POLICY PAPER
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Brucellosis in Animals
Strategies for Prevention and Control

NATIONAL ACADEMY OF VETERINARY SCIENCES (INDIA)
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Preface

India has witnessed accelerated economic growth in the past decades. The livestock sector has played a crucial role in the socio-economic framework of the country. Livestock, Poultry and Fishery sub sectors together contribute 25-30 per cent of agricultural GDP and about 5.5 per cent of national GDP. Although livestock sector has shown incredible growth after independence, the burden of infectious diseases has made our economy and lifestyle stay behind. Among these, brucellosis is one of the major zoonotic diseases with significant public health and economic concern. It has got a serious impact on both human and animal health. There is no vaccine available for human till date. Control of Brucellosis in animals brings down the number of human brucellosis cases. There is a need for an approach and strategies for prevention and control of animal brucellosis. Hence, it is crucial to undertake Brucellosis control program with high priority and sincerity. A strategy of vaccination along with sanitation, good management practices and health education appears to be the need of the hour. Thus a well-planned and operational animal brucellosis control program is an urgent requirement to minimize the economic losses to livestock industry as well as public health concerns.

In view of the gravity of the issue, Indian Council of Agricultural Research, Indian Veterinary Research Institute, and National Academy of Veterinary Sciences (India) jointly organized an "Expert Consultation on Brucellosis" on January 23, 2013 at NASC Complex, New Delhi for an in-depth discussion to review the situation, to formulate recommendations, and suggest suitable management practices and strategies for the National control program and strengthen the research on diagnostics and vaccine(s).

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(Prof. M. P. Yadav)
President, NAVS

BRUCELLOSIS IN ANIMALS

STRATEGIES FOR PREVENTION AND CONTROL

1. PROLOGUE

Brucellosis is considered by FAO/WHO/OIE/ILRI as the most widespread zoonosis in the world with an estimated 500,000 new human cases each year [1, 2]. WHO has recognised it as one of seven neglected, under-detected and under-reported zoonosis [3] with serious health implications, particularly for the poorest segment of human population and in medically under-served regions because of high incidence in developing countries, economic consequences and difficulties encountered in its eradication. The importance of this highly contagious disease is due to its economic impact on the animal industry and severe hazard to human health. Although continuous progress has been made in brucellosis control in many parts of the world, it still remains a major public health hazard and of great economic importance causing an ever-increasing concern in many countries. In India, systematic attempts to gauge the exact problem of brucellosis in animals are yet to be undertaken. Nevertheless, the available epidemiological evidences suggest that brucellosis is prevalent in all domestic animals besides wild animals in all states of India with wide variation in prevalence. The Department of Animal Husbandry, Dairying and Fisheries (DAHD&F), Government of India has recently initiated ambitious National Brucellosis Control Programme. However, for success of the programme, a close monitoring during its implementation along with good husbandry practices is essentially required. Taking cognizance of the serious implications of brucellosis on livestock sector and its public health significance, Indian Council of Agricultural Research, Indian Veterinary Research Institute and National Academy of Veterinary Sciences jointly organized an "Expert Consultation on Brucellosis" on January 23, 2013 at NASC Complex, New Delhi (Annexure-1), with an aim for in-depth discussion to formulate recommendations for strengthening the research on diagnosis and vaccine(s), and suggesting management practices and strategies for the National control program.

2. ETIOLOGY

Brucellosis is an infectious disease caused by members of genus *Brucella of α 2-Proteobacteriaceae family,* which are Gram's negative non-sporing facultative intracellular coccobacilli devoid of classical virulence factors. The disease affects cattle and other domestic animals. Of all known species of *Brucella*, seven, namely *B. abortus, B. melitensis, B. suis, B. ovis, B. canis, B. neotomae* and *B. microti* are terrestrial [4-6], while *B. ceti* and *B. pinnipedialis* are marine species [7]. A novel species, *B. inopinata* isolated from a wound associated with a breast implant has been the latest addition to genus *Brucella* [8] and the BO2 strain as a novel lineage.

3. TRANSMISSION & SYMPTOMS

Many animal species, both domestic and wild, are susceptible to *Brucella*. Cattle, buffalo, sheep, goat, pig and dog are the main reservoirs for maintenance of brucellae. The disease is mainly transmitted through ingestion of organisms via oral and pharyngeal cavities. The disease may also be transmitted through artificial insemination, if semen from infected bull is used. Transmission through inhalation is infrequent in bovines, but is important in humans working in meat processing plant, slaughter house and wool shorter units. The organism is concentrated in the lymph glands of infected animals, particularly those associated with the uterus and udder. Infected females excrete large numbers of bacteria during calving or abortion, from which other animals may become infected with *Brucella* by contact with the expelled tissues, fluids and organisms. Transmission is most likely to occur where animals are densely confined during late pregnancy or calving during late winter and spring. Human may get infected with brucellosis through per-cutaneous, conjunctival or nasal mucous membrane. Factors contributing to the transmission of brucellosis in humans are close contact between human and animal populations, especially in rural areas, occupational settings as well as consumption of raw contaminated milk and milk products.

The disease is largely asymptomatic in most of the animal species. In cattle, buffalo, sheep and goats, brucellosis is characterized by abortions usually during the third trimester of gestation, retention of placenta, orchitis and epididymitis leading to impaired or reduced fertility in bulls. Interference with fertility is usually temporary and most infected animals will abort only once. The udder is often permanently infected, especially in the case of cows and goats. Shedding of organisms in milk is frequent. Sexually immature cattle do not usually show any signs but may remain subclinically infected until maturity and pregnancy. Localized infections in sheep result in orchitis or epididymitis in case of *B. melitensis* and *B. ovis*. Arthritis with swollen joints can also develop in long-term infections.

4. DISTRIBUTION

Brucellosis remains endemic [9] worldwide with the exception of countries where the disease has been eradicated [10]. The global distribution of brucellosis is continuously changing with emergence or re-emergence of new foci [9]. It is an important but neglected zoonotic disease present in all livestock systems in India [3, 11]. The exact incidence of brucellosis in animals and man in India is not known. However, the available literature indicates endemicity of the disease in the country. Bovine brucellosis caused by *B. abortus* has been the most wide spread form in animals including the Indian subcontinent. A recent study on 4,580 animals of 119 dairy farms shows 65.54% (78/119) herd prevalence and 26.50% (1,214/4,580) individual animal prevalence of brucellosis in cows and buffaloes in Haryana and Punjab [12]. A study from Uttar Pradesh conducted in 2000 showed an overall prevalence of 7.25% in bovines with 12.77% seropositivity in cattle and 3.55% in buffaloes [13]. The overall prevalence of bovine brucellosis in Punjab was 11.23% varying from 0% to 24.3% in different villages [14]. The PD_ADMAS (2005-2010) reported presence of the disease throughout the country with varying prevalence in different animal species, viz: bovine (22.15%), sheep (8.85%), goat (6.23%), pig (15.35%), yak (16.0%) and mithun (19.0%). This high prevalence of animal brucellosis is responsible for human infections due to close contact with animals. The disease appears to be on the increase in recent times, perhaps due to increased trade and rapid movement of livestock [15] and increase in more susceptible high producing cross bred cattle population.

In spite of high prevalence of animal brucellosis, the human disease has not been much studied in India where the little data published represents only the tip of the iceberg and the true prevalence remains to be estimated. It is assessed that human brucellosis is greatly underreported in most countries due to lack or weak diagnostic facilities and failures in the reporting systems. Actual prevalence is supposed to be 25 times higher than reported [11]. The prevalence of human brucellosis in India shows wide variation with reported prevalence of 0.8% in Kashmir [16], 6.8% in Varanasi [17], 8.5% in Gujarat [18], 11.51% in Andhra Pradesh [19], 19.83% in Maharashtra [20], and 26.6% in Ludhiana [21]. The prevalence also varies according to the population tested.

It is well established that animal brucellosis is widespread in India and affects both large (cattle, buffalo) and small (goat, sheep) ruminants. There is, however, general agreement that the impact of brucellosis in small ruminants is greater in terms of the adverse effects on human health due to the high virulence of *B. melitensis*. With the exception of the dairy units located in peri-urban areas, the majority of the producers belong to the rural population who are often less privileged with respect to access to public and animal health services.

In India, *B. abortus* biotype 1, 3 and 6 have been isolated from cattle besides *B. melitensis* biotype 1. Relatively higher incidence of brucellosis has been observed in organized farms as compared to the village areas. In India, *B. abortus* biotype 1 has been found to be the major causative agent for brucellosis in organized farms of cattle and buffaloes, whereas *B. abortus* biotype 3 predominates in cattle and buffaloes reared under traditional system of husbandry in villages [22]. All the three biotypes of *B. melitensis* with predominance of biotype 1 have been isolated from sheep and goats besides *B. abortus* biotype 1. Isolation of *B. canis* and *B. suis* have also been made but no isolation of *B. ovis or B. neotomae* has been reported from India.

5. ECONOMIC LOSSES

Brucella is reported to inflict huge economic losses [23, 24] to national exchequer on account of impeding abortion and infertility in animals and loss of precious protein food besides loss of man days and cost of treatment due to human brucellosis. The heavy economic losses to livestock industry results from abortions, sterility, decreased milk production, veterinary attendance and the cost of replacement animals besides being an impediment to free animal movement and export. Though no accurate estimates at national level are available due to brucellosis, the losses have roughly been calculated to cost India at least Rs.350 million every year on account of food animals and loss of man-days [25]. Earlier to this, economic loss due to bovine brucellosis was estimated at Rs.311.47 million [41]. In one study, it was seen that 70 buffaloes aborted due to brucellosis during a period of 4 years on a Government animal farm of Murrah buffaloes located in north India [26]. Altogether 99 infected animals, including aborted ones, were culled and sent to Go-sadan. Keeping other cost aside, culling of 99 buffaloes causes a loss of Rs. 3.96 million if Rs. 40,000/- is estimated as average cost of one buffalo. This clearly suggests that brucellosis causes huge losses on animal farms. Number of dairy farms is increasing day by day and entry of brucellosis on such new farms is very much likely under the prevailing husbandry practices as has been reported recently [12] which results into enormous un-accounted losses. It is estimated that an abortion in female animal costs a farmer Rs. 6000/-, which can be easily avoided by successfully implementing control measures. Prevention of abortions will add 2.63 million new female calves per annum valued at Rs. 2,630 crores. Increase in national milk production by 5 per cent at the end of five year will add an annual value of Rs.7,890 crores. The added advantage of controlling the disease would be in the form of reduced infertility, metritis and production losses.

6. DIAGNOSIS

In the absence of any pathognomonic symptom, clinical diagnosis of brucellosis is difficult. As such, bacteriological and serological tests are used for its diagnosis. The presumptive diagnosis of brucellosis can be done by the exfoliative cytological methods, where smears of placental cotyledon, vaginal discharge or foetal stomach contents are used to detect organisms after staining with modified Ziehl-Neelsen or Kosters' methods [27]. The most reliable diagnosis is based on the isolation and identification of the etiological agent, but this being tedious and time consuming is not practicable under most circumstances [9]. Many a times, isolation is not successful even from known positive cases. Thus, recourse to serological tests becomes imperative. Detection of antibodies is quick but all infected animals do not produce detectable level of circulating antibodies. Also, diagnosis may be impaired by the presence of antibodies to cross-reacting organisms as well as vaccination.

If control programs are to be implemented, testing of animals and/or food products is necessary. There are a large number of serological tests to diagnose brucellosis. Different serological tests commonly used include Rose Bengal Plate Test (RBPT), standard tube agglutination test (STAT), milk ring test (MRT), 2-mercaptoethnol test (2-MET), heat inactivation test (HIT) and complement fixation test (CFT)[28]. Of these, MRT could be used to locate an infected dairy herd, and has been recommended by OIE as a screening test for bovine brucellosis [29]. RBPT is a simple, rapid, cheap and easy test to be performed with high specificity. However, it has reduced performance in chronically infected animals, which require accurate serological tests like CFT and enzyme linked immunosorbant assay (ELISA). ELISA is also an OIE prescribed test and can be conducted on serum and milk samples. In the case of CFT, laboratory and technical expertise requirements make this test unsuitable in many developing countries. Another promising test is fluorescence polarization assay (FPA), which has high sensitivity and specificity [30].

7. VACCINES

Vaccination is an extremely important and effective tool that has been used by many countries to control/eliminate/eradicate animal brucellosis from the area/country. Presently, there are four vaccine strains for use in animals [31]:

i) *Brucella abortus* strain 19 (S19)

The S19 vaccine was developed in 1930 in USA and since then it has been extensively used for controlling and/or eliminating bovine brucellosis from the area/country. It is a reference vaccine and prescribed by OIE. This vaccine has been used in calves, adult bovines including milking and pregnant animals. For calves, standard dose of S19 vaccine is used and given by subcutaneous route, while in adult animals, the S19 vaccine in reduced dose is given by conjunctival route or subcutaneously. The conjunctival route of vaccination is preferred as it overcomes the disadvantages of abortion in pregnant animals, shedding of the organism (S19) in milk in lactating animals and persistent antibody titres [29]. The S19 vaccine is time tested and works in all situations. All those countries that had controlled or eradicated bovine brucellosis used S19 vaccine. Till today this vaccine is considered to be the most effective in controlling brucellosis in bovines in prevailing animal husbandry and management practices in low income or developing countries.

ii) *Brucella abortus* strain RB51 (RB51)

The RB51 is a laboratory derived live-attenuated vaccine strain developed through successive *in vitro* passage of virulent *B. abortus* 2308 on media containing rifampicin and penicillin [32]. It is a spontaneous rough mutant devoid of O-polysaccharide chain hence, lacks the ability to produce antibody in animals/humans. It was licensed by USDA for use as a vaccine against brucellosis in bovines. Inability of RB51 to produce antibody allows an easy differentiation between infected and vaccinated animals. This vaccine is useful in eradication program where identification and removal of infected animals is necessary. However, RB51 is not effective in endemic situation where prevalence of brucellosis is high [33]. Further, it is not effective in preventing natural exposure of *B. abortus* to buffaloes under field conditions [34]. Other disadvantages of RB51 vaccine are: (i) Serological tests like RBPT, STAT, LPS-based ELISA etc. are ineffective in detecting RB51 infections (ii) Monitoring of RB51 vaccination is difficult as antibodies are not produced in vaccinated animals, (iii) Diagnosis of disease is difficult in case of accidental human infections and (iv) Rifampin, a drug of choice for the treatment of human brucellosis, cannot be used. However, RB51 vaccine seems to be useful in low incidence areas/countries when infected animals are needed to be identified and removed with the objective to eliminate/eradicate brucellosis.

iii) *Brucella melitensis* strain Rev.1 (Rev.1)

The *Brucella melitensis* Rev. 1 vaccine was developed in 1950s and since then it is in use for the prevention of caprine and ovine brucellosis, including *Brucella ovis* infections [35]. The vaccination of sheep with the standard dose of Rev.1 vaccine is the most practical means to rapidly reduce the rate of *Brucella melitensis* infection in both sheep and goats. The vaccine can be inoculated by subcutaneous route or conjunctival route with no difference in protection. The conjunctival route is simple and easy to implement with minimum cost. The *Brucella melitensis* Rve.1 vaccine is not safe for human beings as it causes disease in accidental inoculations. Secondly, Rev.1 vaccine carries smooth lipopolysacchride with O-polysaccride that elicits antibodies interfering in sero-diagnosis, a major problem in differentiation between vaccinated and infected animals and, also in eradication campaigns. Because of these problems rough *Brucella melitensis* mutants which are defective in core and O-polysacchride synthesis were generated and tested for their protective efficacy in laboratory models [36]. However, the results of this experiment demonstrated that no vaccine prepared from rough mutant is equal to that of Rev.1 vaccine in laboratory models. This study questions the notion that vaccines from rough mutants are suitable for control of brucellosis in endemic areas [36].

iv) *Brucella suis* strain (S2)

An attenuated strain *Brucella suis* (S2) was developed in China after serial transfer of a virulent *Brucella suis* biotype 1 strain on culture media for years. *Brucella suis* S2 is of smooth type, shows the same level of attenuation as strain 19 shows in guinea pigs, and does not revert to the virulent state after repeated culturing through guinea pigs, sheep, goats or boars. It protects cattle, goats, sheep and pigs when administered orally. Implementation of vaccination programs in semiarid grasslands where sheep and goat breeding is extensive is necessarily difficult. Since in these areas the only source of drinking water is from wells, *Brucella suis* S2 has been administered orally in the drinking water. By this route, the S2 vaccine has been widely used for prevention of animal brucellosis in China [37]. Good results were also obtained with sheep in a trial in Libya [38]. However, in controlled experiments performed in France [39], *Brucella suis S*2 administered subcutaneously did not protect sheep against a *Brucella melitensis* or a *Brucella ovis* challenge under conditions in which the standard *Brucella melitensis* Rev. 1 was effective. The different breeds employed, differences in the challenging strains used, the climatic and nutritional conditions and the difficulties in obtaining reliable data under field conditions may account for the discrepancies.

Limitations of available vaccines include: interference with serology, abortifacient in pregnant animals, and virulence for humans, and shedding in a small proportion of vaccinated animals. Besides, these vaccines are heat-labile and require specific logistics, storage and quality-control precautions when used in remote areas. Moreover, **v**accine for use in canines, swine and man are not available. Therefore, the search still continues to develop a better vaccine particularly one which has no abortifacient properties, can facilitate differentiation of vaccinal and infection antibodies besides being avirulent for man.

8. PREVENTION & CONTROL

Control of brucellosis in human is directly linked to control of animal brucellosis. Humans are the end result of bacterial activity in animals, so any preventive measures aimed at human brucellosis has no impact on the presence of animal disease in an area. Nevertheless, surveillance of human brucellosis is important in the management of brucellosis control/eradication programmes. In fact, the incidence of human brucellosis is a good index of the presence of infection in animal population, and thus, human can be a good sentinel of the infection in animal population in all cases, where a reduced or variable degree of testing is performed.

Before venturing into any control policy enactment, it is vital to identify the important components that are unique to brucellosis and may play an important role in perpetuating the infection in nature. Following important characteristics needs to be considered in case of brucellosis:

1. Disease spreads easily between and within herds and flocks, particularly at the time of calving;
2. Clinical signs are not pathognomonic;
3. Infected females do not always abort;
4. Latent carriers usually exist;
5. Transmission occurs both through direct or indirect contact;
6. No diagnostic tool correctly identifies all infected or non-infected animals;
7. Available vaccines dramatically reduce the spread of brucellosis but do not fully protect against infection, especially in endemic areas where continuous exposure with high number of bacteria takes place.

Any control programme against brucellosis is only fully effective if it is designed for a particular country. This is especially relevant with respect to a country like India which is host to a multitude of geo-climatic conditions; religions and social beliefs, and the problems arising due to their interactions. It is, therefore, important to consider the issues that plague the Indian brucellosis scenario:

1. Animal identification system is non-existent.
2. Growth in dairy venture.

3. Unrestricted movement of animals.
4. Tracing of animals is impossible.
5. No compensation system for culled animals.
6. Brucellosis is a herd disease, and in many circumstances, all herds with positive animals should be culled. However, given the high herd prevalence of brucellosis and ban on cow slaughter, this is inapplicable.
7. No action plan for replacements from certified brucellosis free herds.
8. Testing capacity is not sufficient.
9. Regular testing of all animals is not possible or extremely difficult.
10. Not possible to rapidly cull positive animals.
11. Protection of herd from re-infection is difficult to achieve.

Control is designed to reduce the disease occurrence in populations and can be achieved by reducing or eliminating the causes to a level of little or no consequence and thereby aims to reduce the impact on human health and economy. It is implicit that some “accepted” level of infection remains. Control programmes therefore have an indefinite duration and will need to be maintained even after the “acceptable level” of infection has been reached, so that the disease does not re-emerge. The different components of brucellosis control as described by Smits [40] are enlisted below. These components can be modified as per their suitability in any area.

Components of brucellosis control and prevention

1. Legislation
2. Disease inventory
    - » Livestock census
    - » Risk analysis
    - » Surveillance for assessment of status
    - » Knowledge, attitudes and practices (KAP)
    - » Risk factors for spread and transmission
3. Control and prevention:
    - ♦ Mass vaccination
        - » Vaccine production/procurement
        - » Vaccine storage and distribution
        - » Vaccine quality assurance
        - » Vaccine coverage monitoring
        - » Level of protection
4. Control and prevention:
    - ♦ Complementary measures
        - » Herd and animal identification

- » Information, education and awareness about the disease
- » Animal movement regulation and segregation
- » Test and elimination
- » Farm hygiene and food sanitation
- » Human health, healthcare and disease prevention

5. Post-vaccination control measures
   - » Disease surveillance and monitoring
   - » Test and intervention (vaccination, segregation and elimination)

The brucellosis control and eradication is best achieved by a combination of vaccination with test and slaughter of positive animals. Exclusive test and slaughter strategy should be limited to the regions/ areas with very low herd prevalence supported with well-established veterinary services, adequate budget and the political will. In all other situations, vaccination should be considered as a basic control tool. Since test and slaughter is not practicable in India, eradication cannot be targeted leaving control of brucellosis the only option. *The whole population vaccination should be considered, where the herd prevalence is high and control on animal movement is not effective.*

The brucellosis control programme based on mass vaccination, has to be maintained for at least three generations depending on the species of animal for its effectiveness. Among the different mass vaccination strategies, the safest strategy is the mass vaccination of the entire population in the first year; followed by vaccination of only young replacements in the subsequent years. An individual identification system for identification of vaccinated and non-vaccinated animals is needed. The vaccination campaigns should ensure the critical immunisation level leading to effective control. Ideally, 80-100% coverage should be attained. The success of the immunisation programme largely depends on the vaccination coverage and the vaccine efficacy. Its success greatly depends on activities such as: (i) training of veterinarians, (ii) quality management and (iii) efficacy of vaccination.

To monitor the overall efficacy of vaccination, three surveys need to be conducted: (i) First sero-survey before vaccination, both in animals and humans, to get a baseline sero-prevalence, (ii) Second sero-survey following vaccination of the animals to assess the success of immunisation and the vaccination coverage, and (iii) Third longitudinal sero-survey in humans after the vaccination of animals to assess the effectiveness of the livestock vaccination campaign reflected by decrease in the incidence of human brucellosis. A serological survey in livestock can show the immunisation coverage. The sero-survey should be done between 15 – 45 days, *i.e.*, not before 15 days and not after 45 days of the vaccination campaign, as antibody responses may decline in a relevant proportion of vaccinated animals around this time.

An adequately validated RBPT, with or without a confirmatory test may be adequate (i) to determine the apparent prevalence of brucellosis when applied prior to vaccination, and (ii) to establish immunisation coverage after vaccination. RBPT is also suitable for checking the vaccination quality: 80-100% of vaccinated animals should be RBPT positive when tested 15 to 21 days after vaccination. However, use of RBPT for assessment of sero-prevalence after mass vaccination is not adequate due to the serological interferences induced by vaccination.

A small proportion of the population may remain sero-positive for a long time post-vaccination because of serological response to vaccine and persistent exposure of vaccinated animals to field strains. Therefore, the effectiveness of the vaccination is difficult to be assessed directly at short to medium term by determining the changes of apparent prevalence/ sero-prevalence in the vaccinated livestock. However, it can be assessed indirectly through active surveillance in human beings and requires a close collaboration between the local veterinary and medical authorities.

While using vaccines and diagnostic biologicals, their quality need to be ensured beforehand. Great care should be taken while working within a laboratory situation as live cultures, including vaccine strains, are hazardous and can infect humans. Therefore, all work must be done under containment level III or higher to minimise occupational exposure.

Hygiene/sanitation plays a vital role in the control of brucellosis through reduction of exposure of susceptible animals to the infected ones, or to their discharges and tissues. Factors such as animal husbandry practices (*e.g.*, intensive/extensive husbandry, mixing of herds or flocks), patterns of commerce, type of facilities, and degree of dedication of the owners of animals too, determine the success achieved. For effective animal movement control, identification of individual animals is required. Unauthorized sale or movement of animals from an infected area to other areas should be forbidden. Similarly, import into clean areas must be allowed for those animals that originate from brucellosis free areas and have a herd/flock history of freedom from the disease. Alongside, the risk of transmission, especially reintroduction of disease needs to be monitored where the epidemiological role played by other species of animals including the wild animals becomes important.

9. RECOMMENDATIONS

9.1: Brucellosis Control Policy:

For an effective brucellosis control programme in India, there is need for:

9.1.1: Legislation:

Legislation and/or regulation on brucellosis surveillance and control are needed in order to assure long-term commitment of resources for the programmes, since long-term sustained brucellosis surveillance and control programs are essential to ensure success.

9.1.2: Inter-sectoral collaboration:

The successful implementation of a brucellosis surveillance, prevention and control programme requires strong inter-sectoral collaboration, especially between the public health and veterinary sectors at all levels. To strengthen inter-sectoral collaboration for effective control of brucellosis and other zoonotic diseases, measures of particular importance include establishment of:

a) Advisory committees on zoonoses

b) Veterinary public health units in the Ministry of Health

c) Compulsory sharing of information and cross-notifications of cases

d) Joint out-break investigations

e) Joint training activités

9.1.3: Establishment of surveillance and information systems:

Since brucellosis in India has been shown to be endemic, no further surveys seem to be required prior to the start of the vaccination programme. However, for epidemiological purposes herd and flock prevalence in different regions may be estimated by collecting representative samples and testing at the beginning of programme, if feasible. In any case, this would increase the cost-effectiveness and efficacy of brucellosis control programmes and make better use of the existing limited resources. The following measures need to be considered:

a) Proper surveillance, monitoring and epidemiological database of brucellosis need to be addressed

b) Risk assessment, management & communication needs to be undertaken

c) Role of livestock as well as wildlife in transmission and maintenance of brucellosis needs to be assessed

d) All abortions should be investigated serologically in the first and third week after abortion, and bacteriologically for isolation of *Brucella* organisms from uterine discharge, placenta, stomach contents of aborted foetus and milk.

9.1.4: Vaccination:

Control of brucellosis by vaccination has been shown to be highly effective and beneficial with a Benefit Cost Ratio of 3.2, and may be considered the best option in Indian context by adopting:

a) Calf-hood vaccination should be done in female calves preferably aged between 3 and 6 months with a dose of 4 - 8×10^{10} live organisms of S19 strain. The upper age limit may be extended up to 8 months under certain circumstances.

b) Adult vaccination of females above 8 months of age (heifers, dry animals, animals in lactation and pregnant animals) with a reduced dose of S19 vaccine ($5\text{-}8 \times 10^{9}$ live organisms in 0.1 ml) by conjunctival (ocular) route with a booster after 4 months.

c) Dairy herds of cattle and buffaloes, organized or otherwise, in high milk yielding regions/areas/states of the country should be the first priority for vaccination.

d) Whole herd vaccination should be practiced on dairy herds.

e) Testing of vaccinated animals between 3 and 4 weeks after vaccination to assess the immune response to the vaccine.

f) Mass vaccination should be followed for calf-hood vaccination at 4 to 10 months of age.

g) On the lines of pulse polio control programme, vaccination should be taken up with legal backup to cover up maximum animals in minimum time by involving local administrative departments.

h) Mass vaccination of sheep and goats with *B. melitensis* Rev. 1 vaccine by conjunctival route should be adopted.

9.1.5: Capacity building:

Brucellosis control programme requires sustained political commitment in order to assure that the necessary resources, both human and financial, are made available for medium and long terms. Following issues need to be addressed with regard to vaccine and diagnostics:

a) The Department of Animal Husbandry, Dairying and Fisheries (DAHDF), Government of India should analyze annual vaccine requirement and specify vaccine dose payload in advance. The pharmaceutical companies and State Biological Products Units involved in manufacturing vaccine for brucellosis must come forward to expedite the production capacity as well as expand and upgrade the facilities to meet the demand of the country.

b) Sufficient laboratory capacity and a good laboratory information management system (LIMS) need to be established for timely detection and reporting of disease and to monitor the protective titre in vaccinated animals.

c) Capacity building of vaccine certification agencies for ensuring quality control of the vaccine.

9.1.6: Economic factors:

a) Cost of vaccine needs to be worked out as well as cost for vaccination procedure should also be made available to all the concerned departments.

b) Incentives may be offered to private manufactures for taking up production of quality vaccine in sufficient quantity.

9.1.7: Good animal husbandry practices:

Impact of vaccination is enhanced manifold when associated measures based on good management practices including hygiene/sanitation are put in place. For this, the following measures need to be undertaken:

a) In case of abortion, animal should be isolated followed by cleaning and disinfection to minimize the spread of infection. The aborted material should be properly disposed of.

b) Use of individual calving pens, where the dams near parturition, should be brought and kept at least up to 7 days post-delivery.

c) Proper disposal of uterine discharges and placenta by burning or deep burial with lime and salt. The calving pen should be properly cleaned and disinfected using disinfectant like carbolic acid (phenol) in a concentration of 0.5 to1% after each use.

d) Control of animal movements, implementation of the pre-movement testing in areas of high prevalence, animal/herd identification, and trace-back of the reactors through contact herds.

9.1.8: Education and mass awareness:

Brucellosis control and eradication programmes have invariably been shown to be greatly benefited by health education and mass awareness programs for all the stake holders including the medicos as well as veterinarians and must form an essential component of any programme aimed at control and/or eradication of brucellosis.

a) Health education and promotion programmes for zoonoses prevention in general and brucellosis in particular ensuring an active and strong community involvement and participation with target groups such as veterinarians, physicians and other health personnel, farmers and animal breeders, food handlers, and relevant population groups at risk.

b) Unfounded concerns of contracting brucellosis by use of S19 vaccine must be aggressively addressed among veterinarians, as they fear acquiring disease, S19 being a live vaccine.

c) General concept that brucellosis is a self-limiting disease should be clarified amply as infected animal continues to spread the disease throughout its life, even if it never aborted twice.

d) The problems associated with consumption of raw milk need thorough explanation and awareness amongst masses.

e) Myth relating to reduction of milk yield following vaccination need to be addressed.

f) Veterinarian and animal handlers should adopt proper biosafety measures such as wearing proper protective clothing including gloves, masks, aprons and goggles at the time of vaccinating animals and handling cases of abortion or dystocia.

g) Training of field veterinarians as well as public awareness about the disease need to be given due weightage.

h) Bringing awareness through periodic trainings among dairymen/farmers/vets for (i) proper disposal of foetus, placenta and discharges (ii) disinfection of area/premises/shed etc. (iii) separate management of infected animals (iv) special care of infected animal at the time of delivery (v) use of calving pens and (vi) vaccination of animals.

9.1.9: Research needs

Brucellosis is one of the most prevalent bacterial zoonosis worldwide. It is probably one of the least understood diseases in terms of pathogen immune-biology and pathogenesis. There is a need to elucidate the pathogenesis of *Brucella* in host species. This along with further characterization of its protective and diagnostic antigens is expected to pave the way for developing a better vaccine as well as diagnostic antigen.

In India, there is a need for undertaking research on economic impact and molecular epidemiology of the disease based on isolates from different geographical regions and species including human. Vaccine should be Freeze dried for better storage and transportability to remote corners in the field. A DIVA-based test also needs to be developed.

Claims of Chinese workers in controlling brucellosis in small ruminants using *Brucella suis* S2 vaccine are clear and interesting, however, in controlled conditions *Brucella melitensis* Rev. 1 vaccine has been shown to be superior. There is need to undertake further research on the efficacy of S2 vaccine as this vaccine can be administered orally in small ruminants. The oral route is simple and can be implemented to cover large population of small ruminants in the country.

10. EPILOGUE

The complex nature of brucellosis epidemiology suggests that best disease management practices play an important role for effective control. Control of the disease under certain socio-ecological conditions, where there is poverty and dependence on multiple livestock for livelihood or food, is difficult partly due to the fact that the individuals at risk of exposure are ill-informed about brucellosis, multiple hosts and transmission routes of *Brucella* or have few options available to avoid contact with the causal agent. However, control at the animal-human health interface is likely to yield the best results. Pasteurization of milk and milk products remains the most effective option for preventing infection in human population, whereas control of the disease with accessible cheap effective vaccine applied in the reservoir host (s) population aiming at eradication of the disease in livestock, provides the best long term solution in occupationally exposed communities. In brief, brucellosis in animals can be controlled by adopting three basic principles: (i) test and slaughter of positive animals (ii) maintaining sanitary conditions and (iii) vaccination of animals. Many countries have controlled/eliminated brucellosis by implementing the above principles together. But in India the policy of test and slaughter of cows cannot be adopted due to religious sentiments and, positive animals cannot be culled for economic considerations. Sanitary measures can be adopted but it is a difficult task to be followed. The vaccination of animals is the best workable strategy in the prevailing animal husbandry practices and socio-economic situation of the country.

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