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RESEARCH ON CONTROL OF HEMOPROTOZOAL DISEASES
Texas A and M University
AID-CSD-1947

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Review of Research by Peer Specialists
and RAC Representatives

931-475

Cali, Colombia, September 1-4, 1975
Nairobi, Kenya, September 26-30, 1975

9-30-75

BEST AVAILABLE

1. DEFINITION OF PROBLEM.

Hemoparasitic diseases of livestock constitute as a group one of the most significant obstacles to efficient animal production in the tropics. These diseases all have an affinity for the destruction or alteration of blood cells with a number of secondary adverse affects in the animal host. All are primarily transmitted by biting insects or ticks. The principal pathogenic agents are anaplasma, babesia, theileria and trypanosoma. These diseases are significantly pathogenic as individual entities but they are often highly debilitating or lethal occurring paired or in concert. Babesiosis and anaplasmosis occur throughout the tropics and to some extent in temperate climates. Theileriosis (pathogenic theileriosis or East Coast Fever) is confined to Middle Africa as is African trypanosomiasis transmitted by the tsetse fly. American trypanosomiasis is relatively benign except when it occurs in conjunction with other hemoparasites.

Control of hemoparasitic diseases is accomplished by one or more systems of immunization, chemotherapy or through vector control by the use of insecticides or biological control measures.

At the present time immunization in terms of effective vaccines is still in the experimental stage. It appears that the only pathogen for which there is an effective vaccine is anaplasma and there is some doubt that the vaccine is completely effective against all strains of the organism or that it is effective under conditions of stress or overriding challenge.

There is increasing evidence of insect and tick resistance to insecticides or pesticides (with the exception of the tsetse fly) and a constant need for alternating use of compounds.

Chemotherapy provides temporary protection but it is expensive and not altogether reliable.

Biological control through the use of the sterile male technique, reproductive inhibitors (pheromones, juvenile hormones or insect growth regulators) is still in a research phase but several avenues appear promising.

It is estimated that at least 80 percent of domestic animals are exposed to ticks capable of vectoring disease and an even larger number are exposed to biting flies also capable of transmitting diseases.

2. HISTORY OF TAMU PROJECT.

The Texas A&M University research on hemoprotozoal diseases began in 1967 at the Instituto Colombiano Agropecuario (ICA) under Rockefeller Foundation support. In 1968 AID support was inaugurated and by 1970 the project except for ICA and CIAT support was fully funded by AID. Prior to the inauguration of CIAT at Cali the project occupied research facilities of ICA at the National University in Bogota and ICA field stations at Monteria and Caramagua - the latter two still in use. The Institute

for Tropical Veterinary Medicine at Texas A&M University provides research and training backstop for the project.

In addition to the research that has resulted in systems for protecting animals against anaplasma and babesia and in practical diagnostic techniques a significant number of Colombian and American graduate students have been trained.

In June 1975 sufficient research progress had been made to establish a three year general technical assistance project to demonstrate the practicality of application of the techniques in the field.

3. REVIEW

Purpose

Review of the Texas A&M Project, "Research on Control of Hemoprotozoal Diseases" was proposed at the May 3-9 meeting of RAC (Research Advisory Committee). At that meeting a 3-year extension of the Texas project was under consideration. The RAC recommended, "That the project be approved in the amount and time requested with consideration by AID of the following: (1) narrowing the focus of objectives in the studies to be conducted at Texas A&M University; (2) providing more emphasis and definition to the vector control studies and re-evaluate the budget needs in view of (1) and (2); and (3) arrange for an in-depth peer scientific review as early as possible and report to RAC."

Members

Responding favorably to this recommendation AID appointed a peer review team comprised of the following members:

Immunologists

Dr. S. G. Campbell, College of Veterinary Medicine, Cornell University, Ithaca, NY

Dr. T. O. Roby, Hemoprotozoan Diseases Laboratory, A.P.I., A.R.S., U.S.D.A., Beltsville, Maryland

Entomologists

Dr. R. O. Drummond, U.S. Livestock Insects Laboratory, A.R.S., U.S.D.A., Kerrville, Texas

Dr. Rachel Galun, Director, Entomology Division, Israel Institute for Biological Research, Ness-Ziona, Israel.

Research Advisory Committee

Dr. M. J. Peterson, Professor of Agronomy, Univ. of California, Davis, California

Dr. B. S. Schweigart, Chairman, Dept. of Food Sciences and Technology, Univ. of California, Davis, Calif.

USAID TAB/AGR

Dr. G. H. Beck, Senior Research Specialist

Dr. Nels Konnerup, Livestock Diseases Specialist

Procedure

The review was conducted in two phases: (a) Aug. 30 - Sept. 5 at Cali, Colombia and Falcon Heights, Texas, and (b) Sept. 25 - 30 at Tanga, Tanzania and Nairobi, Kenya. Dr. Schweigart represented RAC at Cali, Colombia and Dr. Peterson at Tanzania and Kenya.

During the first phase, attention was concentrated primarily on the Texas project. Each member of the Texas field Team attached to CIAT in Cali, Colombia reviewed his research interests and activities. Also the project Director, Dr. Fred Maurer and Associate Director Dr. K. L. Kuttler reviewed the work at Texas. Additional reviews were presented of the overall livestock program conducted at CIAT, under the direction of Drs. John Nickel, Ned Raun and E. A. Wells. A copy of the review program is included in the appendix.

Prior to this review in Cali some members of the team attended an International Seminar at CIAT related to animal disease vectors. This provided valuable insight and background information on the specific diseases under study in this project.

The Texas portion of the review was restricted to a site visit to the new facilities at Falcon Heights. This is an ARS-USDA/Texas Dept. of Agriculture laboratory which will be used jointly by Texas A&M for research on tick-disease relationships.

The second phase of the review was concerned primarily with related research activities being conducted in East Africa by EAVRO (East African Veterinary Research Organization), ICIPE (International Center of Insect Physiology and Ecology) ILRAD (International Livestock Research on Animal Diseases) and the Tanga, Tanzania project on the Sterile Male Technique for control of tsetse fly. The Texas project is not linked directly to any of these, but it was felt by RAC that the research being done in Africa is so closely related to the objectives of the Texas project that it should be included in the review. Site visits were made to each institution in Africa and much valuable information obtained concerning possible future directions and linkages that should be encouraged between and among these institutions and American institutions.

4. REPORT

Organization

The Report was organized by individual reports of the peer panel on the technical and scientific discussions and observations of research under way at CIAT/ICA in Colombia, Texas A&M University, College Station,

Texas and related work at ICIPE/EAVRO/ILRAD in East Africa. These reports and the recommendations are summarized by members of the Research Advisory Committee and staff members of TA/AGR-AID. The entire report will be reviewed by the Peer Panel for comments and recommendations and then be submitted to the next meeting of RAC.

Accomplishments

Accomplishments noted by the Panel include the development of a vaccine to protect against anaplasmosis, the development of effective premunition systems against anaplasmosis and babesiosis, investigations of new and more effective chemotherapeutic agents for use in premunition and treatment of the diseases, development of improved diagnostic techniques including a practical card test for anaplasmosis and Babesia bigemina in the field, an epidemiological assessment of the disease agents and vectors in Colombia, parts of Ecuador and Peru, the development of non-bovine sources of babesia from ticks and tissue culture for vaccines, and a beginning of vector control investigations through use of new ixodicides or the use of molasses grass (Melinis minutiflora).

A major effort has been made from the inception of the project to train Colombian and U.S. graduate students. A total of 17 graduate students have been trained to date. In addition, on the job technician level training has been incorporated in the program.

Present Status: Relation to CIAT/ICA

The project is currently staffed by two senior Texas A&M staff members, two Texas A&M graduate students at CIAT and two senior staff members at Texas A&M plus part time staff members at Texas A&M. CIAT provides two full time staff members and ICA provides one full time staff member plus some graduate students. CIAT provides the research facilities at Cali and ICA provides facilities for field research work in the North Coast area at Monteria and in the Llanos at Caramagua. CIAT and ICA inputs including facilities, equipment and local support are considerable as are AID's inputs in equipment and supplies through Texas A&M University.

Related Research and Research Agencies

1) The Falcon Heights Station. This is a triangular site at the base of a dam on the Rio Grande River in Texas. It is isolated by the river spillways on the U.S. and Mexico sides of the river. The USDA and the Texas Department of Agriculture are responsible for conducting research on Boophilus ticks and Babesia bigemina neither of which can be carried out in the continental United States. This site provides a valuable adjunct to the tick-host relationship research suggested by the review panel and the USDA/TAMU staffing will be complimentary to research objectives.

2) ILRAD. This internationally supported (CGIAR) facility at Nairobi, Kenya will provide a basic and applied research laboratory for immunological studies on trypanosomiasis and theileriosis. This institution is in a formative stage and currently occupies temporary

facilities on the 130 acre campus on which the permanent buildings will be erected in 1977. The permanent staff has been selected and post doctoral, post graduate, and visiting scientist are being recruited. While the research emphasis will be strongly oriented to immunology the peer panel and the Director of ILRAD have indicated specifically that the arthropod-disease-host relationship must be addressed. This calls for a close association between ILRAD/ICRPE/EAVRO

3) ICRPE. This institute in Nairobi, Kenya was founded by a group of U.S., European, Israeli and Japanese and African Academia in 1970. It is now carrying out research and training in a number of entomological problems on a broadly based interdisciplinary system. The research on disease vectors includes sophisticated studies of pheromones, juvenile hormones, gene translocation, and insect growth regulators as avenues for biological control. This laboratory has incorporated research support in chemistry, electrophysiology and fine structure units for the entire range of insect research. The research basically carried out by post doctoral and post graduate research staff is strongly influenced and supported by a corp of experienced Directors of Research from various institutions around the world.

4) EAVRO. This organization functions under a mandate of the East African Community and is located at Muguga near Nairobi. A strong program on immunology of trypanosomiasis and theileriasis has been supported at this institution by the USDA and the UNDP. A unit from ICRPE has been incorporated in the EAVRO program at Muguga on the transmission of East Coast Fever by ticks.

These research organizations are all involved in studies related indirectly to the Texas A & M University project on hemoprotozoal diseases located at CIAT. It appears that the most effective way to link these research activities is through periodic workshops or seminars in which staff members of each institution are required to participate.

5. RECOMMENDATIONS -- TEXAS PROJECT

The Texas A & M project initiated in 1967 has substantially advanced the knowledge concerning diagnosis and control of hemoprotozoal diseases of cattle, especially anaplasmosis and babesiosis, in Latin America. The review team feels that this background of knowledge and experience should now be extended into a broader-based global approach involving linkages with institutions in Africa and expanding the research to include more attention to vector and host interrelationships. This is elaborated in greater detail later on. With this in mind the team recommends that the current Texas A & M project be gradually terminated, with special emphasis on completing the current work plans with a minimum of disruption.

Specifically the team recommends the following:

- 1) The Texas A & M project be extended until June 30, 1978.
- 2) The promunition field trials be completed as scheduled under contract No. TA-C-1220. It is suggested that detailed plans for the field trials be reviewed by a team of consultants.

- 3) Continue laboratory trials with the stabilate regarded to be the most promising.
- 4) Perfect the rapid card tests for A. marginale, B. bigemina and B. argentina.
- 5) Provision for more frequent communication between Texas A & M contract coordinators and the field operations team.

6. RECOMMENDATIONS FOR THE FUTURE

1. It is recommended that AID initiate and support the concept of a global approach to research on hemoparasitic diseases of livestock aimed to improve the efficiency of animal production in the tropics. This research network should include studies of the host, the parasite, and the vector, and the interaction among these three parts of the triangular problem. A comprehensive outline of objectives should be developed, priorities established both in terms of importance and timing of specific research projects, and global resources identified in terms of scientific talent, research institutes, and geographical location of the problems.

2. Parasites. It is recommended that AID support research aimed at improving our understanding of cell-mediated immunity in the bovine species with expectation that new types of vaccines (irradiated, host-adapted, tissue culture, etc.) could be developed that are more effective.

3. Host. It is recommended that the following types of studies be supported by AID relative to host resistance to hemoparasitic diseases.

- 1) Immunization of hosts against insects and ticks through the use of insect growth regulators administered directly to cattle.
- 2) Selection of cattle for genetic resistance to these diseases.
- 3) Studies of the interactions between host nutrition and disease control.

4. Vector. The review team had rather strong views regarding the need for imaginative research on vector control. Some of the problems suggested that needed research were:

- 1) A thorough evaluation of the principles involved in molasses grass (Melinis minutiflora) for the inhibition of or toxicity to ticks.
- 2) Ecology of tick vectors of hemoprotozoan diseases.
- 3) Field trials with acaricides and the resistance and susceptibility of various strains of ticks.

- 4) Biological control of vectors by such methods as endocrines, pheromones, and/or a general understanding of vector physiology that might lead to points of vulnerability in the life cycle.

Additionally, it is recommended that there be established a center for the collection and dissemination of literature on ticks and hematophagous insects in Latin America (CIAT) and in Africa (ICRPE). It is suggested that as one step towards this goal, that contacts and working relationships be established with the National Agricultural Library in Beltsville, Maryland for microfilming or other methods of disseminating pertinent literature.

- 5) It is recommended that AID develop a set of principles and procedures for the coordination and partitioning of research which it might fund on hemoprotozoal diseases through the scientific talent of various U.S. universities, this research being conducted at the home based laboratories, at International research centers, or at national research centers, with special consideration to filling in the knowledge and technology required to advance the cause of global health of livestock.

AGENCY FOR INTERNATIONAL DEVELOPMENT
RESEARCH ADVISORY COMMITTEE

Minutes of the Forty-ninth Meeting
(May 8-9, 1975)

The meeting was opened by Dr. Ralph H. Smuckler, Chairman of the Research Advisory Committee (RAC). In behalf of the RAC he expressed appreciation to Administrator Daniel Parker for the Reception held the previous evening, and requested Dr. Long to convey these thanks. Dr. Erven J. Long invited the RAC members to attend the swearing-in ceremony at noon of Charles Mann as Assistant Administrator for Program and Management Services and Dr. Curtis Farrar as Assistant Administrator for Technical Assistance.

Project Review:

Food and Nutrition

Research on Control of Hemoprotozoal Diseases -
Texas A&M University.

Dr. Schweigert, Chairman of the Subcommittee consisting of Drs. Adams, Carter and M. Peterson, reported as follows.

This proposal is for a renewal for a three year period with a funding level of approximately \$1,185,000. The project has been active for a period of seven years, and has emphasized studies in control of blood parasite diseases in cattle in the tropics. This control is crucial in the efficiency and productivity of cattle enterprises in the tropics.

[The leadership of this project appears to be in very good hands at Texas A&M University and the project cooperation with Latin American and international agencies most appropriate.] He noted that the previous review team stressed three years ago the importance of vector control and the present project appears to place the kind of emphasis on this aspect that was suggested by the original review team. [AID would need to review with the project leadership the kind of professional competency to be added to the group to provide the appropriate expertise for this kind of emphasis.] [Professor Peterson has called attention to the finding that cattle grazing on Molasses grass were much less bothered by ticks that carry the hemoprotozoal diseases than cattle grazing on native pasture.] The eight-fold increase in productivity by vector control is most impressive. [This factor is under investigation by CIAT under separate contract with Texas A&M trained personnel. Some reservations have been expressed with respect to concentration of activities in one institution and the need for more emphasis on vector control. A peer review is suggested.]

We see this group as having made major accomplishments. They have been highly productive from many points of view including an excellent series of collaborative publications. The long-range expertise being developed at Texas A&M seems to be excellent. The link with CIAT and other international agencies is extremely important. The committee is generally supportive.

Dr. Adams spoke favorably about his understanding of the quality of the design, the lip-service to environmental issues, and the magnitude of effort involved in the 30-some objectives referenced in the proposal. He was concerned about the difficulty of evaluating the relative emphasis among the many objectives on the basis of only a formal presentation. The staff should take a hard look on the relative balance among the many complex objectives. This is a general problem, relevant to other projects as well, namely, that more attention should be paid to the evaluation of funding for complex objectives, but that the basis for such evaluation is normally not available to RAC members. Possibly this is a topic for discussion in the forthcoming RAC meeting on research issues. He was favorable to the project as presented.

Dr. Carter stated several reservations. He was appalled at the state-of-the-art and the slovenliness of vaccine development for animal diseases. Secondly, he was concerned with the limitation of this complex program of activities to a single institution trying to do all-things-for-all-animals. The objectives are so broad that, by definition, it does not seem possible for one institution to accomplish them all, even if sufficient funds are available.

He expressed his gut feeling that the significant environmental and vector considerations will tend to be slighted by the greater attractiveness to academic researchers of the drug and vaccine investigative work. Further, he believes that vaccine development for these diseases is more complex than for malaria in humans. The recent experience with malaria vaccine development, to the extent relevant, would seem to indicate that there is danger in allowing a scattering of activities. There is need for narrowing the basic objectives. This implies the need for external peer review. Reviews of this project to date have involved in-house reviewers with the exception of Dr. Hansen of the University of Wisconsin. There appears need to effectively examine the environmental and vector control aspects, lower the sights for comprehensiveness, break up the activities into several projects separately funded and evaluated, and open the program up to other investigators.

Dr. Guy Baird, TA/AGR, expressed appreciation for the points made particularly the concern for peer review. A vector seminar is being planned for this August. He pointed out that there are links with other international institutions, namely, ILRAD, the International Laboratory for Research on Animal Diseases just under development in

Kenya, and ICIPE, the International Center for Insect Physiology and Ecology in Kenya.

Dr. Nels Konnerup, TA/AGR, commented on the complete list of published papers in the annual report. Virtually all of those which report on the work in Colombia are coauthored. He commented on the exchange of trained personnel in this field, the delay in vector work now being exploited more actively, and the USDA sponsored work on ticks in this country. AID has just completed a workshop on hemoprotozoal diseases attended by international representatives, and a new vector workshop is planned for August. Outside participation is welcomed for a review to be held at the time of this workshop. There is considerable work on ticks going on at the Israeli Institute of Biological Research and, through its association with ICIPE, there is quite a little benefit in terms of vector control. With regard to the Molasses Grass a research project has been started and some answers are expected by the end of the year. A recent development is the production of a vaccine for anaplasmosis now being field tested with some results expected later this year. Further, work by the University of Illinois in field testing an anaplasmosis vaccine in Mexico, Peru, and Ecuador is being followed by Texas A&M and CIAT. He stated that he believed that this vaccine development is much less complicated than the malaria vaccine work and this promises further development of immunological investigations for other diseases by ILRAD.

Dr. Smuckler referenced Dr. Carter's comment on the possible trade-off between a nicely focused research project which zeros in on an unknown target and on a network approach which tries to mobilize efforts all over the world. This has not been addressed by staff. Dr. Schweigert commented that the subcommittee was not critical of the networking activities, but, rather, was more concerned with the need to focus research activities at Texas A&M. Dr. Montgomery restated the question as to whether there had been any sacrifice of research project goals to network development. Dr. Konnerup stated that in his view the design of the research on anaplasma and babesiasia has been fairly closely focused; while in the work on other hemoprotozoal diseases there have been complicating factors. Dr. Schweigert commented that in the subcommittee review they had found it difficult to sort out the relative importance of the 11 objectives under anaplasma and another 10 under babesia. Further, while the vector seminars and workshops are laudable, they are not by any means the equivalent of peer review and reporting.

Motion: That the project be approved in the amount and time requested with the recommendation that AID consider the following: (1) narrowing the focus of objectives in the studies proposed by Texas A&M University; (2) providing more emphasis and definition to the vector control studies and re-evaluate the budget needs in view of (1) and (2); and (3) arrange for an in-depth peer scientific

review as early as possible, and report to the RAC. On the basis of that report there may be modifications in the program components and priorities.

Motion seconded by Dr. Adams

Dr. Long commented on the review to the effect that (1) it should be held after the seminar to allow time for the conclusions to be considered by the review team, and (2) the peer review should look at the realities of the two approaches of vaccine versus vectors. He was appalled at the undertaking of controlling the vectors of cattle life in Latin America. This peer review of the Texas A&M project must be looked at in the context of the broad program and its application; involving visits to Africa and Latin America, as well as looking at the many technical issues. This is a complex matter, obviously needed, and requiring serious minded planning. It is very important that there be RAC participation.

Dr. Adams asked for clarification of the fact that the proposal refers to prior funding expiring on March 31, 1975, and thus peer review for the extension is literally impossible, particularly if postponed until after the August workshop. Dr. Long replied that there had been a great deal of review activity although not all of the right kind. There is need to move forward now and then to plan for a major review at an appropriate time. Dr. Adams asked if this was essentially a movement into a utilization phase?

Dr. Schweigert stated that this was not what the subcommittee had in mind although that could well be a component and could be the ultimate implications of the review. Rather, he had initially proposed an in-depth, scientific merit, priorities, design of experiment to the issues orientation, at the earliest appropriate time, to have its maximum influence on the ongoing project.

Dr. Smuckler surfaced the basic question whether the peer review was to be considered as a condition of the extension or as a means of continually assessing the directions of the project. Dr. Adams assumed the review was to be a condition of the extension. Dr. Schweigert reread the motion to emphasize the recommendation that AID consider the guidelines including the review with the assumption that this would be considered carefully but that current work would go on by some appropriate contractual means. Dr. Merrill stated that he understood the sense of the discussion to mean that work would move forward as proposed, there would be a review within the year, and a report back to the RAC.

Vote: Unanimously approved.