaccinating only the dogs entering the population after the last campaign should be considered, with revaccination of dogs vaccinated during the last campaign at intervals of about 2 years.

In order to plan, execute and evaluate a mass vaccination campaign, and estimate of the dog population is required (see Annex 4). If possible, a census or a study based on a sample of the dog population should be carried out before starting the campaign or in connection with the first phase of the campaign.

For mass canine vaccination campaigns, the use of inactivated rabies vaccine is recommended. The management of inactivated vaccine in the field is easier than that of live vaccine, since it is less sensitive to changes in temperature. Furthermore, accidents of self-inoculation do not represent any risk for the vaccinator.

With inactivated vaccine, all dogs and cats taken to the vaccinator should be vaccinated, regardless of their age, weight or state of health. Puppies less than 3 months old should be given a vaccine booster at 6 months of age. For live vaccines in particular, the manufacturers' instructions should be strictly followed. (See Annex 4 for parenteral vaccination of other animal species.)

The use of coloured tags or coloured plastic collars individually adjusted to each dog has proved useful in identifying vaccinated dogs and has contributed to the success of vaccination campaigns by motivating owners to take their pets for vaccination. It has also been useful in evaluating the vaccination coverage rate, particularly during the initial phase of the campaign.

Three basic approaches have been used, either alone or in combination, in carrying out mass vaccination campaigns: house-to-house visits, fixed vaccination posts, and mobile clinics. The choice of approach will depend on the specific community and the decision should be taken at the local level.

Research carried out by WHO between 1981 and 1988 as part of the AGFUND/WHO project for the control of human and canine rabies in developing countries revealed that:

- whether owned or not, very few dogs (generally less than 10-15% of the dog population) are able to avoid being caught;
- dog removal programmes (in which stray dogs are captured and humanely killed) are ineffective, as well as costly;
- vaccination coverage rates of 75% or higher can be attained, although this requires special efforts in mobilizing community participation, conducting health systems research and providing support services for vaccination campaigns (23).

High vaccination coverage was attained through strategies consisting of well-designed short-term educational campaigns, mass dog vaccination and marking, followed a few days alter by vaccination of dogs that were missed during the first campaign. In some countries this was combined with the removal of unmarked dogs. In others, adequate population coverage was achieved without dog marking or a second round of vaccination. Informational campaigns and involvement of the community in planning and carrying out these programmes were major factors in their success (see Annex 4).

Fixed vaccination points or mobile clinics should be situated within the communities or neighborhoods they are intended to serve. Experience has shown that such posts will be sufficiently attended only form distances of less than 500 m or about 10 minutes' walk.

2.2.2.4 Dog Population Management

The Committee expressed its appreciation of the long-term engagement of WHO in developing methodologies related to dog ecology and dog population management. Considerable experience has been gained in projects coordinated by WHO in Ecuador, Nepal, Sri Lank and Tunisia and other ecological studies conducted in South America and Asia. However, data collection, health systems and operational research need to be continued in other areas and countries with different social and ecological conditions.

On the basis of the results obtained so far in these studies, the Committee recommended drastic changes in rabies control policies as compared with those previously adopted and practised by most national authorities and communities. There is no evidence that removal of dogs has ever had a significant impact on dog population densities or the spread of rabies. The population turnover of dogs may be so high that even the highest recorded removal rates (about 15% of the dog population) are easily compensated for by increased survival rates. In addition, dog removal may be unacceptable to local communities. Therefore, this approach should not be used in large-scale control programmes unless ecological and sociocultural studies show it to be feasible.

2.3 Economic Concept

2.3.1 Costing in Economic Evaluations [19]

Costing involves identifying; measuring and valuing all resource changes that occur as a certain health care intervention is carried out. The aim is to value the use of scarce resources (materials, drugs, time of physicians, time of patients etc.) that is needed to produce a certain health effect – the outcome of the intervention. In

figure 2.1 we indicate which resource uses may in general e distinguished and need to be identified, estimated in quantitative terms and valued monetarily.

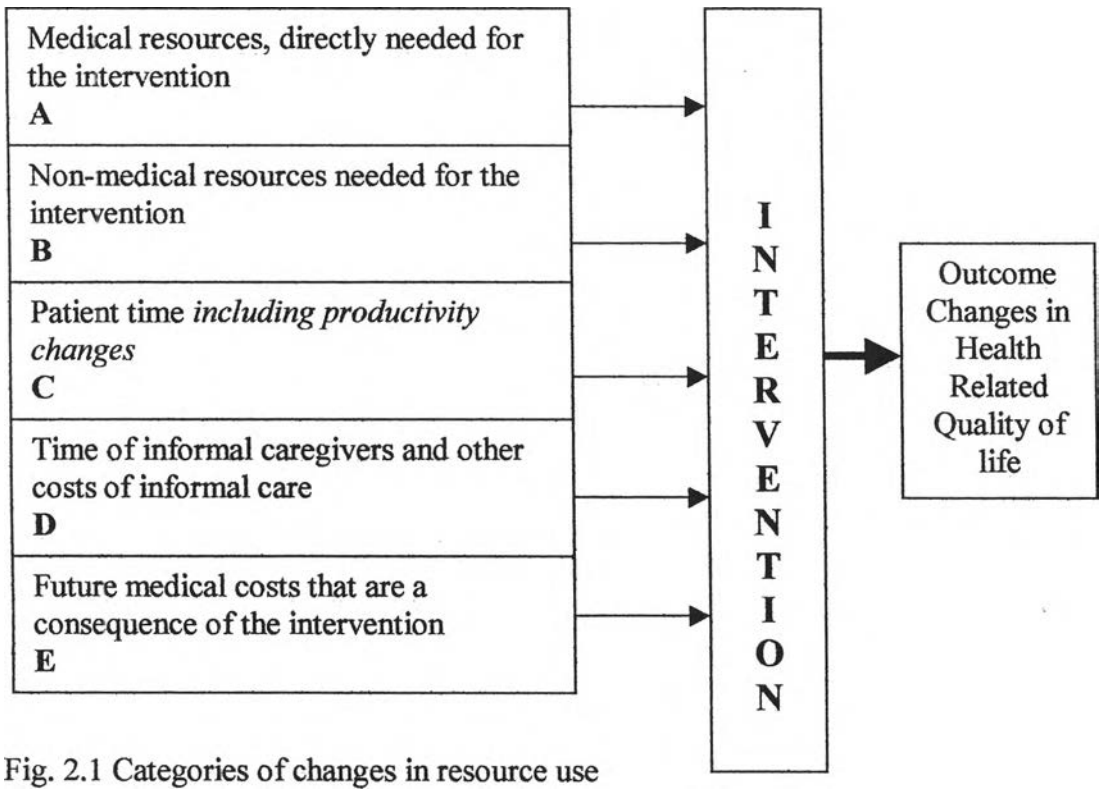


Fig. 2.1 Categories of changes in resource use

The level of detail in the costing method used can be varied with the purpose of a study. If the aim of a study is to give a global impression of total costs, 'gross-costing' may be appropriate.

'Gross-costing' has the advantage of consuming less resources and providing better opportunity for generalization, but at the expense of the level of precision. On the other hand, one could opt for 'micro-costing' which entails detailed inventory, measurement and valuation of all separate cost-items involved. This method is much more laborious, but provides the researcher with more specific insight in the relationships between characteristics of activities and their costs, the economics of scale of a production process, and the relative importance of separate activities. The choice of which costing method to adopt depends on the level of decision required, the desired scope for generalization and the feasibility and costs of adopting either method.

2.3.1.1 The Concept of Costing [19]

2.3.1.1.1 Perspective of the Study

Normally, the perspective of the study is a societal one. This broad perspective ensures that all resource changes and outcomes are taken into account in the determination of whether or not a programme should be implemented as a consequence of a positive or negative change in total welfare.

2.3.1.1.2 Relation to Production Function

An intervention under study requires certain resources to be sacrificed producing a certain outcome. To study the changes in resource use one may consider the different input factors required to produce a good or service in the health care sector. In that way, one may determine a so-called *production function* that gives the relationship between the different inputs (labor, capital and so on) and the outcomes of the intervention. By subsequently determining the valuation of the different cost-items in the production function and incorporating them in that function, we derive a *cost-function* that provides the relationship between costs and outcomes. This cost-function ultimately describes what needs to be sacrificed in monetary terms in order to gain certain outcomes.

2.3.1.1.3 Opportunity Costs

In general, the resources used should be evaluated at their opportunity costs, the value of their best alternative use. These opportunity costs should reflect true societal valuations of the sacrificed resources.

2.3.1.1.4 Average Versus Marginal costs

Average prices include fixed costs, such as costs of hospital buildings and costs of overheads, as well as variable costs. Marginal costs only cover the costs of producing one additional unit of outcome of the intervention. Thus, fixed costs are left out of the calculation.

2.3.1.1.5 Relation to Time

Choosing an appropriate time horizon for the evaluation is important, since shifting the time horizon of the evaluation may have a substantial impact on the results of the study. Ideally, the time horizon should be chosen in such a way that all cost consequences of the intervention under study can be taken into account in the analysis.

2.3.1.2 Identifying and Measuring Resource Use

2.3.1.2.1 The Identification of Resource-items

All relevant resource items both outside and inside the health care sector should be identified and quantified. Amongst other things, this requires both knowledge about the resources needed to perform the intervention, as well as epidemiological knowledge. To build a detailed decision tree specifying all possible courses of the disease and treatment options is a useful step in this phase.

When the analyst has a broad idea of which resource-items will be relevant in the programme under study, he may decide that some resource changes are expected to be too small to incorporate in the analysis (and to measure and value). Although there may be a sound reason to leave out a resource item from further analysis, it is important to indicate its existence in the identification phase.

2.3.1.2.2 Measuring Resource Use

When a study is performed using micro costing, information on resource use on a very detailed level is required. The individual resource components of the intervention under study (e.g. each diagnostic test) need to be identified and measured. For gross costing, the intervention is broken down into larger intermediate products (e.g. hospitalizations) for which resource use is determined.

2.3.1.2.3 Collection of Resource Use Data

The choice of method for data collection depends furthermore on a number of other characteristics of a study, such as the perspective of the study, the requirements for representativeness and generalizability, the (expected) impact of the specific resource item on total or incremental costs, and the availability of existing data and the effort needed to collect additional data.

Regarding perspective, a societal viewpoint is assumed as indicated above. For data collection this means that one should critically assess whether existing data from registries or accounting systems cover all relevant resource items.

Regarding representativeness and generalizability, it is important to consider the objective of the study, which may be targeted to support a decision in a specific setting or to inform national policy. In the first case using data from the specific setting is more appropriate whilst in the latter case the use of data from national registries may be the preferred option.

Third, the estimated impact of a specific resource item should be measured. *A priori* determination of the desired precision can be done by performing a sensitivity analysis up front using best guesses for the different relevant parameters (in terms of resource use and costs).

Finally, given the previous criteria, the availability of data from existing registries may allow shortcuts to be made in the calculation of costs.

2.3.1.3 Estimating the Value of Resources

2.3.1.3.1 Gross Versus Micro-costing and Level of Refinement

The general approach in a costing study is that for a specific health care service one determines the necessary amount of each input: personnel, equipment, material, floor surface, etc. and the costs per unit of each input. Aggregating the product of costs per unit and the number of units of each input gives the costs of the health care service ('bottom up cost calculation'). However, this procedure can be carried out on several levels of refinement and depends on the setting in which a service is being produced.

2.3.1.3.2 Handling of overhead costs

Drummond et al. (1997) give ample advice on different methods of allocating the costs of such resources to final products or services. Direct allocation of overhead costs to final products seems to be the preferred approach. In this method of direct allocation first, overhead costs for the various overhead departments are allocated to a final production centre using an appropriate allocation-key (e.g. square meters for allocating the costs of cleaning services). Second, one should establish what proportion of the capacity of this final production centre is used for the product or programme under consideration. The same proportion of overhead costs is then allocated to product or programme.

2.3.2 Cost Analysis and Cost Allocation

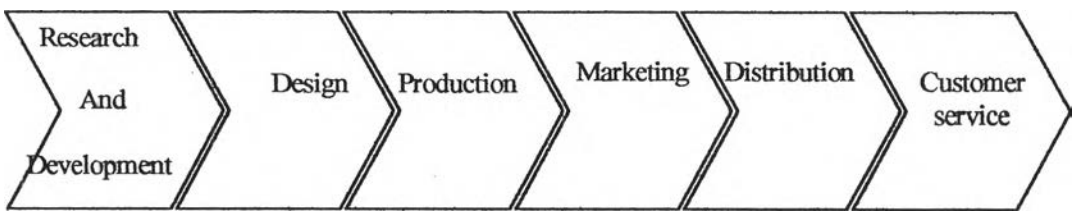
As was mentioned in the previous chapter, the analysis of the comparative costs of alternative treatments or health care programs is common to all forms of economic evaluation. Although many of the issues surrounding costing are context-specific and the analysts options are often limited by the availability of data, it is possible to give some general guidance. Two particularly thorny issues are the

treatment of overhead costs (techniques for allocating shared overhead costs to individual projects) and allowance for differential timing of costs (the technique for discounting and annuitization of capital expenditure).

Purposes of cost allocation [27]

1. To provide information for economic decision
2. To motivate managers and other employees
3. To justify costs or compute reimbursement
4. To measure income and assets for reporting to external parties

Different costs are appropriate for difference purposes. Consider costs of a product in terms of the business functions in the value chain:



Criteria for cost-allocation decision

1. Cause and effect. Using this criterion, managers identify the variable or variables that cause resources to be consumed. For example, managers may use hours of testing as the variable when allocating the costs of a quality-testing area to products. Cost allocations based on the cause-and-effect criterion are likely to be the most creditable to operating personnel.

2. Benefits received. Using this criterion, managers identify the beneficiaries of the outputs of the cost object. The costs of the cost object are allocated among the beneficiaries in proportion to the benefits each receives. For example, consider a corporatewide-advertising program that promotes the general image of the corporation rather than any individual product. The cost of this program may be allocated on the basis of division revenues. The higher the revenues, the higher the division's allocated cost of the advertising programs. The rationale behind this allocation is the belief that divisions with higher revenues apparently benefit from the advertising more divisions with lower revenues and therefore ought to be allocated more of the advertising costs.

3. Fairness or equity. This criterion is often cited in government contracts when cost allocations are the basis for establishing a price satisfactory to the government and its supplier. Cost allocation here is viewed as a "reasonable" or "fair" means of establishing a selling price in the minds of the contracting parties. For most allocation decisions, fairness is a lofty objective rather than an operational criterion.

4. Ability to bear. This criterion advocates allocating costs in proportion to the cost object's ability to bear them. An example is the allocation of corporate executive salaries on the basis of division operating income. The presumption is that

the more profitable divisions have a greater ability to absorb corporate headquarters' costs.

Steps in the overhead application process:

1. Selecting a base for assigning casts to patients and department: the first step is to select an overhead cost application base. This base serves as the denominator for the fraction to be used to calculate that based on the existence of a cause-and-effect relationship between product volume and overhead costs. In addition, the base should be applicable to all patients. Common industrial bases are direct labor hours, direct labor cost and machine hours. Health care organization could use hours or cost for all staff as an application base along these lines. Other bases also could be developed if the result in a more accurate cause-and-effect relationship between overhead costs and volume of patients. Age, sex, and diagnosis were suggested above.

2. Determining budgeted cost and volume: The second step is to determine a budgeted overhead cost and budgeted volume of production. In the case of a health care organization, we would need to ascertain all departmental budgeted amounts that cannot be assigned to patients as either direct labor or direct materials. We would also need to estimate the expected volume. Note that volume does not necessarily mean the number of patients. We are concern here with the volume of the item used for the base. For example, each department would have to estimate the number of hours of housekeeping service that they expect to consume for the coming year, if the housekeeping base is the total number of hours of service.

3. Computing overhead rate: The third step is computation of an overhead rate by dividing the total expected production volume. For example, if a health care organization expects to have overhead cost of $10 million and 500,000 nursing hours, then a rate could be developed by dividing the overhead cost by the nursing hour's base to result in an application rate of $20 per nursing hour. This rate is base on annual budgets. As note earlier, the use of annual rather than monthly budget smoothes out some unwanted seasonal impacts. Similarly, use of monthly budgets for rate calculations would cause us to charge major maintenance costs only to patients rather than spreading these costs across all patients' whole benefit from them over the course of the year.

4. Measuring the actual base: The forth step is to keep track of actual base data as the year unfolds. That is, we must track how many nursing hours are actually consumed for each patient or how many housekeeping hour of service are actually provided to each department.

5. Applying the budgeted overhead application rate to the actual volume: The fifth step is to apply the budgeted overhead application rate to the actual units of the vase consumed to determine the overhead applied. Thus, suppose that a specific department consumed 1,500 hours of housekeeping service. Since the application rate is $10 per hour, a total of $15,000 would be applied to that department. This application would generally be done monthly throughout the year.

6. Accounting for year-end differences between actual overhead and the amount of overhead applied throughout the year: The sixth and the final step is to

account for any year end differences between actual total overhead and the amount of overhead that has been applied to patients throughout the year.

Various methods for allocating shared (or overhead) costs available, namely: [20]

1. Direct allocation (ignores interaction of overhead departments). Each overhead cost is allocated directly to final cost centers. Program X's allocated share of central administration is equal to central administration cost times. Note's program X's proportion is program X's paid hour divided by total paid hours of all final cost centers, not total paid hours for the whole organization. The latter method would underestimate the costs in all final cost centers;

2. Step down allocation (partial adjustments for interaction of overhead department). The overhead departments are allocated in a stepwise fashion to all of the remaining overhead departments and to the final cost centers;

3. Step down with iterations (full adjustment for interaction of overhead departments). The overhead departments are allocated in a stepwise fashion to all of the other overhead departments and to the final cost centers. The procedure is repeated a number of times (about three) to eliminate residual unallocated amounts;

4. Simultaneous allocation (full adjustment for interaction of overhead departments). This method uses the same data as (2) or (3) but it solves a set of simultaneous linear equations to give the allocations. It gives the same answer as method (3) but involve less work.

Allowance for differential timing of costs (discounting and the annuitization of capital expenditure)

Some allowance needs to be made for the differential timing of costs and consequences. That is, economists call this the notion of time preference. There are a number of reasons why individuals may have a positive rate of time preference; that is, a preference for benefits today rather than in the future. First, they may have a short- term view of life; living for today rather than thinking about the future. Secondly, the future is uncertain. Third, with positive economic growth, a dollar today would be of higher value than one in the future. Finally, since most individuals appear to have a positive rate of time preference, one can usually obtain a positive return when making a riskless investment.

A comparison of two programs (adjusted for the differential timing of resource outlays) would be made by discounting future costs to present values. The calculation is performed as follows. If P = present value; F_n = future cost at year n; and r = annual interest (discount) rate, then

$$P = \Sigma F_n(1+r)^{-n}$$

The factor $(1+r)^{-n}$ is known as the discounting factor.

While this approach is the most convenient for many program comparisons, a more common situation is that where most of the costs are easily expressed on an annual recurring basis and it is only capital costs, which differ from year to year. Here it might be more convenient to express all the costs on an annual basis, obtaining an

equivalent annual cost (E) for the capital outlay by an amortization or annuitization procedure. This works as follows:

If the capital outlay is K, we need to find the annual sum E which over a period of n years (the life of the facility), at an interest rate of r, will be equivalent to K. This is expressed by the following formula:

$$K = E\,[1-(1+r)^{-n}/r] \quad \text{or}$$

$$K = E\,[\text{Annuity factor, n period, interest r}]$$

This approach can be generalized to handle the situation where the equipment or buildings have a resale value at the end of the program. If:

S = the resale value;
n = the useful life of the equipment;
r = discount (interest rate);
A (n,r) = the annuity factor (n years at interest rate r);
K = Purchase price/ initial outlay;
E = equivalent annual cost;
then:

$$E = [K - S/(1+r)^n] / [A\,(n,r)]$$

The method described above is unambiguous for new equipment. For old equipment, there are two choices:

Choice 1 – use the replacement cost of the equipment or the original cost indexed to current dollars and a full life;

Choice 2 – use the current market value of the old machine and its remaining useful life.

Choice 1 is usually better as the results are more generalizable – less situational. Note that using the undepreciated balance from the account of the organization is never a method of choice.

2.3.3 Basic Conception of Valuing Lives [25]

For this purpose, two completely different conceptions have been developed: the human-capital approach and the willingness-to-pay approach. In this section, both of them are

2.3.3.1 The Human-Capital Approach

The value of an object can be determined by measuring the owner's financial loss from losing it. This loss, in turn, is measured by the revenue stream that he could have obtained through careful management of the object. The application of this simple accounting rule (productive value principle) to human beings leads to a definition of the value of life based on the loss of human capital result in from the death of that human being. The value of life is therefore equal to the discounted sum of the individual's future (marginal) *contributions to the social product*, which corresponds to his future labor income, provided his or her wage is equal to the value marginal product.

The human capital approach is based on two implicit postulates.

1.An individual's value depends on the contribution that he or she makes to the welfare of its fellow citizens.

2.The appropriate measure of society's welfare is the Gross National Product (GNP).

The main advantage of the human-capital approach is that it can be made operational rather easily. For this reason, it has often been applied in cost-benefit analyses in the past. But it is completely foreign to microeconomic theory, which focuses on individual valuation. In addition, its ethical underpinnings are very much open to attack. One criticism sets in at the result of such a human-capital calculation, which many people consider unacceptable. According to it, the value of the life of pensioners and others who are unable to work is always zero (even negative according to the net human-capital approach).

2.3.3.2 The Willingness-To-Pay Approach

Definition

In contrast to the human-capital approach, the concept of willingness to pay is firmly rooted in the axiomatics of subjective valuation. The preferences of the persons affected and possibly their relatives are in the focus of interest. Asking for the amount of money that is worth just as much to an individual as his own life leads to ambiguities, because the answer depends on whether losing or saving one's life is at issue. These difficulties can be avoided in considering alternatively.

1. Marginal changes in the *probability* π to die within a given period of time;

or

2. Marginal changes of the expected *life span.*

In case (1), one seeks to determine the amount of money Z that the individual is willing to pay for a small *decrease* in the risk of dying $\Delta\pi$ (e.g. 1 percentage point). In full accord with microeconomic theory, Z is called "equivalent variation." By way of contrast, the amount *K* that would be required to compensate the individual for an *increase* in π by $\Delta\pi$ is called "compensating variation" for a change in risk. When $\Delta\pi$ goes towards zero, the two quotients $Z/\Delta\pi$ and $K/\Delta\pi$ converge. Their common limit, that is, the marginal rate of substitution between wealth and the risk of dying, can be interpreted as the individual's marginal willingness to pay for infinitesimal changes in risk.

In case (2), the amount of money that the individual would be prepared to sacrifice in order to prolong his life by one year can be interpreted as his marginal willingness to pay for a year of life gained.

Both of the two formulations have their specific legitimation. From the ex-post point of view, the concept of years of life gained makes more sense than the one of changes in risk. On the other hand, for an individual faced with the ex-ante uncertainty of the time of his death, the concept of life expectancy is less concrete than the one of a change in risk for the subsequent period of time because the life expectancy is determined by the entire probability distribution of death risks over the remaining lifetime.

2.4 Study Design in Prevention Effectiveness [26]

Before beginning a prevention-effectiveness analysis, researchers must address a number of issues. The perspective of the study, the analytic method, and

other key issues affect not only the nature of the analysis but the interpretation and usefulness of the results as well. This process is referred to as "framing the question." Its successful completion is one of the most important steps in a study.

Framing the Question: A List of Key Points

1.Define the *audience* for the evaluation. Identify the users of the results of the analysis, and indicate how the result will be used. Determine the information needs of the target audience in reference to the programme or intervention.

2.Operationally define the *problem or question* to be analyzed. This process will influence the types of effects and costs to be included and will help determine which economic evaluation technique is most appropriate for the analysis.

3.Clearly indicate the *prevention strategies* being evaluated, including the baseline comparator (the strategy that best represents current practice) for the evaluation.

4.Specify the *perspective* of the analysis. The perspective taken will determine which costs and benefits are included in the analysis. Limit perspectives to those relevant to the study question.

5.Define the relevant *time frame* and *analytic horizon* for the analysis. Determine the time period (time frame) in which the interventions will be evaluated. Determine how far into the future (analytic horizon) costs and effects that accrue from the intervention will be considered.

6.Determine the *analytic method* or methods. The three methods widely accepted are cost-benefit, cost-effectiveness, and cost-utility analysis. The choice of analytic method will depend on the policy question, the outcomes of interest, and the availability of data.

7.Determine whether the analysis is to be a *marginal* or *incremental* analysis. A marginal analysis examines the effect of programme scale. An incremental Analysis compares the effects of alternative programmes.

8.Identify the relevant *costs*. Determine whether the health outcomes will be evaluated using the *cost-of-illness* or the *willingness-to-pay* approach. If the cost-of-illness approach is used, determine whether *productivity losses* will be included. Identify other relevant costs or monetary benefits.

9.Identify the *health outcome* or *outcomes* of interest. Determine whether the outcomes of interest are final health outcomes. The number and nature of outcomes will also help to identify the appropriate analytic method.

10.Specify the *discount rate* or time preference for costs and nonmonetary outcomes that occur in the future.

11.Identify the sources of *uncertainly* and plan *sensitivity analyses.* There may be uncertainty about the effectiveness of a programme option in achieving specified health outcomes, or uncertainty about the values of parameters in the model.

12. Determine the *summary measures* that will be reported.

13.If the distribution of the costs and benefits in the population will differ for the prevention-intervention options including the baseline comparator, determine the feasibility of analyzing the *distributional effects* of alternate strategies.

2.5 Previous Studies

1. Bogel K, Meslin FX. Economics of Human and Canine Rabies Elimination: Guidelines for Programme Orientation. Bull World Health Organ 68 (3). (1990): 281-291.

Analysis of the present situation in canine-rabies-infected countries shows that in most cases the levels of activities for controlling the disease in man and in dogs are far too low to prevent human deaths due to rabies and to eliminate the disease in the dog population. This article compares the two major orientations of a rabies control programme, i.e., prevention of the disease in man by intensifying and modernizing post-exposure treatment (strategy A) and canine rabies elimination by controlling the disease in the animal reservoir (strategy B). The operation of both strategies (A + B) together is also analyzed.

Based on the available data and assumptions for calculations of the costs, the results show that when the strategies are applied independently of each other, the annual cost of strategy B amounts to 25-56% of that of strategy A. When the two strategies are applied together, the actual annual spending related to the implementation of A + B becomes less than that of strategy A alone as from the fifth year following programme initiation. The sensitivity of the results was tested against selected fluctuations in the assumptions.

An estimation of the costs of control activities per avoided death, according to the strategy applied, is also given. In countries where resources allocated to rabies control are inadequate in both the health and veterinary sectors, the comparison in costs and effectiveness of the two programme strategies for rabies elimination strongly suggests that consideration should be given to a national programme of dog rabies elimination. On the other hand, for obvious ethical reasons, if attention is paid to improvement of post-exposure treatment, then the national authorities should consider a planning horizon close to 15 years.

2. Fishbein DB, et al. Rabies Control in the Republic of the Philippines: benefits and costs of elimination. Vaccine 9. (August 1991): 581-587.

The authors compared the benefit and costs of eliminating animal and human rabies in the Philippines. If rabies had been eliminated in 1988, economic benefits would total P52.8 (US$2.5) million in 1989.

These benefits would largely arise from the abolition of expenses associated with rabies prevention: P29.7 (US$1.4) million for animal vaccination, P21.6 (US$1.0) million for human postexposure prophylaxis, and P0.3 (US$0.02) million for animal rabies examinations. Benefits also included P1.2 (US$0.06) million in additional earnings of humans whose death due to rabies would be prevented.

Nationwide elimination was estimated to cost between P88.1 (US$4.2) million and P317.2 (US$15.0) million, assuming a canine-to-human ratio of 1:10, vaccine coverage of 60%, and a cost per vaccination of no less than P25 (US$1.19) and no more than P90 (US$4.27).

These costs would be recouped 4.1-11.0 years after the initiation of a one-year elimination campaign. A sensitivity analysis showed that an elimination programme would be economically beneficial in all but the most extreme cases.

3. Belotto AJ. Organization of Mass Vaccination for Dog Rabies in Brazil. Rev Infect Dis 10 (Suppl 4). (1988): S693-S696.

This study reports results of the mass dog rabies vaccination campaigns that took place in Brazil between 1980 and 1985 as a measure of reducing the incidence of rabies in urban areas of the country. Particular focus is given to the organization of these campaigns, which took placed on a singe day in more than 1,000 towns in 20 states, including large metropolitan areas such as Rio de Janeiro.

Three levels of public health services (federal, state and municipal) were involved in the organization of these campaigns. The massive participation of the community is also emphasized. Nearly 100,000 people from different segments of the community, especially students and members of the armed forces and state military police, participated as vaccinators or the other roles on the nation day of the dog rabies vaccination. Another fundamental point is the support given in the media by means of national and state broadcast during the 2 weeks the day of vaccination.

The study shows a progressive decrease in the number of cases of rabies in dogs and in humans during the period, a decrease that can be reasonably attributed to the increase in the number of vaccinations for dog rabies. In 1980 there were reported 4,570 cases of rabies in dogs and 168 cases of rabies in humans; in 1985 the incidence was reduced to 496 and 52 cases, respectively.

4. Chomel B, et al. Mass Vaccination Campaign against Rabies: Are dogs correctly protected? The Peruvian experience. Rev Infect Dis 10 (Suppl 4). (1988): S697-702.

In a mass vaccination campaign conducted in Peru in March 1985, 270,000 dogs (65% of the estimated dog population) were vaccinated over the course of 1 month with an inactivated tissue culture vaccine. Since that time no human rabies cases have been reported; in addition, the number of animal rabies cases has declined to only three from previous mean of 292 cases per year since 1980. Clearly such campaigns should be carried out on a regular basis to reduce enzootic foci of rabies, especially when programs for stray dog control are not well established and maintained. The vaccination of owned dogs and the elimination of stray dogs should always be conducted concurrently. The health authorities should take advantage of large vaccination campaigns to eliminate stray dogs.

A serologic survey was also done to determine the immune response among randomly selected vaccinated dogs, with titers determined 3, 6, 9, and 12 months after vaccination. Twelve months after vaccination, 97% of the dogs had a rabies neutralizing antibody titer of > =0.5 IU/ml, and 87% had a titer of > = 1.0 IU/ml.

Thus, this tissue culture rabies vaccine given under field conditions induced antibodies that lasted for at least 1 year in 97% of vaccinated dogs.

5. Choomkasien P. Epidemiology of Rabies in Thailand; what will we do from now? Available from: http://www.moph.go.th/ops/epi/Monthly/rabies.html[2002,Oct 29]

This article had analyzed epidemiological data of rabies between year 1991-2000. Obviously the number of rabies-related death cases was decreased dramatically after strengthening in dog rabies control program and being widespread use of safety postexposure vaccine. But the way to run out of death case is likely to be more laboratory test taken part in much more than the past. In addition the rabies control in dog should be diffused prevailingly in every area, at least 80% of total dog population

6. Mitmoonpitak C, Tepsumethanon V, Wilde H. Rabies in Thailand. Epidemiol Infect 120. (1998): 165-169.

The prevalence of canine and human rabies in Thailand has decreased significantly during the last decade. This has been associated with an increasing number of human postexposure treatments. Educational efforts, mass vaccination of dogs and cats and the use of safe and effective vaccines have all made and impact.

An estimate of the total dog population, carried out on the basis of random sampling in 1992, was 7.6 million equivalent to 1 dog per 6.7 persons or 0.7 dogs per household. Based on Buddhist ethics, their staffs rarely kill dogs that are brought to the Queen Saovabha Memorial Institute in alive. This practice allowed them to observe a large number [837] of animals during 1985-96. It has been an experience that all their rabid dogs succumb within 10 days of onset of neurological symptoms. Their findings thus support the current WHO recommendation that observation of dog for 10 days is a safe practice. They believe that 'dog rabies survivors', as described by Yasmuth and colleagues may have subclinical illness without aggressive behavior and are simply not detected unless serosurveys are carried out on apparently healthy unvaccinated animals.

It is apparent that some progress with rabies control has been made in Thailand but the battle is far from won. The large population of stray and community dogs, the fact that they have a short life span and often receive only one vaccine injection, contribute to the rabies problem in this country. Cultural and religious barriers to more radical measures for dog control are also hindrance.

7. Meesomboon V, Sagarasaeranee P. Dog ecology Study in Thailand. J Health Science 1. (April 1992): 316-326.

This is the study of dog ecology in Thailand (excluded Bangkok) in 1990 using household questionnaire survey has revealed that the total number of owned dog population was estimated at 7,241,830. There was 585,820 owned dogs in municipal areas and 6,656,010 dogs in rural areas. There were 2,186,847 female dogs at reproductive age (6 months- 7 years old).

The average numbers of dogs per household in urban areas were 0.72, 0.58, 0.63 and 0.35 in Northern, Central, Northeastern and Southern regions respectively and in rural areas were 0.78, 0.93, 0.53 and 0.38 respectively. There were 30.09 reproductive female dogs per 100 owned dog population. Dog to human ratio was 1:6.72.

The annual birth rate of the owned dog population was 12.86 %, and the death rate was 10.91%.

8. Bhanganada K, Wilde H, Sakolsataydorn P and Oonsombat P. Dog-bite injuries at a Bangkok teaching hospital. Acta Tropica 55. (1993): 249-255.

Thailand has a large domestic and stray dog population and Buddhist cultural beliefs encourage feeding and protection of stray animals. Dog bites are common injuries encountered in emergency rooms throughout the country.

A prospective study of such bites seen at a teaching hospital in Bangkok revealed that: (1) dog bites represent 5.3% of injuries seen in the emergency room; (2) the majority occur on the street, are inflicted by stray dogs and are interpreted by the victim as unprovoked. Children and teenagers account for 55% of the victims. The lower extremities (54%) and upper extremities (20%) were the most common sites for bites. 9% of patients were bitten on the face or head. In addition to pain, risk of infection (approximately 13%) and the significant cost of caring for these injuries, victims often experienced prolonged anxiety because of to the generally known risk of rabies in Thailand. Due to the high cost of imported immunoglobulins and vaccines, rabies exposures are not always managed optimally in Asia.