ANIMAL HEALTH RESEARCH IN THE SMALL RUMINANT COLLABORATIVE RESEARCH SUPPORT PROGRAM

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ABSTRACT

Disease is a major constraint in small ruminant production systems in lesser-developed countries throughout the world. Animal health projects have been an integral part of the Small Ruminant Collaborative Research Support Program (SR-CRSP) from its inception. At the onset, these projects were oriented toward herd health care and veterinary extension activities. Later, all the projects developed a sharper focus in that they were directed to more basic studies of infectious disease. Diseases currently being investigated include caseous lymphadenitis, contagious caprine pleuropneumonia, caprine arthritis-encephalitis, ovine pulmonary carcinoma, ovine progressive pneumonia and neonatal mortality of alpaca. Continued, sharply focused studies are projected for the future to take advantage of recombinant technology in the development of multivalent vaccines.

(Key Words: Health, Sheep, Goats, Camelidae, International Cooperation.)

Introduction

Inadequate nutrition often is considered the main limitation for sustainable small ruminant production in lesser-developed countries throughout the world. Rations of poor quality and quantity result from inappropriate management, overgrazing and inadequate resources available to livestock owners. Inadequate nutrition not only results in poor growth and production but also severely reduces vitality and reproductive rate and increases death loss at all ages.

However, disease may represent an even greater constraint on animal production than inadequate nutrition and is more amenable to positive intervention. Occurring in all production systems, disease affects large numbers of animals, and producers observe that fatal disease reduces herd numbers and that obvious chronic disease incapacitates individual animals. Clinically recognized or unrecognized, disease also severely affects growth, general vitality, feed utilization and reproductive capacity. When animal production is examined from a systems analysis viewpoint, (i.e., from energy input-output measurements), any situation that results in the death or morbidity of an animal represents a total loss of the energy investment. Furthermore, in developing countries, the control and possible elimination of disease might be more effective in enhancing the efficiency of animal production systems than attempts to improve productivity by nutritional management.

The broad importance of disease was recognized in the design of the Small Ruminant Collaborative Research Support Program...
(SR-CRSP). Therefore, animal health research, considered to be a prime necessary component from the onset, was planned for inclusion in the programs at all sites.

Discussion

Worldwide, health of small ruminants is predominantly a herd problem inseparably tied to management. Therapeutic treatment of individual animals rarely is of significant importance even in highly managed purebred operations. In developed countries, this concept is recognized in almost all branches of food and fiber animal agriculture including cattle, swine, small ruminants and poultry. Within the last quarter century, the general concepts of "herd health management" have become paramount. These concepts have become established even in individual-animal type production units such as small dairy cattle farms.

From the strong growth of the herd health concept in animal agriculture of developed countries, the professional specialty in veterinary medicine of herd health management emerged. Individuals with herd health management training and skills are specialists who rely on broad veterinary medical knowledge mixed with management acumen and ability. In the developed countries, these specialists are supported by strong diagnostic laboratories providing the disciplinary expertise of pathologists, bacteriologists, virologists, immunologists, toxicologists and parasitologists. With the advances in biotechnology, diagnostic laboratory medicine has become even more complicated and sophisticated, and also more exacting. In addition, herd health specialists of the developed countries have available a broad range of effective pharmaceuticals, including vaccines, that are cost-effective. With the recognition of animal health as an important and necessary component in the SR-CRSP, the planners of the program initially turned to the herd health concept with a health project to be located in each of the projected sites. These projects were led by herd health scientists as the principal investigators. The health projects directed their programs toward the establishment of disease surveys to determine incidence and specific disease prevalence. Based on the results obtained, intervention procedures would then be applied based on developed country experience and technologies. This, in reality, focused the effort on appropriate health care delivery systems, which in many ways is similar to veterinary extension.

Despite some initial vagaries in concept, CRSP by design and intent are to be collaborative research programs, rather than being oriented toward extension. During the first few years, the disciplinary areas other than health were beginning to make research progress. The programs in range science, nutrition, breeding and genetics, sociology and economics were focused and were producing reportable results and appropriate counterpart training. The animal health projects, based on the herd health management concept, were having a difficult time showing research progress. True research in herd health management is difficult to conduct under the best of circumstances. The disease survey programs were hampered severely by acutely inadequate in-country diagnostic laboratory support, which is a necessity. Unavailability or high cost made pharmaceutical interventions impossible or inappropriate. Adequate health care delivery was lacking, and trained personnel for this extension-type activity either were not available or were not adequately supported by their governments. In the meantime, it also had been determined that extension was not a primary CRSP function. The training of herd health specialists was not being accomplished and, in contrast with the other areas of study in the SR-CRSP, the focus of the health projects appeared too broad. Health projects had to look to a new, more focused direction if research progress was to be accomplished.

Progress would entail focusing on specific disease problems because herd health management basically was too broad. To focus on specific disease problems, the program needed other types of scientists such as pathologists, microbiologists, immunologists and parasitologists. Such a change in direction also would facilitate counterpart training and institution building. Scientists with contemporary training in these specialties were few or nonexistent in most of the host countries. It also was recognized that, where possible, there should be more integration of the health research into the other SR-CRSP projects. Within about 2 yr, all the health projects had changed direction and were being lead by principal investigators who were research scientists trained in pathology, immunology or microbiology. With
this change in emphasis, significant research advances were made at all sites of the SR-CRSP where health projects were active.

Brazil

From the onset of the SR-CRSP involvement at the National Center for Goat Research (CNPC) in northeastern Brazil, a cadre of Brazilian veterinarians with research interests in parasitology, pathology and clinical pathology were at the site. Although these workers had limited financial support, they were attempting to develop active research programs. A major deficiency in the research programs was the lack of facilities and laboratory support for the isolation and identification of infectious agents and for the diagnosis and research of infectious diseases. The goals of the SR-CRSP project, after entering the research mode, were 1) to encourage and provide material support and to train technical help from the local labor force for the existing research projects and 2) to develop an infectious disease project that would require the establishment of a functional bacteriology laboratory and isolation facilities for research with agents of infectious diseases. This laboratory would be available for continued cooperation with the other animal health disciplines for bacteriologic and immunologic input into their research and diagnostic service needs.

These goals were accomplished largely in support of a research project on caseous lymphadenitis (CLA), a worldwide disease of sheep and goats, caused by the bacterium Corynebacterium pseudotuberculosis (C. pstb.). The disease is characterized by varying numbers of abscesses in lymph nodes throughout the body, causing clinical signs, which vary depending on the locations of abscesses, and generalized malaise and debilitation of variable severity (Brown and Olander, 1987).

The casual surveys and clinical impressions of SR-CRSP veterinarians who had visited and worked at the Center had suggested that CLA had a high prevalence in sheep and goats in northeastern Brazil. Local goat producers and agricultural officials considered the disease to be the most costly and persistent infectious disease in the region. This opinion was shared by the Brazilian veterinarians at the center, who later documented its prevalence at 27.7% in goats in northeastern Brazil based on clinical and slaughter observations (Unanian et al., 1985). In view of the local importance and the promise of local interest and support, CLA became the main target of research on infectious disease by the SR-CRSP animal health project.

The first studies established the suitability of the synergistic hemolysis inhibition (SHI) test for identification of immune responses to C. pstb. in goats and sheep. The test originally had been developed and used only to study C. pstb. infections in horses (Knight, 1978). The SR-CRSP studies involved the testing of experimentally and naturally infected sheep and goats in California and Brazil and correlation of the results with clinical and postmortem findings (Brown et al., 1985, 1986b, 1987). The studies served to further characterize the prevalence of the infection and its correlation with clinically apparent and inapparent forms of the disease. The SHI test then was used to aid the assessment of the immune response of goats vaccinated with an experimental toxoid vaccine, first in vaccination trials prior to experimental challenge infections and later in naturally infected herds in Brazil. The experimental results suggested some promise for reducing the incidence of disease in vaccinated animals (Brown et al., 1986a). The field trials were not complete when CRSP funding of the Brazilian project was terminated. The last experimentation with the disease at the counterpart institution in the U.S. involved the development of an enzyme-linked immunosorbent assay (ELISA) for the immune response to C. pstb. It was compared to the SHI test under the experimental conditions, but its applicability in field situations had not been tested (Alves, 1988). An examination of the iron kinetics of the goats in these experiments demonstrated that the serum Fe concentration, Fe saturation capacity and total Fe binding capacity of vaccinated goats rose to higher levels that those of non-vaccinates. Unsaturated Fe binding capacities were not different between the groups.

The CRSP animal health project supported research on the seasonal variations of intestinal helminthiasis in sheep and goats in northeastern Brazil. Transmission of infection occurs primarily in the latter part of wet seasons and the early part of the dry seasons (Costa et al., 1987). That work is the basis for ongoing...
research by the CRSP on the strategic seasonal use of anthelminitics in experimental pasture facilities at a Brazilian site remote from the CNPC.

During the tenure of the project it was evident that special problems were created by the uncertainty of climatic changes in the arid tropics. Planning for seasonal control programs was difficult and haphazard and was made especially discouraging when even minimal costs were extreme burdens for the producers. Whereas drought and heat with dehydration and starvation were major constraints on animal health in the arid tropics, the incidence and severity of infectious diseases, such as coccidiosis, foot rot and contagious ecthyma, often were devastating during the drenching floods of the rainy seasons.

**Kenya**

In Kenya, interdisciplinary research efforts were focused on development and evaluation of dual-purpose goats in high-potential areas. A long-recognized disease constraint to achieving this goal was contagious caprine pleuropneumonia (CCPP), which resulted in high mortality among untreated animals. The causative agent of CCPP is a mycoplasma organism (termed F-38) that has been isolated from outbreaks of CCPP in Kenya and in other African and Arabian Peninsula countries. The most important research results were complete protection of contact-challenged goats by an inactivated and lyophilized vaccine that has a shelf life of at least 3 mo and which provided protection from contact challenge by experimentally infected goats when animals were vaccinated with two doses (Rurangirwa et al., 1987a). This work was completed by collaboration among U.S. and Kenyan scientists following research begun several years ago by the Kenya Ministry of Livestock Development and a German agricultural team. The current plan is to conduct large field trials with the vaccine.

In addition to development of the vaccine, researchers have identified a mycoplasmal surface protein that will induce neutralizing antibodies. This protein is a candidate antigen for a recombinant vaccine such as one produced by gene cloning into *Escherichia coli* plasmids with subsequent protein expression. The research team also has isolated a carbohydrate antigen from the causative mycoplasma that will form the basis for a rapid, field diagnostic test for CCPP (Rurangirwa et al., 1987b). Tests now are being conducted in large, centralized laboratories. Current efforts are to evaluate the diagnostic tests and vaccine in other countries where CCPP is a major problem for goat producers. These countries extend from West Africa into Asia.

Scientists in the SR-CRSP and collaborators from various countries demonstrated that caprine arthritis-encephalitis (CAE) virus infection was prevalent in parts of the world and gave insight into the major method of virus transmission (Adams et al., 1983, 1984). Serum samples from Canada, France, Norway, Switzerland and the U.S. had 65% or greater reactors. New Zealand and Peru had 10% or fewer positive samples. Most of the positive samples could be traced to importations from countries with a high occurrence of CAE virus reactors. No reactors were found among serum sampled from Somalia, Sudan and South Africa. The high occurrence of CAE virus infection among dairy goats in countries with intensive dairying practices and the low occurrence in countries with little or no dairy goat industry may be explained by virus transmission in colostrum and milk. It is common practice in some countries to pool colostrum and milk from several does to feed kids. This practice would allow a rapid increase in the percentage of infections after a single infected animal had been introduced into the herd. Other factors also may make transmission under dairying conditions more efficient than under pastoral conditions.

Further studies on the epidemiology of CAE virus infection by the SR-CRSP scientists in the U.S. and Kenya have resulted in methods to control spread of the virus (Adams et al., 1983a,b). Caprine arthritis-encephalitis virus occurs in goat colostrum and milk and is transmitted to kids when they nurse or drink colostrum and milk. Sustained contact over 12 mo between weaned, virus-free goats and virus-infected goats was necessary before horizontal transmission could be demonstrated. Horizontal transmission from infected bucks to negative does during breeding is very inefficient and perhaps nonexistent. The high frequency of transmission to kids by ingesting colostrum and milk and the relative difficulty of horizontal transmission led to a program of
eradication. The program includes removing kids from their dams at birth, feeding virus-free sources of colostrum and milk and complete isolation from other goats until weaning. Results from the eradication program indicate that CAE virus-free herds can be established.

Peru

In Peru, a focus of attention became chronic respiratory disease in sheep. Scientists in SR-CRSP, including U.S. and Peruvian personnel, demonstrated that ovine pulmonary carcinoma (OPC, a contagious lung tumor otherwise known as sheep pulmonary adenomatosis) was responsible for severe losses of adult sheep in Peru and that ovine progressive pneumonia (OPP), caused by an ovine lentivirus (OvLV), was also present (Snyder et al., 1983). A high association between the occurrence of OPC and OvLV infection has been found in both naturally and experimentally induced disease, but the importance of this finding is as yet unknown (DeMartini et al., 1987). Caprine arthritis-encephalitis (CAE), a disease of goats caused by a retrovirus related to OvLV, also was identified in improved-breed dairy goats imported into Peru and in their contacts. These three diseases occur in most areas of the world where sheep and goats are raised, including the U.S. Working with their U.S.-based university, the SR-CRSP scientists developed the capacity to rapidly induce OPC and OPP in neonatal lambs and characterized the resulting lesions and immune responses (Lairmore et al., 1986; DeMartini et al., 1987). More recently, attention has been directed toward virus strain characterization (Lairmore et al., 1987; Rosado et al., 1987), development of improved disease detection methods and analysis of virus-encoded protective antigens. With the cooperation of other scientists, an OPC virus-specific antigen was identified that will be useful in isolating the causative virus of this disease, in developing a serological test for carrier animals, and in developing a vaccine for OPC. Field research in Peruvian sheep flocks has shown that it may be feasible to limit the prevalence of OPC and OPP through flock management and serological testing.

Another focus of health research in Peru was the high prevalence of neonatal mortality in alpaca, which was shown to be related to Clostridium perfringens, type A (CPA), enteropathogenic Escherichia coli (EEC), and an increased susceptibility to infectious disease because of failure of passive transfer of maternal antibody (Garmendia et al., 1987). To improve the methods for diagnosis and prevention of CPA, an enterotoxin produced by the bacterium was purified using monoclonal antibodies, it was characterized, its in vitro and in vivo pathogenicity were examined, and an ELISA assay was developed to detect its presence. The potential usefulness of this enterotoxin as an immunogen to induce protective immunity currently is being investigated.

Communities located at three different ecological levels in Peru were surveyed to obtain information concerning socioeconomic conditions and the status of health in sheep, cameloid and cattle populations. Illnesses of major and minor importance for young animals were identified, as were management and veterinary practices used by these families to control disease. Infertility associated with ram epididymitis and certain other infectious agents was found to be a sizeable problem. On large cooperative farms, ram epididymitis was controlled by use of a vaccine and serological testing. The efficacy of such control methods in community flocks remains to be tested. In an interdisciplinary study in one peasant community, the efficacy of native herbal remedies and preventatives, particularly for internal and external parasitic diseases, is being evaluated. Results to date are particularly encouraging and further investigation in required. A “herd health calendar” appropriate for small communities also is being developed with input and assistance from the sociology, economics, breeding and range SR-CRSP projects.

Morocco

The SR-CRSP did not establish a program in Morocco until the beginning of the 3rd yr of the project. At that time, with programs in four other sites, funding was limited and several disciplines, including health, were not represented in Morocco. However, the University of Minnesota, through a US/AID contract, had established a strong program of support and institution building that included the area of animal health. Thus, the SR-CRSP was able to cooperate with the Minnesota project so that
some health aspects were investigated. Nutritional myopathy (white muscle disease) was identified in animals in the SR-CRSP project and, through collaborative investigation, was determined to be due to a dietary deficiency of selenium (Johnson et al., 1985). This disease previously was unrecognized in Morocco. Collaborative studies are continuing.

**Indonesia**

A project in the herd health mode of investigation was located in the Indonesia site at the start of the SR-CRSP. This site was one of two for which one principal investigator was responsible. With the eventual redirection of all the health projects, the animal health component in Indonesia was discontinued because the Australian agriculture development program, with which the SR-CRSP was cooperating, had strong support in this discipline.

**Education and Training**

Education and training, and hence institution building, have been considered a prime component of the SR-CRSP from its inception. In the area of animal health, 30 individuals have completed graduate programs at the M.S. and(or) Ph.D. level. These students were from both the host countries and the U.S. Technical training in the form of workshops and short courses have been held in all foreign sites.

**Future Directions**

As the SR-CRSP moves into the second decade, an even more focused program in health is being considered. Analysis of mortality and morbidity rates in published studies and at the various SR-CRSP work sites demonstrates that infectious and parasitic diseases continue to be a major constraint for small ruminant production. The economic value of small ruminants and the low incomes of most owners limit the health care interventions that can be applied. For example, frequent treatment of sheep and goats with available anthelmintics will prevent economic problems with internal parasites such as *Haemonchus*, but large numbers of sheep and goat owners either cannot afford these drugs or do not have access to a reliable source of the drugs. With regard to other infectious diseases, vaccines are a possible intervention. However, most current vaccines such as the one for *Brucella melitensis* in goats are univalent, locally produced, variable in quality and poorly distributed. If a minimum of five univalent vaccines is needed to control the major diseases of either sheep and goats, it is clear that they will not be available for small ruminant owners in the countries where the SR-CRSP is operating.

The SR-CRSP experience provides a cogent example of the problem of vaccine production and distribution to sheep and goat owners. The contagious caprine pleuropneumonia vaccine developed by the SR-CRSP is safe because of inactivation, is easily stored because of lyophilization, is efficacious because of the quality and duration of the immune response against challenge and is relatively easy and economical to produce. However, no commercial company will produce the vaccine because of the limited market for univalent sheep and goat vaccines. This leaves production and distribution to individual governments, which have a long list of higher-priority demands for their resources.

Infectious diseases severely constrain sheep and goat production. However, drugs and univalent vaccines, which are used to control cattle diseases, are not suitable for small ruminants in the lesser-developed countries because the value of an individual animal does not justify the cost of these interventions. However, if a single, multivalent vaccine could be produced that would protect against the major pathogens of goats and a similar vaccine could be made for sheep it would have sizeable impact on the control of disease in both developed and lesser-developed countries throughout the world. The SR-CRSP is considering this focus of research for the coming years.

Recombinant vaccinia virus vectors have been made that will induce immunity against multiple infectious diseases (Perkus et al., 1985; Esposito and Murphy, 1988), and there may be no practical limitation on the amount of foreign DNA that can be inserted into the vaccinia virus genome. The research to develop a multivalent, virus-vectored vaccine can be conducted by a program such as the SR-CRSP, and after development the technology does not have to be reinvented in every
country of the world. The vaccine could be stored in a central place and reintroduced into a country if use were interrupted. The technology to produce a virus vaccine exists in most countries, and the production would be inexpensive. Therefore, if governments did not distribute the vaccine at no cost, sheep and goat owners could both afford and economically justify buying a single vaccine that would solve several major infectious disease problems.

Currently SR-CRSP scientists are defining the genes necessary for insertion into a virus vector that would protect against contagious caprine pleuropneumonia of goats and heartwater of goats and sheep (Washington State University and Kenya scientists), ovine pulmonary carcinoma and ovine progressive pneumonia (Colorado State University and Peruvian scientists) and bluetongue of sheep (University of California, Davis scientists). Genes for other diseases could be identified by SR-CRSP scientists and obtained from other researchers as they become available. In this way, the SR-CRSP could amplify the efforts of several other projects by having a defined goal of a multivalent virus-vectored vaccine. However, vaccinia virus is currently not a suitable vector for sheep and goat vaccines because of its potential to infect people, especially people with immunosuppression caused by the human immunodeficiency virus. Research is in progress to genetically alter the vaccinia virus to remove its pathogenic potential for humans, even in cases of immunosuppression. For sheep and goats there is, therefore, a need to develop and evaluate new vectors that pose no threat of human infection. Until a new vector is available, genes can be inserted into vaccinia and the recombinant tested for immunizing potential.

Summary

The health component of the SR-CRSP has undergone significant change during the course of the project, moving from the broad general areas of herd health, health care delivery and veterinary extension objectives to focused research on specific infectious diseases. As the program moves into the second decade, even more focused investigations are planned. Success in these studies would complete the circle to provide significant advances in herd health programs for small ruminants on a worldwide basis in both highly developed and lesser-developed countries.

Literature Cited


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