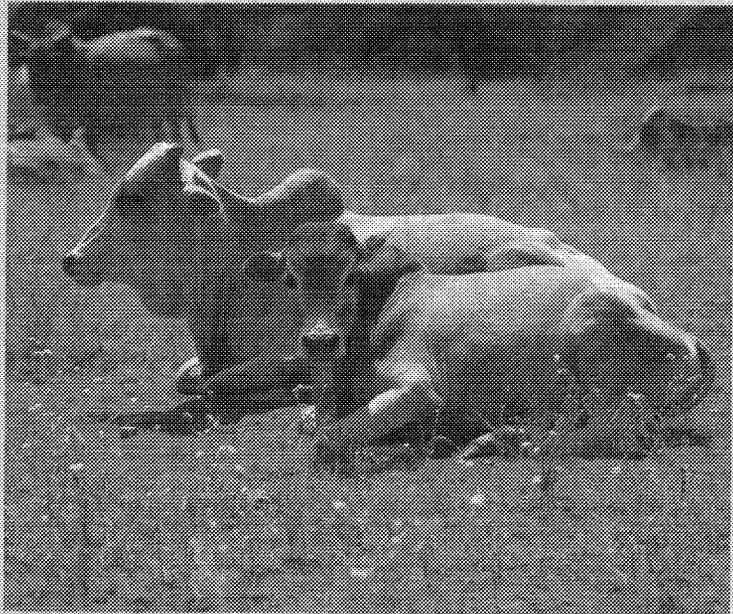
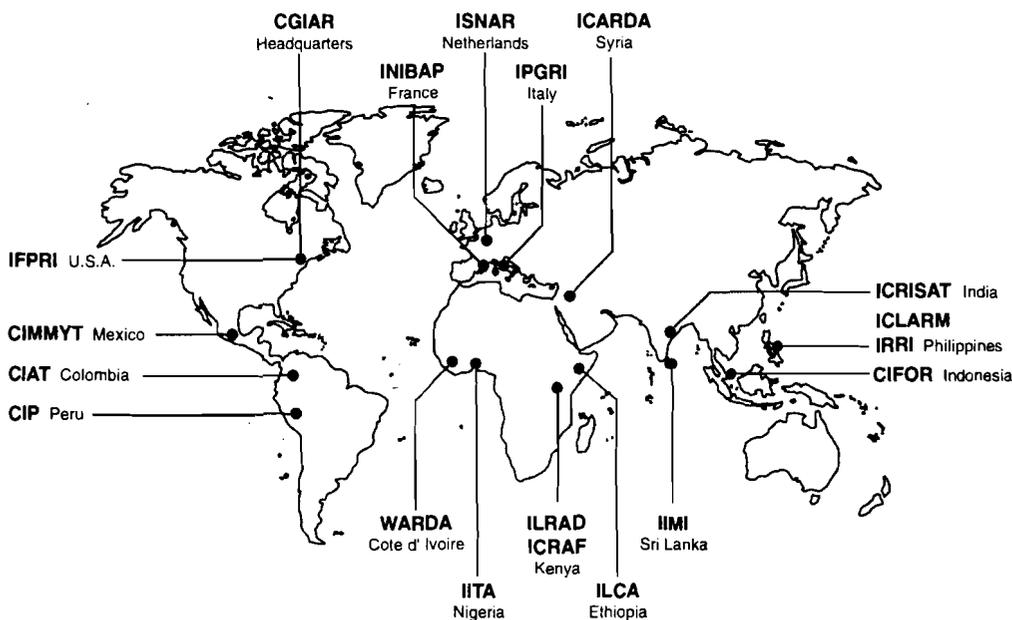


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ILRAD 1993/4 ANNUAL REPORT



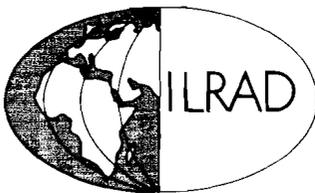
Locations of the 18 institutes that belong to the Consultative Group on International Agricultural Research.

CIAT	Centro Internacional de Agricultura Tropical, Cali, Colombia (International Center for Tropical Agriculture)
CIFOR	Center for International Forestry Research, Jakarta, Indonesia
CIMMYT	Centro Internacional de Mejoramiento de Maiz y Trigo, Mexico City, Mexico (International Maize and Wheat Improvement Center)
CIP	Centro Internacional de la Papa, Lima, Peru (International Potato Center)
IPGRI	International Plant Genetic Resources Institute, Rome, Italy
ICARDA	International Center for Agricultural Research in the Dry Areas, Aleppo, Syria
ICLARM	International Centre for Living Aquatic Resources Management, Manila, Philippines
ICRAF	International Centre for Agroforestry, Nairobi, Kenya
ICRISAT	International Crops Research Institute for the Semi-Arid Tropics, Hyderabad, India
IFPRI	International Food Policy Research Institute, Washington, D.C., USA
IIMI	International Irrigation Management Institute, Colombo, Sri Lanka
IITA	International Institute of Tropical Agriculture, Ibadan, Nigeria
ILCA	International Livestock Centre for Africa, Addis Ababa, Ethiopia
ILRAD	International Laboratory for Research on Animal Diseases, Nairobi, Kenya
INIBAP	International Network for the Improvement of Banana and Plantain, Montferrier-sur-Lez, France
IRRI	International Rice Research Institute, Manila, Philippines
ISNAR	International Service for National Agricultural Research, The Hague, Netherlands
WARDA	West Africa Rice Development Association, Bouaké, Côte d'Ivoire

Cover illustration: The semi-nomadic Borana tribe in north-eastern Africa herd a large and long-legged zebu animal that has considerable potential as a meat breed. On acquiring them early in this century, Kenyan ranchers judiciously crossed the original Ethiopian Boran with European breeds. This scheme to maximize the potential of an indigenous breed rather than attempt to replace it with exotic types has been highly successful. Today, the improved or Kenyan Boran is one of Africa's top beef breeds. Docile and well adapted to hot, dry ranching conditions and to sparse pasture, these valuable animals are now being exported from Africa to other continents.

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ILRAD 1993/4 ANNUAL REPORT

The International Laboratory for Research on Animal Diseases (ILRAD) was established in 1973 with a global mandate to develop effective control measures for livestock diseases that retard food production in developing countries. ILRAD's research program employs the most advanced biological research techniques and knowledge available to develop better methods of controlling African animal trypanosomiasis and tickborne diseases, particularly East Coast fever, a virulent form of theileriosis. Development of better disease control methods will enable livestock producers to increase their milk and beef production, will enable mixed crop and livestock farmers to increase their crop production, and in general will help improve the long-term viability of small-scale farming in the tropics and subtropics.

ILRAD is one of 18 centres belonging to a global agricultural research network sponsored by the Consultative Group on International Agricultural Research (CGIAR), whose headquarters are located in the World Bank, Washington, D.C. The mission of the CGIAR is to increase food production and food security in poor countries, and consequently to reduce world poverty, in ways that are sustainable over the long term and that protect the resource base on which agriculture depends.

In 1993, ILRAD received funding from the African Development Bank, the United Nations Development Programme, the World Bank and the governments of Australia, Belgium, Canada, France, Germany, Ireland, Italy, Japan, the Netherlands, Norway, Sweden, Switzerland, the United Kingdom and the United States of America. ILRAD's total operating expenditure for 1993 was US \$11.8 million.

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FOREWORD

THIS ISSUE of the *ILRAD Annual Report* is unusual in several respects. First, it covers a period of almost two years instead of a single calendar year. Second, it presents an account of activities during a period in which the gradual erosion of funding for international agricultural research, which began to affect operations in 1991, reached crisis proportions and necessitated major program cutbacks. Third, following a phase of extensive review, the Consultative Group on International Agricultural Research (CGIAR), the association of research centres and donor organizations to which ILRAD belongs, initiated changes in the strategy and management of its livestock research program requiring the disestablishment of ILRAD and the International Livestock Centre for Africa (ILCA)—a CGIAR centre based in Addis Ababa that focuses on African livestock production problems—and the creation of a new CGIAR centre, the International Livestock Research Institute (ILRI). Fourth, the installation of a new Chairman of the CGIAR has brought a welcome renewal of appreciation for the need to strengthen food production in developing countries through research and has brought new vigour in fundraising among the donor community to accomplish that. These developments alone provide significant matter for comment. They must not, however, be allowed to overshadow or eliminate comment on the enthusiasm, achievements and progress of ILRAD's staff in the last two years of work to improve animal health and, consequently, animal productivity.

The installation of a new Chairman of the CGIAR whose support of global efforts to increase food security and future food supplies is incisive as well as impassioned will, we hope, persuade donors to reverse the recent fall in support for international agricultural research. Early efforts on his part have already provided ILRAD scientists with new confidence that the CGIAR will continue to play a vital role in agricultural research aimed at solving production problems in poor countries. (A digest of a stimulating address by the Chairman on the future of the CGIAR follows this Foreword.)

ILRAD is deeply indebted to the members of staff who left the Institute in 1993 and 1994 as a result of financial stringencies.

ILRAD is governed by an international Board of Directors comprising 12 members.

In 1993 and 1994, Professor O. Nielsen, from Canada, continued to serve as Board Chairman. Dr. P.T. Englund (USA) and Dr. A.S. Sidibé (Mali) retired after completing two terms each of much-appreciated service to the Board. Dr. P. Angniman (Côte d'Ivoire) and Dr. A. Sher (USA) were elected to fill the vacant Board positions.

In a major review of research priorities conducted in 1993, the CGIAR affirmed that animal products are a vital global food resource and that livestock are a key to improving crop-livestock farming systems and general agricultural development. Three statements in this review alone justify continued major research investment in livestock.

- ① Livestock not only make large and direct contributions to high-quality food supplies in poor countries but also indirectly contribute to the general agriculture of those countries by providing scarce draught power and manure.
- ② The fastest growing sector of the agricultural industry in the near future is expected to be livestock: yearly growth for animal products is projected at 3.4% versus 2.4% for crop products.
- ③ Two-thirds of the agricultural land now in use in the world is rangeland devoted solely to pastoral systems. Domestic animals are also kept in much of the remaining third, where they are a crucial component of mixed crop-livestock farming systems.

We note particularly Dr. Hiroyuki Hirumi and Mrs. Kazu Hirumi, a Japanese-American cell biologist and parasitologist, respectively, who developed the world's first systems for growing trypanosomes in tissue culture in the late 1970s, which led to several international prizes and awards.

We also recognize the many contributions of Dr. Onesmo ole-Moi Yoi, a Tanzanian biochemist and dedicated medical doctor who served ILRAD with distinction and represented Africa's interests on committees of the World Health Organization, the United Nations Educational, Scientific and Cultural Organisation and the prestigious global Human Genome Mapping Project and also served Kenya as Chairman of the Council of Kenyatta University. The long list of distinguished senior alumni now also includes Dr. Wally Fish, American biochemist; Dr. Mike Shaw, British electron microscopist; Dr. John Curry, American anthropologist; Dr. Diana Williams, British immunologist; Dr. Phil Toye, Australian immunologist; and Mr. Mike Holt, British engineer. As these alumni and their colleagues contemplate the transition of ILRAD to ILRI and continue their careers, they may take pride in the words of Mr. Ismail Serageldin, Chairman of the CGIAR, addressing the staff of ILRAD during a recent visit to the Laboratory.

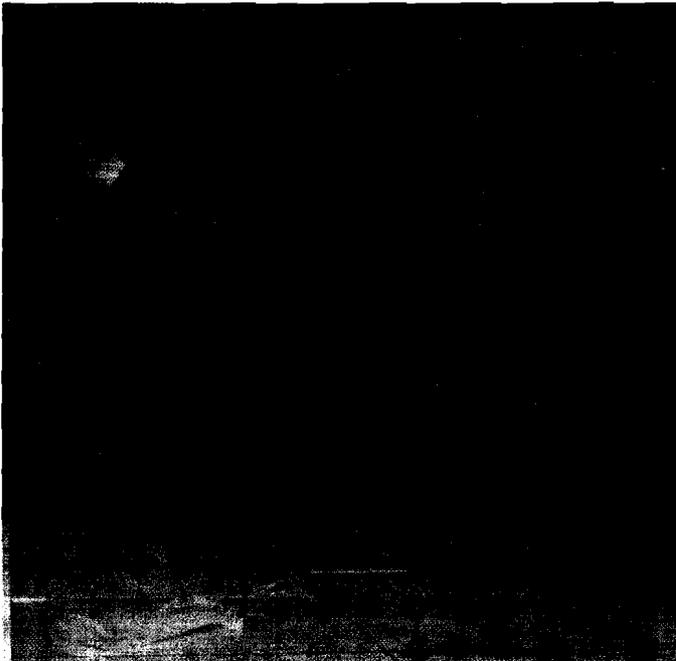
'Let me say that you have been, in fact, the embodiment of the best that there is in terms of the science in the CGIAR. It is the best of the science in the CGIAR not only because it has been so vigorous but also because it has been, I think rightly, held up as being at the cutting edge of thinking about these problems. And it is the best in another sense, not just because it is good science, but because it is focused on the problems of the poor.'

There can be no better tribute to their contributions.

With profound regret we note four tragic deaths. Mr. Hassan Yunis, an ILRAD messenger, died on 3 June 1993. Mr. Ged Lamb, a British research associate who worked at the institute for 13 years, died on 1 May 1994. A former Zimbabwean ILRAD staff member, Dr. Andy Norval, who ran ILRAD's Tick Unit from 1987 to 1989, died on 11 April 1994. Mrs. Lindsay Doyle, wife of ILRAD Director Dr. Jack Doyle, died on 14 August 1994.

THE FUTURE OF LIVESTOCK RESEARCH supported by the CGIAR has been under intensive review since early 1992, when the Third External Program and Management Reviews of ILRAD and ILCA were completed. Both Reviews commended the scientific and development achievements these Centres had made since their foundations in 1973 (ILRAD) and 1974 (ILCA). However, the Reviews expressed concern that the ongoing programs of the Centres, which are predominantly concerned with problems in African livestock production, inadequately addressed global agricultural priorities. These include counteracting environmental degradation and maintaining the productivity of land over the long term through improved natural resource management. Donor nations, anxious to broaden the impact of their investment in livestock research by including other important regions of the developing world, believed more could be achieved by building stronger collaborations between international and regional research centres and stronger links between research workers and end-user producers.

A donor working group appointed in October 1992 by the Chairman of the CGIAR reported in May 1993 on the need for, and possible approaches to, a more global and holistic livestock research strategy. Between May and October 1993, a Livestock Steering Committee, with input from the CGIAR livestock research centres, confirmed the need for new approaches. In October 1993, the CGIAR decided to move ahead on development of a new global livestock research strategy and appointed the Rockefeller Foundation as the implementing agency.



THE FUTURE OF LIVESTOCK RESEARCH IN THE CGIAR

In January 1994, the British High Commissioner in Kenya, His Excellency Sir Kieran Prendergast, and his wife, Lady Prendergast, visited ILRAD and toured the laboratories.

In this picture, Dr. Subhash Morzaria, an ILRAD molecular biologist from Uganda, and Dr. Declan McKeever, an immunologist from Ireland, demonstrate to the British High Commissioner and his wife use of a technique developed at ILRAD to diagnose East Coast fever in cattle and to determine the species of theilerial parasite that has infected an animal.

Outputs of ILRAD's research such as this have greatly advanced epidemiological research and have improved veterinary care.

Mr. Eliud Owour Were receives a Long Service Award from Dr. Ross Gray, Director General of ILRAD. For 16 years Mr. Were has provided high-quality back-up services to support the institute's laboratory research.

Mr. Were was one of 56 ILRAD employees who were presented in 1993 with a Long Service Award for serving ILRAD for 15 years.

The awards were presented at the institute's annual Christmas barbecue.

In previous years, 52 other ILRAD employees were given these awards. Nearly a third of ILRAD's staff members have worked at the institute for 15 years or longer.



Rockefeller adopted recommendations for a 'fast-track' approach to effecting the desired changes in CGIAR-sponsored livestock research; it aims to have new arrangements in place by January 1995. A global strategy for livestock research has been elaborated, an *Indicative Medium-Term Plan* has been drawn up that sets out principal future research activities and appropriate resource dimensions, and a *Program of Work and Budget* has been developed for the first year of operations of a new centre and an associated inter-centre CGIAR system-wide research program. Administrative needs for the new Centre, designated the International Livestock Research Institute, have also been considered and an Establishment Agreement providing for the Centre's foundation has been prepared for government signing in Bern in September of 1994. These activities have been supervised by an Implementing Advisory Group, which will transfer responsibility for the further development of CGIAR livestock research activities to a newly empowered Board of Directors towards the end of 1994.

THE REVISED CGIAR
LIVESTOCK RESEARCH
STRATEGY

THE REVISED LIVESTOCK RESEARCH STRATEGY has two principal elements. First is the establishment of a new institution to undertake research on global constraints to livestock productivity. The Institution's research program will span a full spectrum of research, from strategic work to reveal the molecular physiology of immune responses to disease pathogens in farm animals, for example, to socioeconomic studies to determine the constraints farmers and livestock producers face in adopting new technologies in livestock production. The program will encompass selected activities of current ILRAD and ILCA programs as well as new strategic and ecoregional activities.

The second element of the revised strategy is a CGIAR System-Wide Livestock Research Program. This will require close cooperation among international and regional agricultural research centres serving different regions of the world. The program will address problems of livestock productivity jointly where pooling resources and expertise is deemed practical and expedient. Research to improve forages has been identified as a possible focus for such system-wide attention. The new livestock research centre will play an important convenor role in this global and collaborative program.

The effectiveness of this dual approach will depend critically on effective links being made between staff of the International Livestock Research Institute and other international agricultural research centres as well as the many other professionals involved in livestock research, such as scientists funded by national governments and bilateral donors, academics and staff of development agencies and non-governmental organizations. Future progress in CGIAR-sponsored livestock research will thus depend heavily on an increased and improved flow of information among farmers, researchers and appropriate intermediaries.

The following documents setting forth the agenda and budget of the new CGIAR livestock research centre and related CGIAR activities became available in August 1994:

- *Strategic Plan for a New CGIAR Global Livestock Research Institution*
- *An Indicative Medium-Term Plan for the International Livestock Research Institute: 1995–1998*
- *ILRI Program Plans and Funding Requirements for 1995*
- *Systemwide Livestock Research Programme: A Proposal Submitted to TAC*

THE CGIAR'S REVISED STRATEGY to improve tropical livestock production, and the establishment of the International Livestock Research Institute in January 1995, mark the end of a decade and a half of productive livestock research at ILRAD and the introduction of several fresh research approaches in the new institute. Before embarking on the new program, it is fitting to reflect for a moment on the old.

ILRAD's many achievements in over a dozen scientific disciplines over the last 18 years provide authoritative scientific, technical and methodological bases for future animal health research at ILRI. It has been clear for many years that no easy solutions will be found to the problems caused by the vector-borne blood parasites of the tropics. In looking so rigorously for solutions, however, ILRAD scientists have found during their studies answers to one important scientific question after another. The steady accretion of fundamental knowledge that ILRAD's work has produced is a solid foundation on which to build future tropical animal health programs.

The pathogens ILRAD has focused on—trypanosomes (genus *Trypanosoma*) and tickborne parasites of the genera *Theileria*, *Babesia*, *Anaplasma* and *Cowdria*—continue to retard livestock and agricultural development throughout the tropical regions. Developing ways to control these parasites effectively and to immunize livestock against them will depend on continuing ILRAD's dissection of the molecular components of the parasites and the immune responses infected animals make to them.

THE ACHIEVEMENTS
OF ILRAD

ILRAD scientists have been pathfinders in many respects. They were among the first to investigate and unravel the complex interactions between trypanosome and theilerial parasites and the bovine immune system. And they were among the first to bring the latest advances of molecular biology to bear on research on tropical protozoan parasites of livestock.

ILRAD has become a major institute in Africa where developing country postgraduates can receive rigorous training in the biological disciplines needed to develop better ways of controlling widespread protozoan livestock diseases of the tropics. A cadre of African biochemists, molecular biologists, molecular geneticists, immunologists and pathologists working to improve livestock health has been built largely on ILRAD resources and expertise.

Many of these former ILRAD students today are collaborating with ILRAD scientists in major research projects, are managing research departments of their own, and are shaping livestock research policy across Africa and in other developing regions of the world.

ILRAD has played a major role in advancing knowledge in both of these areas. Pioneering work on the pathogenic African trypanosomes, which led to the development of methods for cultivating all three major species, was a major step forward in the quest for vaccines against the trypanosomiasis disease complex. The elucidation of a trypanosome phenomenon known as antigenic variation made the trypanosome parasite a workhorse model for studies of gene expression in advanced medical laboratories around the world. Although this same phenomenon presents obstacles to developing a conventional vaccine against trypanosomiasis, it has opened the door to other vaccine strategies, such as one that would work against the development of disease rather than against the parasite. In this area, the increasing power of molecular biology has allowed increasingly detailed examination of the vital life processes of the parasites, the location of important parasite genes and the production of sufficiently large quantities of parasite molecules, using genetic engineering techniques, to test the ability of these antigenic molecules to induce protective rather than harmful immune responses in the host animal.

ILRAD's research on theileriosis, better known as East Coast fever, has been similarly consequential and has moved research even further towards a vaccine against this debilitating, often fatal, disease. The bases of the antigenic structure of *Theileria parva*, the cause of East Coast fever, and its many variants have been determined. Methods of immunizing livestock against this disease with attenuated live parasites have continued to be improved and tested in the field. A genetically engineered first-generation vaccine for East Coast fever has been developed and is being refined.

Since its foundation, ILRAD has been at the forefront of research on the immune system of ruminant livestock. Published work on the humoral and cellular elements of the bovine immune response is now being supplemented by groundbreaking work on cytokines—intercellular hormones whose perturbation can make the difference between an immune and a diseased animal. Molecular genetic analysis is revealing the basis of resistance to trypanosomiasis.

In other fields, ILRAD's research has enhanced the long-term viability of chemotherapy to control both disease complexes. Improved disease surveillance technology has also been developed and is being introduced for general use through international development agencies. Use of such technology in agricultural development projects is throwing new light on disease transmission and strengthening links among epidemiologists, economists and extension specialists.

ILRAD staff identify, transfer and tailor emerging technologies in industrialized countries to accelerate and enhance their research work. Early in the development of such important technologies as monoclonal antibody preparation, gene cloning,

MHC peptide stripping, immuno-electron microscopy, geographical information systems and embryo transfer technology, ILRAD scientists have brought technological material and expertise to Africa to benefit tropical animal health research. Scientists and technical workers from Africa and other developing regions have had early access to such important innovations in biological research through collaborative research work, research fellowships and individual and group training at ILRAD.

These are some of the strengths that ILRAD brings to the new International Livestock Research Institute in January 1995. In some fields, cooperation with our major partner, ILCA, is already in place and will simply continue or be expanded. In others, there will be opportunities for making new and wider links to other institutions and organizations as the new research program to develop improved crop-livestock systems to support sustainable agricultural productivity gets under way.

UNCERTAINTY, it is said, harms the morale of an organization more than any other factor. It is as surprising as it is gratifying, then, to be able to report that in this period of substantial institutional changes and uncertainty, the Laboratory's staff were more productive than ever before. The staff publication list, which appears at the end of this *Annual Report*, is one indicator of this heightened productivity. A total of 106 publications were produced in 1993 by some 50 ILRAD scientists. A record number of these, 87, were published in international refereed journals. Readers will find a compilation of these research results in the *ILRAD 1993 Annual Scientific Report*, published earlier this year. (The *1994 Annual Scientific Report* will be published early in 1995.)

ILRAD'S SCIENTIFIC
PRODUCTIVITY

I can therefore commend for your attention, as I have every year in the last thirteen, the report that follows of the outstanding research, research support and outreach activities of ILRAD. This record of the progress made at ILRAD to improve control of tropical livestock diseases in the last year and a half of the Laboratory's existence (1993 through mid-1994) will, I trust, be as enduring as the records of previous years have proved to be.



A.R. Gray
Director General

'THE NEW ABOLITIONISTS'

SUMMARY OF A TALK
GIVEN AT ILRAD
ON 14 JULY 1994

BY MR. ISMAIL SERAGELDIN,

CHAIRMAN OF THE CGIAR
AND
WORLD BANK VICE PRESIDENT
FOR ENVIRONMENTALLY
SUSTAINABLE DEVELOPMENT

MR. ISMAIL SERAGELDIN, Vice President of the World Bank, has called for massive reinvestment in—and recommitment to—agricultural research to solve problems of the poor. Fiscal deficits and complacency over food supplies, he said, have led to severe cuts in funds for agricultural research. 'We must act', the Vice President said, 'not to save a bureaucratic structure, not to stabilize an instrument of our policy, not even to save research centres of excellence. We must act for the poor and the hungry of the world, and for the children of the poor and the marginalized of today, who will be hungry a decade from now, if we do not act now.'

Mr. Serageldin, the Vice President for Environmentally Sustainable Development and the Chairman of the Consultative Group on International Agricultural Research (CGIAR), was speaking at the International Laboratory for Research on Animal Diseases. After holding discussions with scientists, research administrators and students on the problems they are tackling, he disclosed World Bank plans for revitalising international agricultural research.

THE AIM OF THE CGIAR is to develop innovations that can be used by farmers in developing countries to gain greater food security. As Chairman of the CGIAR, Mr. Serageldin guides the decisions of 40 international agencies, national governments and private foundations that make up the consultative group, which funds 18 research centres around the world. The 1,700 scientists in these centres and their research colleagues in developing and developed countries are producing drought- and pest- and disease-resistant varieties of the staple food crops of tropical countries. They are tailoring agricultural production methods to sustain increased production over the long term. They are determining better ways of managing natural resources in fragile environments. They are improving methods to control fatal livestock diseases. These and other innovations help small-scale farmers increase the amount and the quality of the food they produce in ways that protect their soils, their water and the genetic resources of their diverse plant and animal species.

By 1991, all but two donor countries (Denmark and Japan) were running into severe financial difficulties and as a consequence reduced or barely held steady their contributions to the CGIAR. Understandably loath to cut expenditures to ameliorate full-scale emergencies, such as the holocausts in Bosnia, Somalia and Rwanda, donor organizations have instead reduced their investments, including those committed to long-term research. But we reduce support for agricultural research with no impunity, Mr. Serageldin argued. Research conducted to provide the world's poorest people with the means to make lasting improve-

ments in their lives, and in the lives of their children, is not a luxury, he stated. It is a necessity. 'Each time we cut funds to keep research alive, we mortgage the lives of future generations.'

Complacency about food security among the poor is, he warned, grossly unwarranted. A billion people today—nearly one person in every five—lives with the deadening weight of constant hunger. In just ten years, the world will have a billion more people to feed.

Since taking up his appointment as Chairman of the CGIAR in January this year, Mr. Serageldin has already substantially increased donor support for international agricultural research. He has insisted that an equation operating in the CGIAR for the last few years—'the budget drives the research'—be reversed so that problems of highest priority will again determine the research agenda of the CGIAR centres, which in turn will determine their budgets. He has placed World Bank commitment solidly behind this renewal program and has drawn the CGIAR donors with him in a reassertion of the importance of international agricultural research.

MR. SERAGELDIN has accomplished these things virtually single-handedly and armed virtually with a single idea. The idea is that the world's intellectual and natural resources are sufficient to feed the one billion people who go hungry every day. The idea is that these resources might be marshalled in an imaginative application of science and technology to solve agricultural problems of poor countries. The resources would be mobilised in a network of research centres established in developing countries around the world. The centres would use research to solve big problems faced by small-scale farmers in poor countries. The centres would be emphatically apolitical and international in character. The research conducted would be first-rate: rigorous, systematic and at the cutting edge of scientific endeavour. The scientists would tackle consequential problems strategically and conduct research over the long term to yield long-term solutions.

That idea became a reality when the first such research centres began to function under the auspices of the CGIAR in 1971. For almost a quarter of a century, the Vice President said, the CGIAR has operated on consensus and good will rather than legal treaty. Such a non-political, non-bureaucratic and truly international enterprise, he said, is unique in the annals of development. The successes of the CGIAR include helping to avert the catastrophic food shortages predicted in the 1950s by introducing high-yielding wheat and rice varieties, which produced record-breaking harvests in South Asia and Latin America in the 1960s, ushering in what is now called the Green Revolution. Whether this informal consultative group will continue to be empowered to help stem hunger and environmental degradation is now uncertain because of enduring financial constraints.

Mr. Serageldin's mission in visiting CGIAR institutes in Africa was to learn first-hand about the work of the centres, to affirm his and the World Bank's commitment to long-term research in agriculture, and to raise the morale of those involved in this global enterprise—the scientists whose years of basic research, whose scientific breakthroughs are the cornerstone of future improvements in food production and resource management. 'The CGIAR is not an all-purpose development tool,' Mr. Serageldin reminded his audience; 'it will not solve all the problems of developing country agriculture.' What is certain, he said, is that if we fail to commit ourselves to long-term investments today, we will not solve the problems of tomorrow. 'Soon or late', the economist John Maynard Keynes wrote his influential 1936 publication, *General Theory*, 'it is ideas, not vested interests, which are dangerous for good or evil.' An idea a quarter of a century old, vigorously reasserted and promulgated by Mr. Serageldin, is demonstrative proof that Keynes was right—ideas are potent. Whether the idea that modern science can be directed to help people gain access to more food and a better life survives the next quarter century is now in question. The fight to gain support for that idea, the Vice President said, will take place in donor and developing nations alike over the next 18 months.

CLOSING HIS TALK with an analogy as strong as it is fitting, Mr. Serageldin reminded his audience of how dangerous an idea can be to evil—how a single idea, taken root, can change the course of human history, and change it for the better.

'More than a hundred years ago, some people looked at slavery and said that it was unconscionable, unacceptable. They held that it shouldn't exist. That it degraded free and enslaved men and women alike. These people called for the abolition of slavery and they were known as abolitionists. The idea took hold. Political and economic pressures were brought to bear. Slavery was legally abolished.

'I ask you to look around the world today. To see 20 per cent of humanity living off 1.4 per cent of the world's income, to see a billion people malnourished—to see that hunger and poverty exist on this scale in the world today—that, too, is unconscionable and unacceptable. We must today become the new abolitionists. All of us.

'If we are going to abolish hunger, a lot of things need to be done. But fundamental to the task is to leave aside ideology and romanticism and to focus on bringing to bear the best that science has to offer to achieve that better future.'

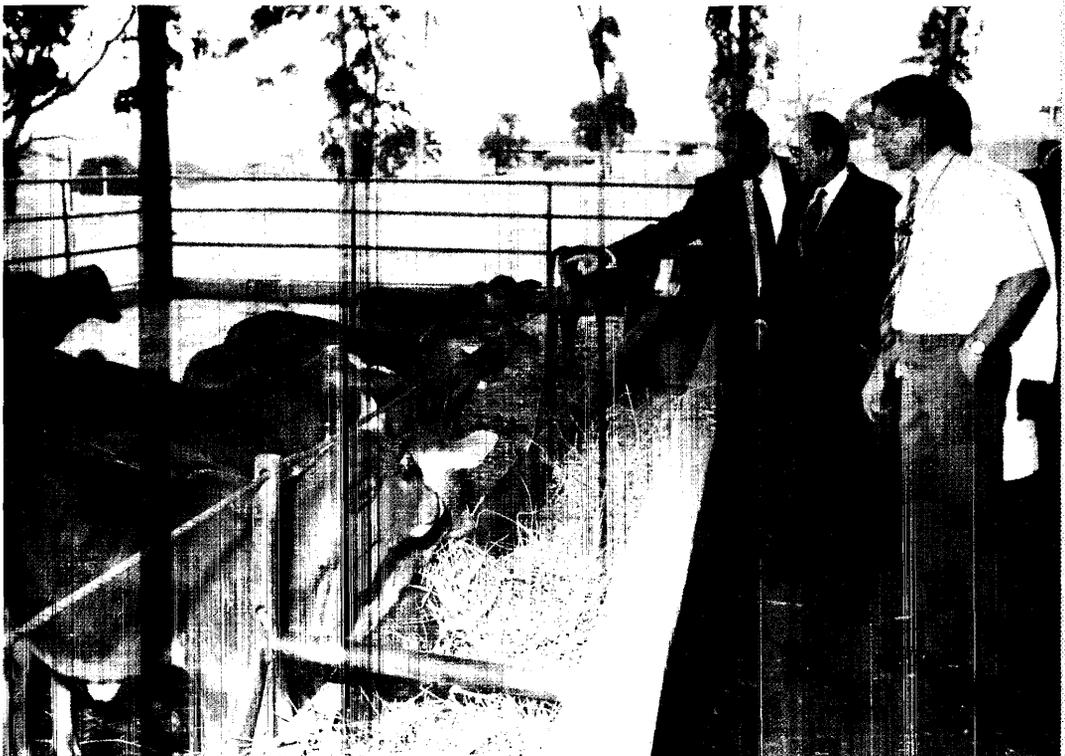


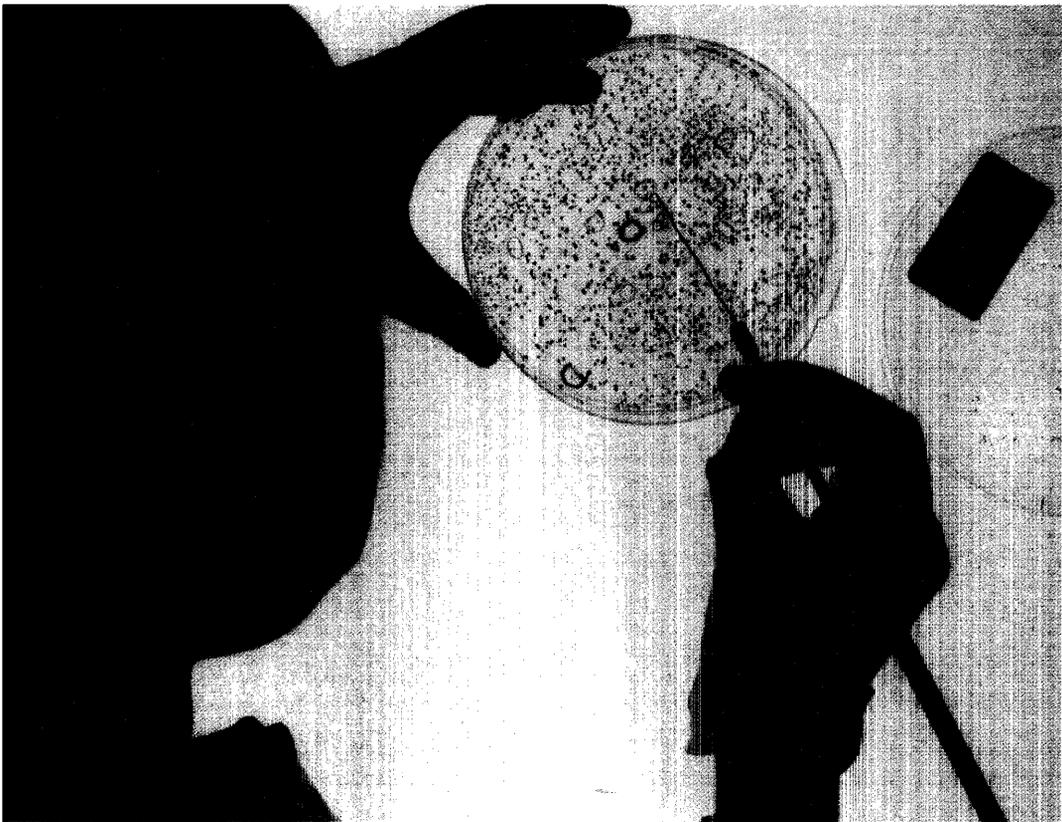
Focusing on the agricultural problems of the poor

'is what the CGIAR is all about. That was the driving vision that started the CGIAR and kept it going for almost a quarter of a century. And it is the driving vision that must be recaptured today.

We want to recapture the spirit of Belaggio in a new generation of decision-makers, and get them committed to the problems of the world— as they exist today.'

—Ismail Serageldin, July 1994





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TICKBORNE DISEASES

THE MAJOR TICKBORNE DISEASES of livestock occur throughout the world, where habitats exist that are suitable for the tick vectors that transmit disease-causing parasites. Anaplasmosis (gall sickness), caused by the *Anaplasma marginale* parasite, and babesiosis (redwater/tick fever), caused by *Babesia bigemina* and *Babesia bovis*, are widely distributed between 40 degrees north and 32 degrees south of the equator. Cowdriosis (heartwater), caused by *Cowdria ruminantium*, afflicts livestock throughout sub-Saharan Africa and was introduced to the Caribbean islands in the last century. Tropical theileriosis, caused by *Theileria annulata*, extends from the Mediterranean and northeastern Africa to China.

Throughout the tropics, an estimated 600 million cattle are exposed to anaplasmosis and babesiosis and 200 million to tropical theileriosis. In Africa, 175 million cattle are exposed to cowdriosis. In eight Latin American countries, anaplasmosis and babesiosis cause annual economic losses estimated at US\$1.5 billion. In Southeast Asia, 2–20% of the region's 337 million cattle are affected by anaplasmosis or babesiosis.

The most economically important tickborne protozoan parasite in Africa is *Theileria parva*. This parasite causes theileriosis, commonly known as East Coast fever, Corridor or January disease. The disease debilitates and kills infected livestock in 11 countries of eastern, central and southern Africa. Some 24 million of the 63 million cattle raised in this region are at risk from the disease, which ILRAD has calculated killed over a million cattle and cost US\$168 million in 1989.

The ravages of tickborne diseases are seen most dramatically when exotic cattle, such as genetically improved *Bos taurus* breeds, are introduced to tick-infected areas. In an attempt to improve their livestock industries, developing countries introduce about 70,000 high-quality breeding stock each year and each year more than 50% of these animals die from tickborne disease. The economic losses sustained include not only the purchase price of expensive imported breeding animals but also the contribution these animals would have made to greater productivity and the genetic improvement of national herds.

(*Opposite*) The bacterium *Escherichia coli* is a workhorse of modern molecular biology. In this photograph, a scientist in ILRAD's tickborne diseases program selects a colony of *E. coli* that contains a plasmid DNA molecule. The plasmid carries a gene from the *Theileria parva* parasite. The parasite gene codes for a protein molecule that is 'seen' by cells of the immune system of cattle.

Bacteria harbouring parasite genes encoding such antigenic molecules can be induced to synthesize large quantities of standardized recombinant antigen. Antigens produced in this way at ILRAD are assessed for their potential use as the base of a vaccine against cattle disease or as a target in an improved test to diagnose parasite infection of cattle.

Vaccines based on inoculation of attenuated live parasites have been developed for *Theileria annulata*, *Anaplasma marginale*, *Babesia* species and *Cowdria ruminantium*, in addition to *Theileria parva*.

These live vaccines have effectively controlled tick-borne diseases under some circumstances. All, however, are limited by their reliance on a cold chain delivery and the risk they carry of introducing extraneous pathogens to vaccination areas.

EPIDEMIOLOGY AND BIOLOGY

The brown ear tick, *Rhipicephalus appendiculatus*, transmits *T. parva* parasites as the tick feeds on animal hosts. Two wild animal hosts, waterbuck and Cape buffalo, show no signs of disease while infected. Most domestic cattle, on the other hand—particularly highly productive exotic breeds, animals crossbred with these and genetically improved indigenous cattle that encounter *T. parva* for the first time—develop severe disease from infection and die if untreated.

The only immunization method developed to date against East Coast fever is to inoculate cattle with a potentially lethal dose of live parasites while simultaneously administering a long-acting antibiotic drug to reduce the severity of the ensuing infection. While effective in many circumstances, this method, known as 'infection and treatment', has several drawbacks. Chief among them is the need to keep the parasites frozen in liquid nitrogen to remain viable and the limited immunity produced: although an animal is protected against the stock or stocks used in the immunizing dose, it will not be protected against infection with many other stocks the animal may encounter in the field. ILRAD's tickborne disease research program is therefore focused on developing a safe, relatively cheap and broadly effective vaccine against East Coast fever, which will in addition lay the groundwork for the development of advanced methods to control other tickborne diseases.

THE FIRST STEP in implementing effective tickborne disease control is to define the disease problem in a given area as precisely as possible. Tickborne diseases often occur together and in different combinations. Understanding this complexity has been made difficult by lack of reliable, standardized diagnostic tests. ILRAD has made good progress working alone and in collaboration with other institutions in developing serological and DNA-based techniques for parasite detection and discrimination.

Most field isolates of *T. parva* prepared as stabulates in the laboratory are mixtures of different parasite stocks. To provide better-defined parasites for characterization and immunological studies, staff in 1993 used a method developed at ILRAD to isolate clones from four of six *T. parva* stocks selected for detailed study.

Stocks of *T. parva* have been distinguished using restriction fragment length polymorphisms (RFLPs) in the genetic material of the parasite. The RFLPs were identified by their hybridization with *Tpr* repetitive, ribosomal and telomeric nucleic acid sequences. These sequences have also been exploited to characterize recombinant parasites derived following sexual reproduction in different stocks. ILRAD scientists recently identified a novel polymorphic multicopy gene sequence, LA6, which is transcribed in the schizont stage of *T. parva* and is believed to

code for a protein. This sequence also has a mixed genotype in one of the recombinant *T. parva* parasites and will complement a group of probes that has been selected for stock characterization and transfer to national and regional laboratories in Africa.

Previous work at ILRAD indicated that the p67 gene of *T. parva*, a candidate for a novel vaccine (see below), is conserved among different stocks of this parasite. Experiments conducted in 1993 confirmed that the gene is identical among all cattle-derived *T. parva* stocks tested. The gene in *T. parva* derived from infected buffalo, however, was discovered to have a 129 base-pair insertion not found in the cattle-derived parasite. If on-going experiments confirm that buffalo and cattle *T. parva* do have different allelic forms of the p67 gene, it may be possible to exploit this polymorphism in the production of a useful epidemiological tool.

An important short-term goal of the program is to develop a group of standardized enzyme-linked immunosorbent assays (ELISAs) that detect parasite-specific antibodies and antigens in the host. This technology is being widely adopted for diagnostic use by both international development agencies and national agricultural research systems in developing countries. The assays being developed at ILRAD have potential global application.

Collaborations have been established with Australian and American laboratories to develop the assays, and sera for their validation is being provided by laboratories in Brazil, Canada, South Africa, the UK, Uruguay and West Africa. Emphasis in 1993/4 was placed on selecting the most suitable antigen for *T. parva* antibody detection. A polymorphic immunodominant antigen, known as p85, or PIM, demonstrated the highest sensitivity and specificity and is being used to develop the assay. The effectiveness of these assays in the field will be tested in validation exercises conducted with the Food and Agriculture Organization of the United Nations (FAO, Rome) and the International Atomic Energy Agency (IAEA, Vienna).

The next generation of diagnostic reagents will be based on nucleic acid technologies. Probes developed at ILRAD that employ repetitive DNA sequences and small and large subunit ribosomal RNA sequences in the *Theileria* genome have been used to identify species of this parasite with unprecedented precision and to disclose new epidemiological information. The *T. parva* ribosomal RNA sequences were used to develop synthetic oligonucleotide, radioisotope-labelled probes that specifically identify *T. parva*, *Theileria mutans*, *Theileria taurotragi*, *T. annulata* and *Theileria buffeli*. Commercially developed non-radioactive systems for labelling the probes are being examined at ILRAD to determine their suitability for widespread diagnostic and epidemiological use.

ILRAD scientists require a regular supply of highly infected ticks to isolate and study antigenic molecules of *T. parva* that are

Methods used to control tick-borne diseases vary from strict tick control, achieved in parts of Africa by spraying or dipping cattle regularly with acaricides, to vaccination with live parasites, chemotherapy and selection for tick-resistant cattle.

Reliance on tick control is becoming increasingly difficult for developing countries because of high acaricide costs, development of tick resistance to these compounds, poor management of cattle dips and civil unrest. There is also growing concern about the damaging environmental effects of widespread acaricide use.

Vaccination coupled with strategic rather than intensive tick control and administration of drugs to treat cattle that develop disease is a sustainable control strategy that would improve survival rates among 'grade' cattle as well as the productivity of indigenous animals.

promising bases for novel subunit vaccines. Highly infected ticks are also needed to produce improved stabilates for live infection-and-treatment immunization. The researchers also need lowly infected ticks that mimic natural field infection rates; these ticks are used to assess the levels of protection afforded cattle by immunization with experimental vaccines.

ILRAD maintains tick colonies for these experimental purposes. Producing ticks with defined infection rates, however, has been problematical: the rates with which *T. parva* parasites infect their tick vectors as well as the competence of the vectors to transmit the parasites vary greatly. Recent investigations revealed several factors that determine tick infection rates and the efficiency of *T. parva* transmission. This information will be used to create optimal conditions for producing batches of ticks with predictable infection rates, to improve understanding of the epidemiology of East Coast fever and to refine disease-transmission models being developed at the Laboratory. (See also the section on ILRAD's Tick Unit, in the Research Support Chapter, below.)

SUPPORT FOR THE
NATIONAL AGRICULTURAL
RESEARCH SYSTEMS OF
DEVELOPING COUNTRIES

STAFF MEMBERS OF ILRAD's tickborne diseases program give advice and support to the national and regional animal disease research and control programs of developing countries. ILRAD helps these programs particularly in applying new technologies in integrated control strategies. ILRAD intends to validate new epidemiological tools and vaccines with these research partners.

In 1993 and 1994, ILRAD continued to support tickborne disease control projects in Zanzibar, Zambia and Zimbabwe. To help widen use of the infection-and-treatment method of immunization against East Coast fever on smallholder farms on Unguja and Pemba Islands, the institute provided disease control workers on the Zanzibari islands with characterized stabilates for the immunization and with parasite antigen for monitoring the effectiveness of the immunization. To support a Belgian-sponsored project in eastern Zambia, ILRAD characterized passage stabilates of the immunizing Katete stock and a possible breakthrough parasite. Five tissue-culture isolates of southern Zambian parasites stored at ILRAD since the 1980s were revived to provide national disease control researchers with a range of parasites from which to select an immunizing stock for this Zambian region.

To support theileriosis control in Zimbabwe, staff of the tickborne disease program in 1993 completed characterization of over 40 tissue-culture isolates and stocks of *Theileria*. Results of this work confirm the remarkable homogeneity observed the previous year among cattle-derived *T. parva* from widely divergent areas of Zimbabwe. In more general support for immunization against theileriosis within the endemic region, ILRAD staff characterized working stabilates of the *T. parva* Muguga, Kiambu 5 and Serengeti-transformed

combination of stocks employed in an FAO-supported regional vaccine production facility in Malawi.

IL RAD'S RESEARCH on *T. parva* antigens previously identified a parasite molecule with vaccine potential. The molecule elicits antibodies that neutralize the ability of sporozoite forms of the parasite to infect bovine lymphocytes. The molecule is a protein of 67 kilodaltons (kDa) mass and is expressed on the surface of *T. parva* sporozoites. Previous experiments at ILRAD have demonstrated that immunization with a recombinant form of the p67 antigenic molecule protects about 70% of cattle from subsequent challenge with a dose of *T. parva* stabilate that would be lethal in most non-immunized cattle.

Stable expression of the p67 recombinant antigen was achieved in 1993 by targeting the protein to the periplasmic space rather than the cytoplasm of the bacterium *Escherichia coli*. Another construct of the gene, a truncated p67 derivative targeted to the periplasmic space and expressed at higher levels, was also made for testing in cattle.

Use of overlapping peptides that span the entire *T. parva* p67 molecule enabled ILRAD scientists to determine that B-cell epitopes are clustered at either end of the molecule; no clear relationship, however, was observed between protection and the specificity of the antibody response. Two T-cell epitopes were also identified this year, using another set of peptides and lymphocytes from a single animal.

In research to augment the protection induced by p67, staff identified five other major sporozoite antigens that might complement p67 in a vaccine. Antibodies raised against three of these antigens have been demonstrated to partially neutralize sporozoite infectivity. These antigens are being characterized further.

A major effort was made in 1993/4 to identify antigens of *T. parva* schizonts that bear epitopes for bovine cytotoxic T cells and thus provoke bovine cellular immune responses. By eluting naturally processed peptides from *T. parva*-infected cells, ILRAD scientists identified a peptide fraction that contains the epitope of a cytotoxic T-cell clone. The fraction was sent to the University of Virginia for sequence analysis. Program scientists are also screening schizont gene libraries with immune cytotoxic T cells to identify the relevant genes directly. This approach has been used successfully to identify human and mouse tumour antigens that are recognized by tumour-specific cytotoxic T cells.

The gene encoding an immunodominant *T. mutans* 32-kDa piroplasm antigen used to diagnose *T. mutans* infections in cattle was cloned in 1993 and three complementary DNA (cDNA) variants were sequenced. Two of the clones were expressed in the pGEX bacterial expression system. The recombinant antigen is being assessed for its potential as a protective antigen and is being used to develop improved diagnostic ELISAs.

PARASITE ANTIGENS WITH
VACCINE OR DIAGNOSTIC
POTENTIAL

The availability at ILRAD of suitable cattle on which to conduct research—as well as ILRAD's tropical location, excellent laboratory facilities and ability to work on a variety of pathogens—make tickborne disease research at the Nairobi Laboratory advantageous. The institute's expertise in tickborne disease parasitology and epidemiology, its progress with antigen identification and isolation, and its understanding of the requirements for inducing immune responses in cattle, which have been established in research on the *T. parva* organism, can be exploited to develop vaccines for other tickborne diseases in collaboration with laboratories in both developed and developing countries.

A 200-kDa antigen of *Babesia bigemina* was selected this year as a candidate molecule for development of an improved antibody-detection ELISA. A single copy gene of 3.8 kilobases was isolated and cloned into a pGEX expression plasmid vector. The fusion protein produced and the parasite lysate gave similar results in the ELISA using sera of known reactivity to *B. bigemina*. This suggests that the critical diagnostic 200-kDa epitopes are encoded in the 3.8-kilobase insert. Work is under way to complete the sequence and to express components of the gene with the aim of circumventing cross-reactivity with an antigen that has been identified in sera from areas free of *Babesia*.

VACCINE DEVELOPMENT

IN 1993, ILRAD STAFF produced a recombinant vaccinia virus that incorporates a chimaeric p67 gene in which the final 228 base pairs of the *T. parva* gene have been replaced with base pairs of the gene encoding variable surface glycoprotein (VSG) in the *Trypanosoma brucei* parasite. Cells infected with the virus express p67 determinants on their surface in greater amounts than the original recombinant virus.

The new recombinant virus has been assessed in two *Bos indicus* cattle, the species employed in previous trials, for the capacity to induce enhanced immune responses to p67. The antigen-specific antibody and T-cell responses these animals produced were of the same order as those produced with previous constructs. These results suggest that vaccinia virus may not be an effective antigen delivery system for *Bos indicus* cattle. The usefulness of these constructs in *Bos taurus* cattle, the likely target for genetic improvement of production traits, will be assessed.

Efforts continued in 1993/4 to construct and characterize recombinant vaccinia viruses that incorporate cattle genes encoding cytokines, the messenger molecules secreted by cells of the immune system that activate and inhibit immune cell functions. Constructs were produced incorporating interleukin-2 (IL2), IL4 and IL6 genes. The IL2 and IL4 constructs were shown to be biologically active. In a preliminary attempt to influence the nature of the immune responses to the p67 antigen, cattle were co-infected with the IL2 or IL4 construct and the p67 recombinant virus. No clear effect has yet been observed.

In 1994, research was directed to generating attenuated *Salmonella* bacteria incorporating the p67 gene. Several recombinants are now available and are being assessed for their stability in inoculated animals. Recombinant *Salmonella* strains that prove stable will be evaluated in cattle immunizations.

Other studies continued to focus on identifying the cellular interactions required to stimulate *in vitro* *T. parva*-specific cytotoxic T cells derived from immune and naive cattle. Recent experiments indicate that naive *T. parva*-specific cytotoxic T cells need contact with immune helper T cells to be activated. These results strengthen accumulating evidence that induction of

Use of limiting dilution assays established in 1993 demonstrated strong helper and gamma/delta T-cell responses in young cattle challenged with *T. parva*. Additional studies of the gamma-delta T-cell reactivity revealed that causing the stimulators heat stress enhances these responses *in vitro*. This result suggests that some if not all *T. parva*-specific gamma/delta T cells recognize stress proteins. The possible role of these cells in protection is being investigated.

parasite-specific helper T cells will be required to generate cytotoxic T-cell immunity in vaccinated cattle. Future studies in this area will be advanced by the availability of a panel of parasite-specific helper T-cell clones that was generated during 1993. These reagents will also be used in screening exercises to identify antigens of the parasite that provoke helper T-cell responses.

TICKBORNE DISEASE RESEARCH COLLABORATIONS AND NETWORKS

The international tickborne diseases research community is a relatively small one with many overlapping interests. It is served by many formal and informal networks. In the eastern and central Africa region, ILRAD, the Food and Agriculture Organization of the United Nations (FAO) and the Organization of African Unity (OAU) together regularly convene workshops on national and regional tickborne disease control. ILRAD also has on-going collaborative research activities in disease control with national projects in Kenya, Tanzania, Zambia and Zimbabwe and gives support to an FAO-supported regional live vaccine production laboratory in Malawi.

ILRAD's tickborne diseases program has established agreements with American and Australian laboratories for the joint development of diagnostics and is collaborating in research on a cowdriosis vaccine with the United States Agency for International Development (USAID). This work is being conducted at the University of Florida, in Zimbabwe and through the offices of the Southern Africa Development Coordination Conference. Other collaborative research on *Cowdria* is being undertaken with CIRAD (Centre de Coopération Internationale en Recherche Agronomique pour le Développement) and IEMVT (Institut d'Élevage et de Médecine Vétérinaire des Pays Tropicaux).

The largest information network in tickborne diseases has been the Anaplasmosis Babesiosis Network based at Washington State University. This network is funded by a USAID project linking four US universities that are using biotechnology to develop improved animal vaccines and that are working with national programs in Africa, Asia and South America. A *Cowdria* network is sponsored by CIRAD-IEMVT. Several efficient networks are in place in Latin America, one on diagnosis sponsored by the Swedish International Development Authority through FAO/IAEA (International Atomic Energy Agency). The European Union funds a consortium of UK universities to work on *Theileria annulata* control in collaboration with relevant organizations in India, Morocco, Tunisia and Turkey. ILRAD has linked up with this consortium to conduct comparative studies of the sporozoite antigens of *T. annulata* and *T. parva*. Australia supports tickborne disease research and control in Asian countries, particularly live vaccine production in Sri Lanka. Australia also supports collaborative work on diagnosis in Asia and, with ILRAD, projects in Malawi and Zimbabwe.

It is clear that extensive and suitable links exist for testing, validating and applying new technologies in tickborne disease control as they are developed. These links are also crucial for investigating differences in host animals, tick vectors, parasite isolates and laboratory facilities in different regions, some of which might compromise the application of new tickborne disease technology developed at ILRAD and elsewhere.



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TRYPANOSOMIASIS

TRYPANOSOMIASIS occurs across more than a third of Africa. It is arguably the most important livestock disease on the continent. Like East Coast fever, trypanosomiasis is caused by infection with a protozoan parasite. In Africa, trypanosomes are usually transmitted to domestic and wild animals, as well as to people, by tsetse flies as they take a blood meal. The wide occurrence of this disease in people and their livestock retards agricultural and economic development on the continent.

The tsetse fly occurs only in Africa. It transmits four parasite species—*Trypanosoma brucei brucei*, *Trypanosoma congolense*, *Trypanosoma simiae* and *Trypanosoma vivax*—that cause trypanosomiasis in cattle, sheep, goats, pigs and horses. The fly also transmits two parasite species—*Trypanosoma brucei rhodesiense* and *Trypanosoma brucei gambiense*—that cause human trypanosomiasis, commonly known as sleeping sickness.

Thirty percent of Africa's cattle population, estimated to be 160 million, and comparable numbers of small ruminants are at risk from trypanosomiasis. Losses in meat production, milk yield and tractive power and the costs of running programs to try to control the disease are estimated at US\$500 million each year. Adding to this figure estimates of the lost potential in livestock and crop production raises the cost of this disease in Africa to some \$5 billion a year. In addition, 50 million people are exposed to the risk of contracting human trypanosomiasis.

The trypanosome parasites that cause disease in livestock and people also infect wildlife species, which are a source of infection for tsetse, which then infect domestic animals and people. Many wild animals tolerate trypanosome infections with no apparent ill effects. In humans and most domestic livestock, however, the pathogenic effects of infection are severe.

One to two weeks following infection with trypanosomes, animals that are susceptible to the disease develop intermittent fever and anaemia. Bitten repeatedly by tsetse flies and commonly infected with different kinds of trypanosomes, cattle deteriorate for months before dying.

(*Opposite*) A relief carving taken from a monument built in 1450 B.C. in the necropolis of ancient Thebes, on the west bank of the Nile, at Luxor, Egypt. The sandstone carving depicts a cow of the humpless, taurine (*Bos taurus*) type, which first arrived on the African continent about 7,000 years ago.

ILRAD molecular immunologists are studying the immune responses of descendants of these animals, the N'Dama cattle of West Africa, to infection with trypanosome parasites to determine how these animals resist trypanosomiasis when most other breeds develop the disease.

ILRAD molecular geneticists are analysing and mapping the genes of this ancient breed as part of an international search for cattle genes responsible for important traits, including those that control resistance to livestock diseases.

EPIDEMIOLOGY

ILRAD'S TRYPANOSOMIASIS PROGRAM strengthened its outreach activities with the appointment in 1993 of an epidemiologist charge with coordinating the application of ILRAD's diagnostic tests by national agricultural research organizations in developing countries. These tests include species-specific assays to diagnose trypanosome infections and assays to quantify levels of the trypanocidal drug isometamidium in cattle sera. These improved tests will be used to acquire epidemiological data for developing computer-based models of trypanosomiasis and to design improved control strategies. Staff recently undertook consultancies for the Onderstepoort Veterinary Institute/Kwazulu Government, in South Africa, and for an FAO/IAEA-supported trypanosomiasis control project on the island of Unguja, Zanzibar.

Unguja Island has a natural tsetse barrier and only one tsetse species, *Glossina austeni*. Here the project is attempting to eradicate the tsetse fly. Blood samples obtained from cattle in the northern part of the island, believed to be free of tsetse, were analysed at ILRAD using antigen-detection ELISAs and species- and strain-specific DNA probes on parasite material amplified by the polymerase chain reaction (PCR). The results show a high prevalence of trypanosome infections in the area, perhaps caused by mechanical transmission of the parasites by biting flies other than tsetse and by cattle movement. Investigations are being conducted to establish if tsetse-transmitted infections do occur in this area; if so, the area will have to be included in the tsetse eradication project.

The program also continued to collaborate with ILCA in the Ghibe Valley, in southwestern Ethiopia, where drug resistance to trypanocidal drugs had become an important problem. Studies were carried out to determine the efficacy of controlling trypanosomiasis by treating cattle with insecticides. By September 1994, monthly applications of a synthetic pyrethroid had reduced tsetse populations from pre-control levels by more than 93%. Trypanosome prevalence in cattle was also reduced, by 74%, despite continued demonstrations of high resistance to all available trypanocides. Populations of other biting flies were reduced by 88%. These promising results suggest that insecticide 'pour-ons' will be an important component of trypanosomiasis control packages in some areas.

DIAGNOSIS

DEMONSTRATING the presence of an infective agent in a host animal remains a key element in diagnosis. Advanced biotechnologies are regularly being tailored at ILRAD to develop new reagents for identifying trypanosomes and diagnosing trypanosomiasis. Monoclonal antibody-based antigen-detection ELISAs, DNA hybridization assays and the PCR technique have all been successfully adapted for these purposes. The unprecedented high sensitivity of these methods has made epidemiological studies more accurate and has enabled scientists to ask new research questions.

Diagnostic antigens of *Trypanosoma vivax* and *Trypanosoma congolense*—the antigens specifically recognized by monoclonal antibodies in antigen-detection ELISAs—were cloned into a baculovirus expression system in 1993. Tests confirmed that the recombinant form of the *T. vivax* antigen is seen by the monoclonal antibodies raised against it in the laboratory and also by antibodies induced in cattle infected with *T. vivax*. DNA sequence information revealed that the *T. congolense* antigen is a thiol protease probably related to a cysteine protease under immunological study at ILRAD for several years.

HOMIDIUM AND ISOMETAMIDIUM are related trypanocidal compounds widely used in cattle, sheep and goats. In 1993, in collaboration with the University of Glasgow, staff simplified an ELISA developed to quantify levels of the trypanocide isometamidium in serum samples taken from cattle treated for trypanosomiasis. The assay is now more robust and ready for wide-scale testing.

Previous ILRAD research showed that uptake of isometamidium by trypanosomes is accomplished by a saturable transport process. Experiments in 1993 revealed that drug uptake is inhibited by purine nucleosides and by a nucleoside transport inhibitor. Other studies indicate that the mitochondrion plays an important role in drug uptake and that the transport process is driven by an electrogenic mechanism rather than being sodium-linked.

Work was undertaken in 1994 with the Technion-Israel Institute of Technology to isolate a population of sealed membrane vesicles from plasma membranes of *T. b. brucei*. This preparation was demonstrated to take up glucose by a transport-mediated process. The vesicles will be used to study the mechanisms responsible for transporting trypanocidal drugs. Recent data indicate that homidium and isometamidium are transported by the same mechanism.

Further progress was made towards identifying genetic changes in trypanosome populations associated with the development of resistance to quinapyramine, another trypanocide. Differences in profiles produced by the RAPD (randomly amplified polymorphic DNA) technique with target DNA of resistant and susceptible populations derived from a common parental clone of *T. congolense* appear to be due to mutations at the DNA priming site. The genomic fragments containing target DNA sequences that possibly mutate as resistance to quinapyramine develops will be cloned for further analysis.

ILRAD SCIENTISTS are now analysing in detail the molecular events associated with the switch made by *T. congolense* from non-dividing infective metacyclic insect forms to actively dividing bloodstream forms. Understanding the molecular events involved in this switching process and the avail-

CHEMOTHERAPY AND
DRUG RESISTANCE

PARASITE-HOST
INTERACTIONS

The differential display method recently developed at ILRAD, called RADES-PCR, for 'randomly amplified developmentally expressed sequences by PCR', is used to quickly identify parasite gene sequences expressed in given stages of the trypanosome's development. This method is proving exceptionally sensitive and powerful in molecular studies of trypanosome differentiation.

The technique also represents a significant advance in parasite biology. It enables scientists for the first time to look at differences among large numbers of parasite samples, it reduces the time needed to identify genes by 500 to 1,000-fold, and it reduces the amount of parasite material needed by at least ten-million-fold. Modifications to the technique are opening up new research approaches of critical importance in molecular investigations.

ability of molecular markers to follow it both *in vitro* and *in vivo* are enabling staff to dissect early important processes in the onset of a trypanosome infection.

Two innovations made this molecular scrutiny possible. First was the development of axenic (feeder-layer free) culture systems for propagating and isolating pure populations of all life-cycle stages of *T. congolense*. Second was ILRAD's development of a differential display method, dubbed RADES-PCR—standing for 'randomly amplified developmentally expressed sequences by PCR'—which allows the rapid identification of developmentally expressed trypanosome genes.

Observations of the consequences of trypanosome infections in 'trypanotolerant' cattle, which control the disease effects of such infections, and 'trypanosusceptible' cattle, which develop disease, suggest that these different cattle types make different responses in the early days of an infection. An understanding of the mechanisms by which the parasites differentiate and of the different responses these cattle types make to the infecting parasites is crucial to determining the mechanisms involved in tolerance and to identifying candidate parasite targets for new intervention and control strategies.

Using the RADES-PCR method, ILRAD staff have isolated about 250 products derived from differentially expressed genes in metacyclic and established bloodstream form parasites. These products are being cloned, characterized and genetically mapped. Other studies are examining differential gene expression during the transition from metacyclic forms to early and late bloodstream forms. By September 1994, over 30 of the products were cloned and sequence information had been derived from 20. The sequenced products are being analysed in detail to determine if they encode sequences that have homologues in current sequence databases. This work is leading to a clear understanding of the strategies adopted by these parasites to establish and maintain an infection. The work is also helping to identify parasite targets for intervention and control of trypanosomiasis.

TRYPANOSOME ANTIGENS

WORK ON TRYPANOSOME ANTIGENS continued to focus on two heat-shock proteins and an immunodominant cysteine protease of *T. congolense*. One of the heat shock proteins is recognized by sera of all infected cattle. The gene encoding this immunogenic molecule has been cloned and the product shown to be homologous to mammalian immunoglobulin-binding proteins (BiP). After repeated attempts using various bacterial strains, the full length BiP was expressed in the bacterium *Escherichia coli* and purified.

The cysteine protease, named congopain, has been the focus of several projects in the institute because of the different immune responses trypanotolerant and susceptible cattle make to it, its potential pathogenic effects in host animals, its use as a diagnostic

reagent and its potential as a vaccine candidate molecule. Characteristics of the enzyme make it particularly difficult to isolate from the parasite in sufficient quantities and in an active form to study its effect on host cells. Expression of active congopain in *E. coli* would greatly facilitate such studies. The complete DNA sequence of the gene encoding congopain was derived in 1993 and experiments undertaken in 1994 to express the encoded protein in *E. coli*. Expression of two recombinant fragments representing the catalytic, central domain and the C-terminal extension was successful. A monoclonal antibody raised against native congopain reacted with the C-terminal extension, the non-conserved region of the protease. Attempts to express the full length active molecule in commonly used expression vectors failed. Use of eukaryotic expression systems, such as the baculovirus system, is being explored.

ASSAYS WERE DEVELOPED for studies of T-cell responses to *T. congolense* variable surface glycoprotein (VSG), the cysteine protease and the BiP homologue. These revealed T-cell responses in cell populations from lymph nodes draining the infection site but no responses in peripheral blood lymphocytes. Responses to VSG appear to occur predominantly among helper T cells, whereas responses to the invariant antigens appear to occur in a range of T-cell populations.

Research on macrophage activation and its consequences in trypanosomiasis revealed that the amount of a cytokine known as tumour necrosis factor alpha (TNF α) produced by macrophages prepared from peripheral blood is related to the severity of anaemia that develops during an infection. Soluble VSG was shown to stimulate *in vitro* production of TNF α by macrophages primed with interferon γ —but not by unprimed macrophages. Membrane-form VSG was found to be a good stimulator of TNF α production even in unprimed macrophages. To facilitate further studies of the consequences of macrophage activation, bovine TNF α was cloned and expressed and the recombinant product shown to be biologically active. Expression was achieved using the pMAL-P vector, in which the cloned gene is fused to a gene coding for a maltose-binding protein. Following introduction in *E. coli*, the fusion protein was purified from bacterial products by affinity chromatography. This expression procedure was scaled up in 1994 to produce sufficient quantities of active recombinant protein for the production of polyclonal antisera needed for neutralization studies.

To monitor the effect of bovine helper T cells on the progress of trypanosomiasis in terms of parasitaemia, anaemia and antibody responses to trypanosome infection, helper (CD4) and cytotoxic (CD8) T cells were depleted in the blood, spleen and lymph nodes of cattle. These complete depletions were achieved by intravenous injection for at least two weeks of large amounts of mouse monoclonal antibodies to bovine CD4 and CD8.

HOST RESPONSES
TO INFECTION

The protozoan trypanosomes that cause trypanosomiasis are generally transmitted by tsetse flies in Africa. Some ten million square kilometres of the continent are inhabited by tsetse. Agricultural development over much of this area is restricted because the fly and the disease it transmits preclude people from keeping ruminant livestock, which are the backbone of many of Africa's small farms.

Four trypanotolerant N'Dama and three susceptible Boran were used in the experiment. Two N'Dama and two Boran were depleted of CD4 T cells. The next day, all seven animals were infected with *T. congolense*. Parasites appeared in the blood at the same time in CD4 T-cell-depleted and non-depleted animals and in both breeds.

CD4 T cells were absent from the blood for two weeks after depletion, but they reappeared to levels of 25% of those in the control (non-depleted) animals. The IgG antibody response to trypanosome antigens in the control animals appeared five days after infection. This response was delayed in the depleted animals until after the second week and never reached the same levels as in the controls. However, in both breeds parasitaemia and packed cell volume (PCV) were similar in depleted and non-depleted animals over the six weeks that they were monitored.

Previous studies showed that the first parasitaemic peak is slightly higher in Boran than in N'Dama and that PCV drops faster in Boran than in N'Dama. Similar differences between the two breeds were found in this experiment three weeks after infection. Within each breed, PCV and parasitaemia did not differ between depleted and non-depleted animals. Thus, total depletion of CD4 T cells for the first two weeks of the infection and partial depletion thereafter did not affect susceptibility or resistance to infection despite a significant effect on immunoglobulin responses.

ANAEMIA

THE SEVERITY OF ANAEMIA in trypanosome-infected cattle is a good indicator of whether an animal will survive or succumb to an infection. Evidence suggests that macrophage activation contributes to the development of anaemia. These cells are derived from the bone marrow. Recent experiments indicate that although the bone marrow of susceptible Boran cattle responds in the early stages of trypanosomiasis in an attempt to rectify the anaemia, the response may be sub-optimal. In a new approach taken to identify the ways in which genotypes of different cattle breeds affect responses to trypanosome infection, staff have produced eight N'Dama-Boran bone marrow 'chimaeras' by splitting bovine embryos and implanting one each of the resultant N'Dama and Boran embryos into a single surrogate dam. Seven of the pairs produced in this way were challenged by infection with *T. congolense*. The results demonstrate that bone marrow plays an important role in trypanosomiasis and in trypanotolerance. *In vitro* bone marrow cultures were developed to facilitate a search for the molecular mechanisms that determine the different responses to parasite infection made by trypanotolerant and trypanosusceptible cattle. Staff also continued to develop reagents needed to examine cytokine responses to infection made in the bone marrow and elsewhere. In addition to cloning and producing active bovine TNF α and IL4, staff cloned the stem-cell factor and IL3 and made further progress in cloning bovine erythropoietin.

WORK TO DEVELOP AND PHENOTYPE a trypano-tolerance resource cattle population has progressed well. (See the following pages for the research uses to which this special herd is being put.) Production of the first (F₁) generation of an N'Dama-Boran crossbreeding herd was completed in 1993. The first second-generation (F₂) animals were born at the end of 1992; at the end of 1993, staff began to challenge members of this second generation with trypanosomes. During 1994, two full-sibling families of F₂ cattle were completed, with 39 and 32 calves born and 9 confirmed pregnancies in surrogate dams. Two further F₂ families were brought to an advanced stage, with 16 and 12 calves born and 5 confirmed pregnancies. Several other families were initiated, giving an overall total of 116 F₂s born and 39 *in utero* at the end of August 1994.

Phenotyping of the first group of animals for trypanotolerance was begun in December 1993; this work continued as successive groups of animals also reached the age of one year, when they were ready for challenge by the bites of *T. congolense*-infected tsetse flies. By the end of 1994, about 27 animals will have completed the phenotyping exercise and another 38 will be at various stages in the challenge process.

Considerable variation in response has been observed in the 14 animals whose phenotyping was completed by September 1994. Considerable variation also occurred in the levels of parasitaemia, especially at the first peak. Generally, there was close correlation between parasitaemia levels and clinical illness.

ILRAD is developing a consensus map of the bovine genome in collaboration with other research institutions, notably in Australia, Israel, the UK and the USA. By the end of 1993, ILRAD's molecular geneticists had produced over 100 polymorphic bovine microsatellite markers for this map. Production of microsatellites ceased at that point and their mapping and characterization was begun. Screening the markers—a majority of which will also be useful in genetic research on sheep and goats—confirmed their high level of informativeness. Markers for several type I anchor loci were also developed. When added to those produced by other laboratories, these will link the physical and genetic maps of the bovine genome.

Linkage mapping of the markers is under way, with 22 markers incorporated in the linkage map to date (in collaboration with the Commonwealth Scientific, Industrial and Research Organization, in Australia). Another 20 markers have been typed against approximately 300 animals that comprise the international bovine reference panel. This information will be used to linkage map these markers before the end of 1994.

Arrangements have been made with GenBank, USA, for large-scale submission of the marker sequences and associated information. About 100 mapped and characterized ILRAD microsatellite markers are expected to be in the public domain before 1995.

EXPANDED RUMINANT
GENETICS PROGRAM

Livestock account for almost 40% of global agricultural productivity and provide an invaluable source of income for many of the world's poorest and most disadvantaged people. Ruminant animals are invaluable in large areas of the world where they are the only species able to convert the locally available cellulose-rich feeds into meat, milk, hides, wool, manure and tractive power.

As a result of unprecedented human population growth, consumer demands for meat, milk and milk products, hides, wool, manure and tractive power are not being met. Without a dramatic change in the situation, the production shortfall will inevitably increase.

Traditionally, superior genetic combinations, or genotypes, have been developed by careful selection of breeding stock, allowing only those animals with the best performance to breed.

Selection over a period of generations has served the animal breeder and the consumer well. However, use of traditional selection methods for ruminant species—cattle, buffalo, sheep and goats—improve productivity very slowly. Although in the past this approach managed to increase production to keep pace with increasing food demands, it will not continue to do so in the future. Today's unprecedented human population growth demands a much faster increase in livestock, and particularly ruminant, productivity than has been achieved previously.

WHILE MUCH CAN BE DONE to improve livestock productivity by implementing better management methods and disease control, the productive capacity of an animal is ultimately limited by its genetics. Every aspect of farm animal health and performance is affected by one or more of the 100,000 or so genes in the genomes of each livestock species. The goal of ILRAD's expanded ruminant genetics programme is to provide animal breeders with the means to combine these genes in new ways to develop new breeds of farm animals with greater fitness and higher productivity than their predecessors.

Some genes are particularly influential in terms of animal health, while others control important livestock characteristics such as growth rate, milk and egg production, meat quality and fertility. The problem facing livestock geneticists and animal breeders is that different breeds and individuals within breeds carry different versions of these important genes. Almost invariably, any given individual or breed does not carry all of the most desirable forms of the genes, such as those endowing disease resistance, adaptation to heat and drought, efficient usage of food and high growth rate. The challenge is to bring together in all individuals of a herd or flock particular combinations of genes that collectively provide optimal health and productivity.

Although often small in number, some animal populations carry genes controlling resistance to some of the most seriously limiting livestock diseases remaining to be conquered, such as trypanosomiasis. Genes bestowing heat and drought tolerance and the capacity to utilise very poor quality feeds also occur in livestock populations that have adapted over long periods of time to harsh environments. However, there has been relatively little selection for populations of livestock naturally adapted to difficult environments and constant disease challenge. The best adaptation and productivity genes are therefore distributed around the world and throughout the spectrum of livestock breeds.

These valuable genes need to be brought together in new combinations to create new breeds with desirable environmental adaptations and the capacity to be productive in demanding circumstances. Three things are required to achieve this quickly.

- Tools must be developed to identify regions of the genomes of livestock where the most desirable genes are located.
- The new genetic tools must be applied in animal populations carrying useful genes so as to identify those genes.
- Loss of livestock biodiversity must be halted before genes of potential value in future livestock systems are lost forever.

To this end, ILRAD has established a livestock molecular genetics research program. ILRAD's scientists have collaborated with a network of research institutions in North America, Europe and Australia to use biotechnologies developed for the human genome effort to create a map of the genome of cattle. The map comprises hundreds of genetic markers, which can be used to identify and isolate specific regions of the genome.

IL RAD SCIENTISTS have used modern animal breeding and embryo manipulation technologies to establish a population of the trypanotolerant N'Dama breed of cattle that can be used at the Laboratory for experimental purposes. A breeding herd was established ten years ago from a few frozen embryos transported from West Africa. In the decade since, one hundred N'Dama have been born at ILRAD. Some of these animals have been crossbred with local East African cattle, which, like most cattle, are very susceptible to trypanosomiasis.

The resulting crossbred animals constitute a unique genetic resource—a trypanotolerance herd in which genes controlling resistance to trypanosomiasis are passed to some individuals of each successive generation and not to others. Challenging animals with the disease identifies those that are resistant. Using the genetic markers to type samples of DNA from the animals, scientists are identifying the regions of the genome that carry trypanosomiasis resistance genes. Once this is completed, DNA markers will be available to animal breeders to select directly for individuals (even before they are born) that carry parts of the genome containing the disease resistance genes.

Identification of these valuable genetic regions will enable ILRAD scientists to make another important advance. Rather than attempting to look through all of the 100,000 genes of cattle for those bestowing resistance to trypanosomiasis, they will be able to restrict the search to manageable proportions.

Using the same tools and approaches that ILRAD's scientists are using to find important disease resistance genes, genes controlling other valuable livestock traits can be identified. With advances in the techniques used to insert genes into embryos safely and effectively, it will become possible to bring together in a precise manner the most useful genes for a given livestock production system in a few embryos destined to become future breeding stock.

Financial limitations make the conservation of every rare breed impossible. The conservation process must be rationalized to allow selection of the minimum number of populations of animals that together represent the broad range of diversity. This requires the development of new forms of DNA typing that will rapidly and accurately provide estimates of the degree of genetic differences among animal populations. ILRAD scientists have developed a range of new markers and technologies for this purpose.

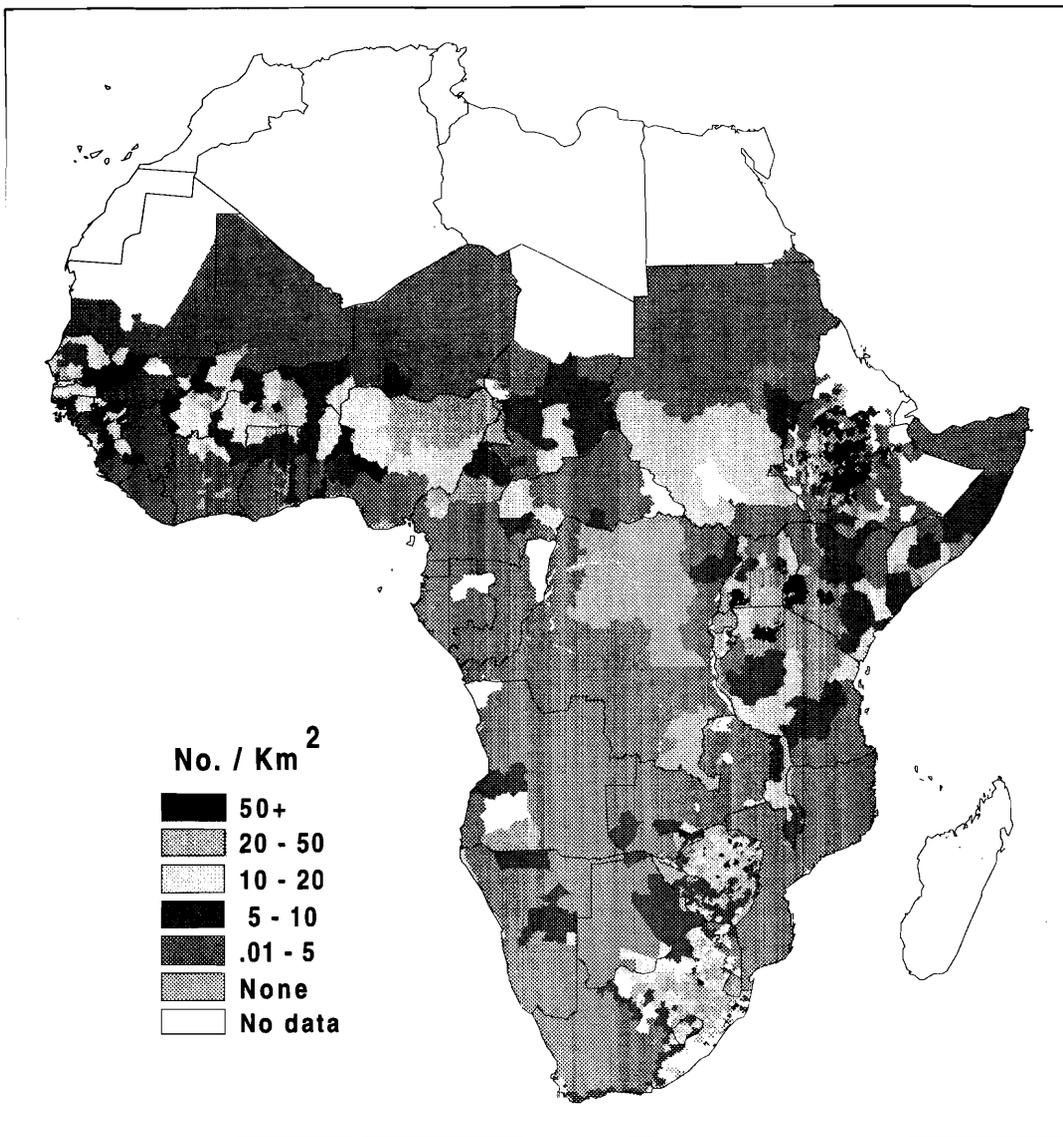
The Food and Agriculture Organization recently established a Global Programme for Conservation of Domestic Animal Diversity. ILRAD's expertise and unique links to organizations and countries holding some of the rarest breeds of ruminant livestock in the world make it well placed to play a significant part in the FAO initiative to safeguard the global store of livestock biodiversity, which is so important to the future development of the agricultural communities of developing countries.

Livestock genes are being lost at an alarming rate worldwide as rare livestock breeds disappear. The Food and Agriculture Organization estimates that 30–40% of all livestock genetic resources are in imminent danger of extinction.

The rare breeds and populations that are fast disappearing may carry genes of great usefulness to future animal breeders. Recognizing this, the international community has enacted legislation to conserve livestock biodiversity. This legislation has now been ratified as an international treaty through the Convention on Biological Diversity.

Conservationists as well as animal breeders need better tools to halt further loss of livestock biodiversity. ILRAD scientists and their colleagues in advanced laboratories around the world are helping to develop such tools in the form of genetic markers and improved technologies, methodologies and protocols developed to accelerate their molecular analyses of the genomes of important domestic livestock.

The text for this section of the Annual Report, on ILRAD's Expanded Ruminant Genetics Program, is excerpted from an article written by Dr. Alan Teale, Head of ILRAD's Trypanosomiasis and Ruminant Genetics Programs. The article was written for the occasion of the signing of an international agreement in Berne, Switzerland, on 21 September 1994, to establish the International Livestock Research Institute, sponsored by the CGIAR.



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SOCIOECONOMICS AND ENVIRONMENTAL IMPACT PROGRAM

ILRAD'S SOCIOECONOMICS and Environmental Impact Program conducts research to quantify and predict the probable epidemiological, economic, socio-cultural and environmental impacts of diseases on livestock production. The program also evaluates the merits of applying alternative improved disease control interventions in different production systems and agroecological zones. Originally focusing on East Coast fever, the program has broadened application of the generic methods it has developed to other important livestock diseases.

Staff of this program develop and employ strategic epidemiological, socioeconomic and ecological models. The models are fed by data derived from case studies carried out jointly by ILRAD and the national research organizations of developing countries. Understanding disease impacts at the regional and continental levels improves as more case studies are included in the models. Outputs generated by the case studies are used not only by ILRAD but also by the national research and development programs of the countries in which the studies were conducted.

EPIDEMIOLOGICAL RESEARCH has been conducted to determine and quantify the production effects of vector-borne infections and the influence of different control options on these effects. For example, although tickborne diseases are widely prevalent worldwide, their effect on productivity varies greatly. Heavy losses due to mortality and morbidity occur in endemically unstable situations, whereas few or no deaths and sickness occur in some situations of endemic stability. Location, production system, climate and cattle type are the main factors that determine the effect tickborne infections have on cattle productivity. In the future application of a new generation of vaccines against tickborne diseases, cattle populations that most warrant vaccination will have to be carefully targeted.

To help identify suitable targets for new and integrated control strategies, ILRAD staff have used strategic models to predict the distributions of diseases, the infections they transmit and the infection dynamics in different production systems. The program has

(Opposite) This map shows the distribution and density of cattle in Africa by administrative boundary. ILRAD compiled these data from over 60 sources. This is the first high-resolution, digital, geo-referenced database on cattle populations in Africa. Like the other databases under construction at ILRAD, this one will continue to be refined as more accurate and up-to-date data are obtained.

ASSESSING THE IMPACTS
OF LIVESTOCK DISEASES
AND THEIR CONTROL

explored the use of several vector distribution models, such as CLIMEX, BIOCLIM, HABITAT and, most recently, DOMAIN, as well as statistical procedures such as discriminant analysis. To investigate infection dynamics, staff from ILRAD and Warwick University (UK) developed a mathematical model of *Theileria parva* transmission under conditions of endemic stability. This model is being tested in other production systems of the region.

Two complementary economic modelling procedures developed by the program were further applied in 1993/4. The first is a computer spreadsheet model that assesses the economic impact of a disease on livestock production and evaluates the merits of implementing alternative control options. Originally used to assess the costs of theileriosis in eastern and southern Africa, this model predicted high economic returns from widespread use of the infection-and-treatment method of immunizing cattle.

Between 1991 and 1993, staff from ILRAD and national agricultural research systems in Kenya, Tanzania, Uganda and Zimbabwe conducted case studies on both smallholder and large-scale beef and dairy farms to compare estimates of the costs of controlling theileriosis by immunization and a concomitant reduction in acaricide use with the actual costs of intensive acaricide use, the control method currently employed. The results suggest that an immunization-based control strategy would reduce the economic cost of the disease in the whole affected region by 43%. Immunization at the vaccine-cost level evaluated in the model, although financially viable in the eight production systems studied, would not yield greater benefit:cost ratios than the current acaricide-based strategy—and thus would not be the intervention of choice—for indigenous zebu cattle in two Kenyan study sites, one in the highlands (Uasin Gishu) and one at the coast (Kilifi). For the other six production systems and for all cattle types, implementing immunization-based control would give benefit:cost ratios greater than those of the current acaricide-based control strategies.

The spreadsheet model was adapted and applied in 1994 to assess the economic impacts of heartwater and its control at a case study site in Zimbabwe. The model estimated the costs of heartwater in the country in 1992 to be \$8.7 million and predicted that an immunization-based control strategy would reduce national costs of the disease to \$1.4 million. These results are being validated jointly by ILRAD and a heartwater research project in Zimbabwe funded by the United States Agency for International Development.

ILRAD's computer spreadsheet model is also being adapted to assess the economic impacts of trypanosomiasis and the economics of employing alternative strategies to control it. Using this model and collaborating with national agricultural research systems in Africa and with AP Consultants (UK), ILRAD continued in 1993/4 systematically to quantify the economic costs of trypanosomiasis in Africa. Studies completed in The Gambia and Zimbabwe have been supplemented by a third study in Côte d'Ivoire; a fourth study, in Cameroon, is nearing completion.

Two indirect benefits of theileriosis immunization are particularly important.

- (1) Lowering the risk of the disease will encourage adoption of genetically improved and higher producing cattle by more farmers, thereby increasing food production and consumption, employment and trade.
- (2) Reduced use of chemical acaricides will improve the environment, reduce government expenditure and allow time currently spent dipping or spraying cattle to be applied to other productive farm household activities.

Results show that the costs of the disease in The Gambia are predominantly due to production losses (99.9%), most of which is decreased milk yield; trypanosomiasis costs in Zimbabwe are largely control costs (98%), most of which is expended to control tsetse populations; and the disease costs in Côte d'Ivoire are a mixture of production losses (90%) and control costs (10%).

The situation in Côte d'Ivoire thus falls between that in Zimbabwe and The Gambia, with the disease per head of cattle estimated to be \$4.88. Effective tsetse control in Côte d'Ivoire may allow an expansion of cattle production in the southern part of the country. In regions with more widespread tsetse infestations, notably in coastal and central Africa, reducing the risk of trypanosomiasis by employing more effective control methods may increase areas available for livestock and crop production.

These analyses will be used to develop inputs for other African countries where the disease occurs so that continent-wide economic losses may be calculated. The reliable estimates of trypanosomiasis costs produced as a result of these country studies will help policymakers choose the most cost-effective, appropriate and sustainable control measures for specific areas and circumstances.

CONVENTIONAL WISDOM has held that implementing more effective control of trypanosomiasis will open vast areas of Africa to livestock raising and, through increased use of animal traction, to mixed crop-livestock production as well, with two important results: an increase in food production at the expense of biodiversity and the environment. A Rockefeller-supported investigation of the environmental and socio-economic impacts of improved trypanosomiasis control was initiated in late 1992 to test this assumption. Staff began by uniting the often disparate views of ecologists, economists, epidemiologists and anthropologists in a conceptual model developed to examine the effects disease control may have on changes in land use. This model is a framework for a research approach integrating continental and national-scale GIS analysis with field case studies in eastern, western and southern Africa.

If the conventional wisdom is right, both human populations and land-use intensity should be negligible in areas infested with tsetse. Initial results show that, overall, it is true that fewer people live where the fly occurs. The presence of tsetse, however, does not prevent people from using land. In Burkina Faso and Mali, for example, the intensity of cultivation is higher in areas infested with the fly than in adjacent areas that have no tsetse. In these countries, flies infest land with the greatest potential for agriculture (better soils, more groundwater), and farmers have evolved ways to conduct agriculture in the face of trypanosomiasis.

AT FIELD SITES in the Ghibe Valley, Ethiopia, and the Zambezi Valley, Zimbabwe, staff are measuring the impacts of disease control on livestock numbers and land use, and, in turn, the influence of land-use changes on vegetation structure and biodiversity. Field work at the Zambezi site has just begun. In Ghibe Valley, ILRAD and ILCA are comparing areas

DETERMINING LINKS
BETWEEN TSETSE
DISTRIBUTION
AND LAND USE

THE ENVIRONMENTAL
IMPACTS OF
TSETSE CONTROL

In recent years, mathematical modelling has played an increasing role in the life sciences. Such models use mathematical language and logic to represent, for example, the behaviour of a physical system or the dynamics of disease transmission.

Mathematical representations, or models, are providing ILRAD scientists with the means to investigate the variables that determine how severely a disease will affect livestock production in a given area, to test a hypothesis about links between the presence of tsetse flies and land use in Africa, and to compare the costs and benefits of implementing alternative disease control strategies in different areas and circumstances.

This year ILRAD published the proceedings of an international workshop that was organized by ILRAD and FAO in November 1992 on 'Modelling Vector-Borne and other Parasitic Diseases'.

GIS DATABASE DEVELOPMENT FOR DETERMINING THE IMPACTS OF DISEASE CONTROL

ILRAD has been designated a lead centre in the CGIAR on use of computer-based geographical information systems.

with similar physical and ecological characteristics where effective tsetse control has and has not been implemented. Preliminary results from a cross-sectional household survey and measurements of farmer's fields show that, as expected, cattle populations (particularly oxen) are greater, cattle deaths fewer and more land cultivated in tsetse-free than in tsetse-infested areas. It thus appears that tsetse control is spurring expansion of agricultural land use in Ghibe Valley. Staff are now using an historical series of satellite images to determine if these land-use changes are also occurring in other areas of Ghibe Valley. The aim of this work is to develop the means to extrapolate results from detailed field studies such as these to other sites and to larger areas.

Staff compared how changes in land use caused by tsetse control have in turn changed vegetation structure and biodiversity—in the forms of numbers of tree, bird and large mammalian species—at sites along a gradient of land use. These ecological properties were chosen to reflect the nature of the controversy about tsetse, namely, that the fly is the guardian of wildlife and its habitat on the continent. Vegetation abundance, structural complexity and biodiversity in Ghibe Valley were expected to be greatest in lesser-used woodlands and grasslands and to decrease as human use intensified. The study confirmed that relatively little-used riverine woodlands represented unique habitats, being structurally complex and sheltering species found nowhere else in Ghibe Valley. Converting these woodlands to cultivated land as a consequence of tsetse control would indeed reduce biodiversity, perhaps radically. Cultivation had no impact, however, on biodiversity or vegetation when grasslands were converted to smallholder, oxen-ploughed farms as a result of tsetse control. These observations must be interpreted cautiously: farmers state that well before tsetse control started in the area, populations of large mammals had been decimated due to increased human use of the land. It appears, even so, that introducing tsetse control could adversely affect populations of large mammals if the reduced disease risk encouraged an influx of people into ecosystems now largely unpopulated.

ILRAD'S RESEARCH ON THE EFFECTS of improved control of animal diseases requires extensive geo-referenced databases integrated in computer-based geographical information systems (GIS). The latter are used by the program to build prototype animal health decision-support systems that will put available knowledge and technologies to better use in the control of animal diseases. In collaboration with national veterinary departments in Zimbabwe and Uganda, ILRAD is conducting case studies to obtain further information for the development of these systems.

A series of climatological, environmental, demographic and land-use data layers at local, national and continental resolutions of scale were developed at ILRAD or acquired from other institutions in 1993/4. Substantial collaboration in database develop-

ment was enhanced by a 1991 initiative of the CGIAR and United Nations Environment Programme. ILRAD is playing a major role in helping this CGIAR/UNEP project identify and develop digital databases of common interest to the international agricultural research centres.

Extensive databases have been developed to determine land-use changes resulting from tsetse control in the Ghibe Valley study site. A Landsat Thematic Mapper image of the Ethiopian area and ground survey information were analysed to develop a land-use classification layer for March 1993 for tsetse and non-tsetse control areas. This effort is part of a time-series analysis that will eventually include snapshots of land-use before and after fly control began.

To put the high-resolution research results from Ghibe in a national context, Ethiopia-wide databases were acquired. The International Centre for Research in Agroforestry, in Nairobi, recently developed interpolated climate surfaces at 1-km resolution for the country, including long-term monthly mean minimum and maximum temperature and rainfall. The United States Geological Survey and the Famine Early Warning System (FEWS-USAID) provided land-use, soils, human population, agricultural productivity and administrative boundary data layers.

Other national datasets ILRAD acquired include detailed 1994 land-use and human population layers for Zimbabwe, developed by FEWS, Harare. This was an important addition to the animal health decision-support system installed by ILRAD in the Zimbabwe Veterinary Research Laboratory in early 1994 and will facilitate ILRAD's work to model the changing epidemiology of tickborne diseases in that country. The animal health information system consists of over 100 geo-referenced data layers, including national and veterinary infrastructures, disease outbreaks, vector distributions, wildlife host distributions, natural resources, and climatic and demographic themes. In addition, databases on land use, human population distribution, geomorphology and vegetation types for northwestern Zimbabwe were acquired from the Natural Resources Institute (UK). These data will be used to conduct a case study of the environmental impacts of tsetse control in that region.

At the continental level, ILRAD acquired from FAO a detailed administration boundary layer for Africa. Containing updated political boundaries, this has been used as a framework for developing cattle population and distribution data for sub-Saharan countries. The GIS was then used to calculate cattle density on the continent (see the map that opens this chapter). A similar approach was used by staff at the University of Southern California to estimate human population densities in Africa; this updated (1994) information was recently acquired by ILRAD. Other continental layers obtained by the program include three layers of vegetation distribution from UNEP and the status and distribution of protected areas, forests, wetlands and endangered species from the World Conservation Monitoring Centre.

To accelerate its acquisition of data and construction of databases, ILRAD's Socio-economics Program in 1993/4 exchanged information with a variety of organizations that have developed databases relevant to the research objectives of the program. Secondary data at the finest resolution possible were also obtained in this period and digitized into new GIS data layers.

With the International Centre for Research in Agroforestry (Nairobi), the International Institute of Tropical Agriculture (Ibadan, Nigeria) and the Australian National University, ILRAD collaborated in developing Africa-wide interpolated climate surfaces at 0.05-degree (4-km) resolution. These include long-term monthly mean minimum and maximum temperature, rainfall and elevation. Only coarse-resolution surfaces (25 km) or meteorological station data were available before this.

Climatic variables essential for discriminating the biological requirements of parasite vectors were derived from these monthly surfaces and are being used to develop computer-based models and animal health decision-support systems.

COOPERATIVE PROGRAMS, TRAINING AND INFORMATION

COOPERATIVE PROGRAMS UNIT

ILRAD'S OUTREACH ACTIVITIES fall under a Department of Cooperative Programs, Training and Information. The broad aim of the Cooperative Programs Unit is to initiate and facilitate research studies conducted jointly by ILRAD staff and scientists working in the national agricultural research systems of developing countries. These collaborations accelerate research progress both at ILRAD and at the collaborating institutions and—through transfers of the latest scientific information and advanced technologies to the national systems—enhance control as well as research of tropical diseases of livestock.

Staff from this unit and ILRAD's research programs regularly visit Africa's national and regional agricultural research institutions. On these visits, they explore the merits of possible collaborative research projects and inform developing country research managers about ILRAD activities and outputs that have potential for exploitation by national and regional livestock disease control organizations.

Cooperative Programs staff also help to coordinate the transfer of ILRAD's research findings and products to the institute's stakeholders. The latter include national governments, universities and research institutes; regional and international research organizations; and funding agencies. Examples of the technologies developed or refined at ILRAD in 1993/4 that are of potential benefit to these stakeholders are:

- A newly developed artificial membrane system for *in vitro* feeding of laboratory colonies of ticks.
- An improved *in vitro* assay, developed in collaboration with the University of Glasgow Veterinary School, for determining levels of the trypanocidal drug isometamidium in cattle.
- New reagents that have improved diagnosis of tickborne diseases and trypanosomiasis.
- Computer-based decision-support systems for research and disease control organizations produced with empirical data on the epidemiology of tickborne diseases and trypanosomiasis. Such a system is currently being used in the Veterinary Research Laboratory of the Department of Veterinary Services, in Harare, Zimbabwe.

ILRAD's Department of Cooperative Programs, Training and Information helps to transfer the institute's research products to potential users in other organizations. The main objectives of this transfer are to promote research and application of improved control methods for livestock diseases, particularly tickborne diseases and trypanosomiasis.

This department uses ILRAD's scientific resources to initiate collaborative research projects, to run training programs, to disseminate scientific information, and in general to help enhance the research and control work conducted in national and regional organizations of developing countries.

- Computer models for assessing the impacts of diseases and the costs and benefits of implementing alternative disease control options. A spreadsheet model and a farm-level simulation model are currently being employed by visiting scientists in Kenya (Muranga), Zambia and Zimbabwe.



Dr. Ross Gray (left), Director General of ILRAD, with Mr. Simeon Nyachae, Kenyan Minister for Agriculture, Livestock Development and Marketing, who gave the opening address at an FAO 'Technical Consultation on Trypanosomiasis' held at ILRAD from 16 to 19 February 1993.

Sixteen experts in tsetse and trypanosomiasis control in 9 African countries participated in the meeting, as well as 71 observers from ICIPE, ILRAD, ILCA, KARI, OAU/IBAR, World Bank Livestock Services, regional offices of international drug companies, the Ugandan Commissioner for Tsetse Control, Kenya Veterinary Research Laboratories, Kenya Veterinary Association, Kenya Tsetse Control Unit, Kenyatta University and the University of Nairobi Veterinary Department.

ILRAD hosts and makes substantial contributions to several outside meetings each year. Such gatherings of high-level policy-makers benefit ILRAD because they expose staff directly to the priorities of the national agricultural research systems of developing countries. At the same time, senior staff from those systems are introduced to ILRAD's research agenda and to its technical and scientific resources.

TRAINING UNIT

THE GOAL of ILRAD's Training Unit is to enhance the scientific and technical capacity of developing country national agricultural research systems, which include universities and other centres of higher learning, by training individuals at ILRAD and by supporting relevant training conducted elsewhere. The clients of ILRAD's training activities are scientists, technicians, personnel from national agricultural research systems on staff development and future trainers in livestock research and disease control. The Training Unit's activities address the needs of these clients who, with their colleagues in their home institutions, are likely to be instrumental in testing, evaluating and using new products and methodologies developed at ILRAD.

In 1993 and 1994 to date, scientists and senior laboratory technicians from 32 developing and 3 developed countries came to ILRAD for periods of one week to six months to receive individual training in techniques and methodologies specified by their research institute or disease control project.

ILRAD provides several kinds of training:

- (1) advanced research work for post-doctoral fellows;
- (2) full-time graduate research studies towards master's and doctorate degrees;
- (3) specialized training courses for groups; and
- (4) individual training in skills and techniques acquired in short-term attachments to the Laboratory's research programs.

Individual training at ILRAD in 1993 and 1994 (through September); number of participants in different types of training by country of origin.

Nearly 10% of ILRAD's budget is spent each year on training and related outreach activities.

ITT = individual technical training
GTT = group technical training
RF = Research Fellows
SRF = Senior Research Fellows



Simon Mwangi, an ILRAD Research Fellow from Kenya. Up to 25 doctoral and master's students have been given full-time training and support at ILRAD at a time.

Most ILRAD Research Fellows are staff members of universities and research institutes in developing countries who have previously received a Master of Science degree or its equivalent. These Research Fellows undertake full-time laboratory bench research at ILRAD towards a doctorate. On completion of their studies, they return to work in their home institutions.

Country	ITT	GTT	RF	SRF
Bhutan		1		
Brazil		1		
Burkina Faso	1	2		
Cameroon	1	1	1	
Canada	1		1	
Chad		1	1	
Côte d'Ivoire		2		
Ethiopia	1	3	1	
France	1		1	
Gambia		1	1	
Germany	1			
Ghana		2	1	
Guinee	1			
India	1	1	1	
Indonesia		1		
Kenya	11	6	13	1
Malawi		4		
Mali		2	1	
Mexico		1		
Morocco		1		
Namibia		2		
Nigeria	1	1	1	
Senegal		1	1	
South Africa		4		
Sudan		1	2	
Tanzania	5	5	2	
Tchad			1	
Thailand		2		
Uganda	3	6	2	1
UK		1		
USA			1	
Zaire	1		1	1
Zambia	3	2		
Zimbabwe	3	6	2	
Totals	35	61	35	3

Thirty-five students—most of them from Africa and supported by ILRAD fellowships—conducted research at ILRAD during all or part of 1993 and/or 1994 towards Ph.D. and M.Sc. degrees. ILRAD provided three additional fellowships to senior African scientists to do post-doctoral research at the institute.

In this period, ILRAD held four group courses. In June 1993, ILRAD and the University of Nairobi conducted a three-week course on 'Quantitative Epidemiological Methods in the Study of Tickborne Diseases', which was attended by 14 individuals from 7 African countries. From May to June 1994, ILRAD conducted a four-week regional course on 'Use of Diagnostic Methods for Trypanosomiasis'; 17 individuals from 16 African countries participated. From October to December 1994, ILRAD conducted a six-week course on 'Tickborne Diseases Diagnostic Validation'; the 11 people came from 11 countries: Brazil, Burkina Faso, India, Indonesia, Mexico, Kenya, Malawi, Mali, Morocco, Uganda and Zimbabwe. Several individuals from Namibia and South Africa participated in ILRAD courses and workshops for the first time in 1993/4.

The last group course was conducted a week before the '7th International Symposium for Veterinary Epidemiology and

Economics', which over 400 delegates attended in Nairobi in August 1994. The course, entitled 'Introduction to Quantitative Veterinary Epidemiology', was held at ILRAD and conducted jointly by ILRAD, the universities of Nairobi and Guelph, and the Overseas Development Administration of the UK. Nineteen people from 12 countries—from Bhutan, Côte d'Ivoire, Ghana, Kenya, Malawi, Namibia, South Africa, Tanzania, Thailand, Uganda, Zimbabwe and the UK—took the course.

ILRAD workshops are largely think tanks attended by ILRAD staff involved in a particular research area and selected world experts in that area. Because the latest information in a field of particular interest to ILRAD's research programs is exchanged at these high-level meetings, the workshops contribute much to program planning by ILRAD and its collaborating institutions. ILRAD hosted two scientific workshops in 1993 attended by a total of 31 international scientists from 11 countries. Jointly with the International Livestock Center for Africa, ILRAD held a workshop on 'Increased Utilization and Adoption of Trypanotolerance' in April 1993. In November of that year, ILRAD conducted a workshop to explore 'Novel Immunization Strategies against Protozoan Parasites'.

ILRAD hosted and made major contributions to two other workshops. The first workshop was the first research coordination meeting of a joint project of the Food and Agriculture Organization (FAO) and the International Atomic Energy Agency (IAEA) held in February 1994. The 14 African representatives who attended the five-day workshop, entitled 'Use of Immunoassay Methods for Improved Diagnosis of Trypanosomiasis and Monitoring of Tsetse and Trypanosomiasis Control Programs', reviewed ILRAD's enzyme-linked immunosorbent assay for diagnosing trypanosomiasis and assessed new project proposals submitted by candidates for IAEA research contracts in charge of monitoring trypanosomiasis control programs. The second workshop ILRAD contributed to was conducted by FAO in August 1994 to plan tickborne disease training activities and impact assessments as part of a regional coordination and training project ('Integrated Tick and Tickborne Disease Control') in eastern, central and southern Africa. This workshop was attended by FAO representatives from the project and by country coordinators.

ILRAD's relationships with its trainees do not end when they leave the institute. For example, ILRAD has strengthened its ties with former trainees, and has helped the trainees stay in contact with each other, through publication of a newsletter, *Contact*. ILRAD works to stay in touch with its former trainees for two main reasons. One is that the success of a post-graduate training program is better measured by the productivity of its former students after they have received their degrees than by the number of degrees awarded each year. The second is that former ILRAD trainees are the most appropriate vehicles for broad and effective transfer of ILRAD products, methodologies and information

Representatives from training programs at ten Africa-based CGIAR institutions—CIAT, CIMMYT, CIP, IFPRI, IITA, IPGRI, ISNAR, WARDA, ILRAD and ICRAF—met at ICRAF in Nairobi in November 1993 to determine ways of increasing their collaborative activities. This is especially attractive in areas such as development of databases built with geographic information systems, analyses of biostatistical data, and choice and use of advanced information hardware and software. Plans were made at the meeting to pool resources in these and other areas for training purposes. A common training schedule for 1994/5 was prepared for distribution to African national agricultural research systems. Plans were made to compile databases of CGIAR trainees, resource personnel and facilities by African country and to produce a catalogue of training materials in agricultural research available in Africa.



INFORMATION UNIT

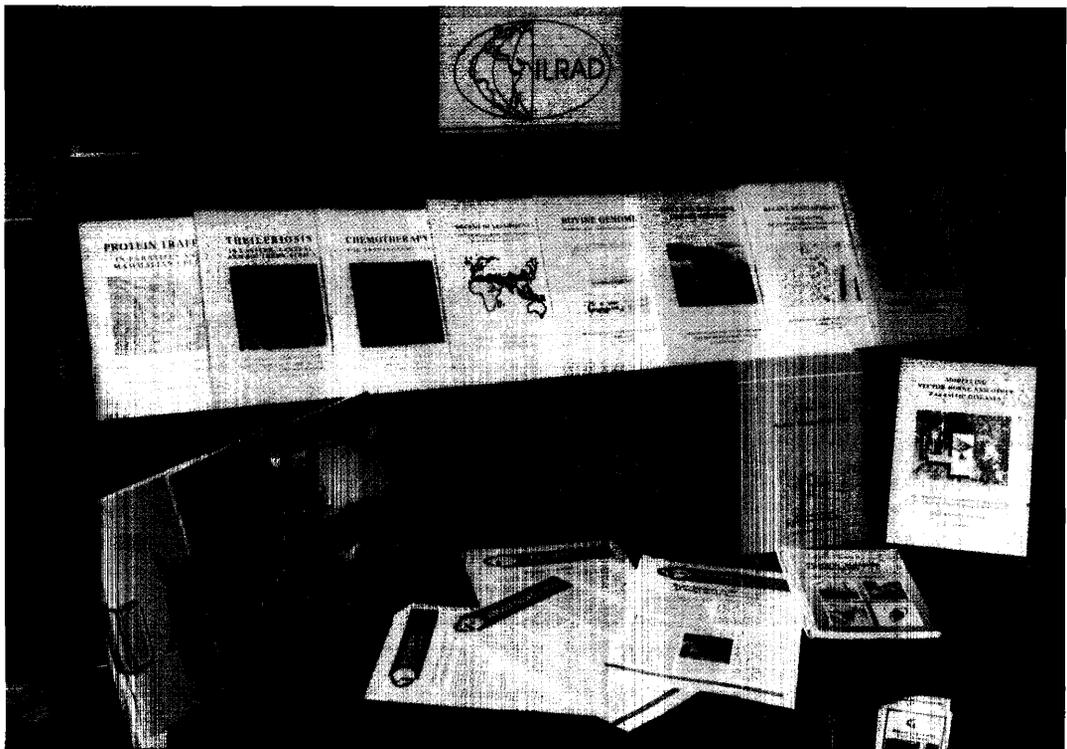
THE BASIC TASK of ILRAD's Information Unit is to produce and distribute publications that (1) inform readers of the research and outreach programs of the institute, (2) disseminate new information and experimental results, (3) facilitate the transfer of research outputs, and (4) increase public awareness of the importance of ILRAD's work.

Each year the unit publishes an *ILRAD Annual Report*, an annual *ILRAD Highlights* and a quarterly scientific newsletter, *ILRAD Reports*, in French as well as English. In English only it publishes an *ILRAD Annual Scientific Report*, an annual list of scientific publications produced by staff, two or three proceedings of international scientific workshops or meetings conducted by ILRAD, an annual *Program and Budget* document and a weekly *Internal Newsletter* distributed to all staff members and to the Board of Directors. In the last two years, the unit in addition gave editorial support to a *1994-1998 Medium Term Plan* for ILRAD and to a *Program and Budget* document covering the same years for the new institute that will replace ILRAD and ILCA in January 1995, the International Livestock Research Institute.

All of the institute's English publications are written, edited, designed and electronically laid out to camera-ready stage in-house and printed locally, in Nairobi. Translation and typesetting of French publications is contracted to a biomedical translation company in the USA.

Publications from ILRAD.

Over 75% of ILRAD's 4,068 readers—which include individuals and libraries in research institutions, veterinary departments, universities and national development and disease control organizations—are located in developing countries.



The annual report, annual highlights and quarterly newsletter are intended for a wide range of readers, with emphasis on scientists and policymakers in national agricultural research systems. ILRAD's annual scientific report comprises abstracts describing the aims and results of each research project conducted at the Laboratory during the year. This book and the annual list of staff publications are intended for scientists and highly technical staff working in areas related to ILRAD's research programs as well as for new ILRAD staff. ILRAD's readership comprises about 3,500 English and 500 French readers in developing and developed countries worldwide.

Proceedings of the institute's international workshops are also intended mainly for a scientific readership. Publication of the presentations, discussions and recommendations of ILRAD workshops is a useful reference for workshop participants, donor representatives and staff of national agricultural research systems, who use the information compiled in the proceedings for their own research planning. In 1993, ILRAD published summaries of papers presented at a September 1991 workshop, *Ticks and Tick-Borne Disease Control* (49 pages, ed. Tom Dolan). This meeting, held in Kampala, Uganda, was the fourth in a series of workshops held since 1984 to discuss recent research findings in tick-borne diseases and to address problems encountered in their control. The workshop was organized jointly by ILRAD, the Food and Agriculture Organization of the United Nations and the Inter-African Bureau of Animal Resources of the Organization of African Unity. ILRAD also published in 1993 the proceedings of its November 1992 workshop, *Genome Analysis of Protozoan Parasites* (189 pages, ed. Subhash Morzaria).

In 1994, ILRAD published three proceedings volumes and one book. The first proceedings was of a workshop on *Modelling Vector-Borne and other Parasitic Diseases* (369 pages, eds. B.D. Perry and J.W. Hansen), which was organized jointly by ILRAD and FAO and held at ILRAD in November 1992. With ILCA, ILRAD is publishing the proceedings of a workshop on *Increased Utilization and Adoption of Trypanotolerance*, held at ILRAD in April 1993 (in press, ed. G.J. Rowlands and A.J. Teale). The experts attending this workshop reviewed research on trypanotolerance, determined future research and extension needs in this area and set up mechanisms to enhance and widen inter-institutional collaborations in work on trypanotolerance. The Laboratory is also publishing the proceedings of its November 1993 workshop on *Novel Immunization Strategies against Protozoan Parasites* (in press, ed. D.J. McKeever). With ILCA and FAO, ILRAD this year also co-published a second edition of a handbook on *The Epidemiology, Diagnosis and Control of Helminth Parasites of Ruminants* (171 pages, by J.W. Hansen and ILRAD scientist B.D. Perry).

ILRAD's Information Unit endeavours to produce publications that:

- encourage cross-fertilization of ideas and collaborations among scientists working in different institutes and countries
- communicate the significance of results of ILRAD's research to the institute's financial supporters and those who influence their decision-making
- transfer the latest scientific information obtained in ILRAD research to stakeholders in the national research programs of developing countries

LIBRARY

The relatively small ILRAD Library is sufficiently specialized, comprehensive, up-to-date and advanced in its communications systems to serve the multidisciplinary interests of ILRAD's scientific staff, many of whom are at the forefront of international work in their research areas.

The Library also serves scientists working outside the institute by disseminating worldwide and upon request publications, reprints, abstracts, research results and other information produced and collected at ILRAD.

Information services provided upon request include:

- retrospective searches (retrieval and printing of bibliographic information on given topics)
- selective dissemination of information (profiles of interests of scientists are designed and bibliographic information on user-specific topics sent to them regularly)
- specialized bibliographies (on animal trypanosomiasis and tickborne diseases)
- accessions lists published weekly (a list of recent accessions is distributed internally and to local research institutions)
 - document delivery and referral (the Library holds most of the original documents in ILRAD's databases and refers users to other sources when appropriate)
- inter-library loans to local universities and research institutes

THE ILRAD LIBRARY provides fundamental support for the institute's research by acquiring, organizing and disseminating information, most of it in the form of printed books, scientific journals and computer databases. The emphasis of the collection is on the livestock diseases ILRAD focuses on, animal trypanosomiasis and tickborne diseases, as well as veterinary medicine and the biochemistry, chemotherapy, cytology, epidemiology, genetics, immunology, molecular and cell biology and pathology of these diseases and their causative parasites.

Journals form the main part of the Library's collection. In 1994, the Library subscribed to 150 specialized scientific journals, 25 monographic serials and 15 indexing or abstracting journals. A total of 100 books were received this year, bringing the total book stock to some 4,155 volumes. A *Weekly Alert* newsletter is produced and distributed to staff and other local libraries to highlight important new accessions in the Library.

The Library also maintains access to several international agricultural and biomedical databases stored electronically on CD-ROMs (compact disks-read only memory). These include Current Contents, Life Sciences (on computer disk, 1991-1993, on CD-ROM, 1994), CABI Abstracts (1984-1991), Medline (1966-present), Science Citation Index, SESAME and Veterinary Science and Animal Health (1973-1991). The Library this year installed MICRO CDS/ISIS for managing all its databases. ILRAD scientists access the databases using a local area computer network established in 1991, and they now conduct most of their own literature searches using office personal computers.

In the first half of 1994 and on staff request, the ILRAD Library photocopied 6,500 journal articles, borrowed 448 articles from other libraries, lent out 447 publications, and bought from the British Library 400 photocopies of journal articles. The Library also undertook 26 literature searches for ILRAD staff and 81 searches for external users.

Because the Library's extensive, up-to-date and highly specialized journal collection is unique in Kenya, its services are extended to staff of other research institutes, as well as to government departments and universities, in Nairobi. Library staff helped strengthen the country's agricultural information services in 1994 by providing short-term practical training to 11 library students from Kenyan universities, research institutes and polytechnics. The Library fulfilled in this period requests for over 586 reprints and other publications written by ILRAD scientists and it donated to local libraries 1,020 books and journals. Over half of the literature searches undertaken during 1994 were conducted for, and sent by post to, users from other African countries. A total of 586 reprints and photocopies of journal articles written by non-ILRAD scientists were sent to researchers in other developing countries in Africa, Asia and Latin America.

RESEARCH SUPPORT

ILRAD'S TSETSE UNIT establishes and maintains colonies of tsetse flies for research on trypanosome parasites. Trypanosomes normally pass through several stages of their life cycle in the tsetse fly. Although it is possible to maintain trypanosomes *in vitro* and to infect laboratory animals and livestock by injecting parasites into the animals, trypanosomes maintained and transmitted artificially differ from those transmitted naturally through the bite of an infected tsetse fly. Thus, a great deal of the trypanosomiasis research conducted at ILRAD requires trypanosomes that have developed in tsetse flies.

Five tsetse breeding colonies were maintained at ILRAD in 1993/4. These were *Glossina morsitans centralis*, originating from mainland Tanzania; two colonies of *G. pallidipes* obtained from Kenya's Coast and Rift Valley Provinces; *G. brevipalpis*, from Kenya's Eastern Province, and *G. longipennis*, from Kenya's Rift Valley Province. These five production colonies, fed five days a week using rabbits, provided all the tsetse required for trypanosomiasis research at ILRAD in these years.

A colony of *G. fuscipes fuscipes* initiated in January 1992 with 500 wild puparia from Kenya's Nyanza Province is in an expanding phase. By the end of September 1993, the colony had 955 breeding females and had produced 11,688 puparia. A colony of *G. austeni* initiated in September 1992 with 200 wild puparia from Kenya's Coast Province a year later had reached a target of 1,500 breeding females and had produced 13,417 puparia.

As well as providing services to ILRAD scientists, staff members of the unit conduct research on tsetse flies as vectors of trypanosomiasis. Studies were conducted in 1993, for example, to determine differences in the susceptibility of four laboratory-bred *Glossina* species to three stocks of *Trypanosoma simiae*, a parasite that causes acute disease in pigs. The differences observed in infection rates are partly responsible for differences in the epidemiology of *simiae*-trypanosomiasis.

Another study was conducted to compare infection rates of *G. morsitans centralis* and *G. brevipalpis* with procyclic forms of *Trypanosoma brucei brucei*. Procyclic *T. b. brucei* from

TSETSE UNIT

ILRAD's Tsetse Unit supplies surplus tsetse puparia to outside research groups on request. In 1993, the unit provided a total of 21,570 tsetse materials to colleagues working in Kenya at the International Centre of Insect Physiology and Ecology, the Kenya Trypanosomiasis Research Institute, the University of Nairobi, Kenyatta University, and the Kenya Medical Training College, and to scientists working abroad at the universities of Bristol and Wales, the Swiss Tropical Institute and Texas University.



A tsetse fly (*Glossina morsitans*), the vector of trypanosome parasites, resting on a tree branch.

TICK UNIT

susceptible *G. m. centralis* could not complete cyclical development in refractory *G. brevipalpis*, whereas those from *G. brevipalpis* developed to metatrypanosomes in the salivary glands of *G. m. centralis*. Results of this work suggest that maturation of *T. b. brucei* in tsetse is probably not determined by a single lectin-procyclic interaction but rather is the result of complex interactions among many interrelated physiological factors of the trypanosome and tsetse vector.

The ILRAD Tsetse Unit regularly trains staff from institutions in Africa's national agricultural research systems on the management of tsetse colonies, on dissection of tsetse flies to identify infecting trypanosome parasites, and on aspects of tsetse biology and ecology pertinent to the vector's role in the transmission of trypanosome infections to livestock. Personnel trained at ILRAD in 1993 include a technician from Zaire, a doctoral student from Mali and an animal disease control officer from Kenya's Ministry of Agriculture, Livestock Development and Marketing.

THE TICK UNIT supplies ILRAD researchers with tick-borne disease pathogens that infect domestic ruminants. Regular provisions are required of ticks and tick salivary glands infected with the sporozoite form of *Theileria parva*, which causes theileriosis, commonly known as East Coast fever. *T. parva* sporozoites can be obtained only following infection and development of the parasites in tick vectors.

Rhipicephalus appendiculatus is the most important tick species in East Africa, where it is the principal vector of *T. parva*. Stocks of this species maintained at ILRAD include those from Muguga, Kenya; Ol Pejeta, Kenya; McIlwaine, Zimbabwe; Chipata, Zambia; and Entebbe, Uganda. Colonies of other tick species maintained at ILRAD include other *Rhipicephalus* species—*R. evertsi*, *R. pulchellus* and *R. zambeziensis*—as well as *Amblyomma variegatum* and *Amblyomma gemma*, vectors of *Cowdria ruminantium*, which causes heartwater, and two relatively benign *Theileria* species, *T. mutans* and *T. velifera*, as well as *Boophilus decoloratus*, vector of *Babesia* and *Anaplasma*, which cause redwater and gall sickness, respectively.

In 1993, a new tick feeding apparatus was developed jointly with scientists at the Nairobi-based International Centre of Insect Physiology and Ecology. This consists of an artificial membrane that incorporates added olfactory and tactile stimuli and is supplied with blood every eight hours. Ticks fed more efficiently on this system than on other *in vitro* systems. Furthermore, most nymphal ticks that were fed on *T. parva*-infected blood using this system became infected with that parasite. The system is now being refined to produce ticks whose engorgement, moulting and transmission characteristics are similar to those of ticks fed on cattle. When this is achieved, the feeding system will be used to

ILRAD continued to collaborate with scientists at the International Centre of Insect Physiology and Ecology to optimize feeding techniques employed to produce infected ticks *in vitro*. This work has demonstrated that most species of ixodid ticks can probably be fed on artificial feeding membranes rather than animal hosts, thus generating considerable savings in time and expense as well as obviating the need for experimental animals.

conduct *in vitro* experiments of parasite biology and transmission dynamics that require the feeding of known numbers and mixtures of defined parasites.

Since 1986, in collaboration with scientists at the Universities of Florida and Strathclyde, ILRAD staff have been constructing a database on experimental transmission of *T. parva* by *R. appendiculatus* ticks. A General Linear Model was used to determine the relative importance of variables that determine levels of tick infection. The analyses revealed 14 factors and interactions that affect infection levels significantly. This information will be used to devise methods for producing tick batches with relatively predictable infection levels. Related research demonstrated that some of the variability in tick infectivity is under genetic control and that it should be possible to select ticks with high and low susceptibilities to *T. parva* infections. Such standardized infections are needed to conduct trials of prototype vaccines and to clarify the epidemiology of parasite transmissions in the field.

In collaboration with biomathematics research conducted at the University of Warwick, ILRAD's Tick Unit fed ticks on infected cattle to compare the competence of six stocks of *R. appendiculatus* ticks and one stock of *R. zambeziensis* to transmit *T. parva* (Muguga) and *T. parva* (Boleni) parasites. (Vector competence is assessed by determining the levels of infection that develop in tick salivary glands.) A series of experiments disclosed significant variation in the competence of these ticks to transmit the different *T. parva* parasites, indicating that relationships among these parasites and their tick vectors in the field probably vary greatly. In a second series of experiments using the same two *T. parva* stocks, nymphal/adult parasite transmission was shown to be more efficient than larval/nymph. ILRAD is also collaborating with Warwick to identify the factors that determine the survival and infection of *T. parva* in *R. appendiculatus* ticks. When complete, the data set will be used in computer models to predict tick and parasite survival and parasite transmission under different conditions.

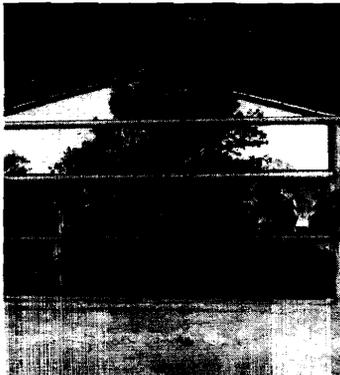


With the help of microscopes, technicians in ILRAD's Tick Unit dissect *Rhipicephalus appendiculatus* ticks infected with *Theileria parva* parasites. Sporozoite forms of the parasite, which are able to infect animal hosts, are located in the salivary glands of the ticks. The technicians extract these glands from the ticks and gently grind the glands to release the sporozoites. The sporozoites are preserved as stabulates to be used later to immunize livestock by the infection-and-treatment method and to infect animals in experiments.

SMALL ANIMAL UNIT

In 1993/4, ILRAD's Small Animal Unit supplied a total of 4,038 mice and rats to outside research groups in Kenya, including the:

- Institute of Primate Research
 - Kenya Agricultural Research Institute
- Kenya Medical Research Institute
- Kenya Society for the Prevention of Cruelty to Animals
 - Kenya Trypanosomiasis Research Institute
 - Kenyatta University
 - Museums of Kenya
 - ODA-funded research project in Busia,
- University of Nairobi Departments of Veterinary Pathology, Veterinary Medicine, Zoology and Public Health
- Veterinary Laboratories at Kabete



LARGE ANIMAL UNIT

THE SMALL ANIMAL UNIT provides ILRAD's research and training programs with regular supplies of mice, rats and rabbits. Throughout 1993 and through mid 1994, ILRAD continued to be self-sufficient in the production of all of these laboratory animals. Rabbit demand remained stable while rat and mice demand fell dramatically from the previous year. Rat usage fell by 33% and mice usage by 51%. The percentage used of small animals also improved: of mice weaned, 43% were used in 1992 and 55% in 1993/4; of rats weaned, 60% were used in 1992 and 78% in 1993/4.

A meticulous balance in the supply and demand of small laboratory animals for experimental use is impossible to maintain over an extended period. While discouraging overproduction of animals, for which there may be no demand, ILRAD also discourages buying animals when surplus demands arise due to exorbitant importation costs. No other suppliers of experimental animals exist in Kenya should ILRAD's production fail or fall short of required numbers. For these reasons, ILRAD consistently produces a surplus of animals. When not needed by the institute's scientists, these excess animals are provided to other research organizations and projects in Kenya.

In December 1993, ILRAD formed an Animal Care and Use Committee to advise management on the institute's animal care and housing facilities and to guide scientists on proper procedures for animal experiments.

Following European and North American guidelines, the committee prepared a set of standard operating procedures. Staff conducting any experiment involving animals request approval from this committee to have the animals allocated. The committee follows the principles of good laboratory practice in determining the necessity of using a given number of animals in an experiment and the appropriateness of the experimental procedures to be undertaken.

THE LARGE ANIMAL facilities on the ILRAD Farm, located next to ILRAD's laboratory, at Kabete, had an average population of 520 head of cattle and 250 goats during 1993/4 that were allocated for research projects at ILRAD. The average age of the cattle held on the farm has been reduced. Drought conditions in the country caused irregularities in the supply of animal feeds, which created management difficulties.

The institute's ranch, Kapiti Plains Estate, located about 70 km from Nairobi, in 1993 carried an average of 2,328 head of cattle. The ranch supplied 365 cattle to the ILRAD Farm and sold 283 cattle to local farmers and butchers. A total of 712 calves were born in 1993, compared with 829 in 1992 and 1,061 in 1991.

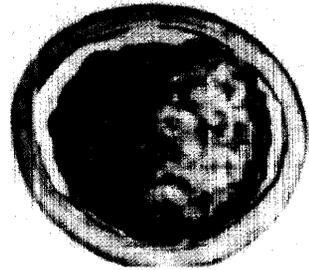
ILRAD's embryo transfer program has continued to do well. From January 1993 through May 1994, 74 embryo collections were performed on 27 donor cows, yielding 299 viable embryos.

The embryos are either transferred or cryopreserved and stored in liquid nitrogen for later use. The transferred embryos are implanted individually into the uteri of heat synchronized recipient cows, 75% of which subsequently give birth to calves.

The 75% pregnancy rate achieved is a dramatic improvement on previous years. This is largely due to use of an improved culture medium in which the embryos are held between collection and transfer. The same medium has improved the success rate of splitting embryos: 6 sets of identical twins and 2 singles were born from the first 8 embryo splits of 1993. That totals 14 calves from the original 8 embryos.

Purebred, trypanotolerant, N'Dama cattle are required for research into the trypanotolerance trait. ILRAD began its N'Dama breeding program in June 1983 by importing N'Dama embryos from The Gambia. The first N'Dama calves (5 heifers and 5 bull calves) were born at ILRAD in March/April 1984. In 1993 and the first eight months of 1994, 24 N'Dama calves were born, bringing the total number of N'Dama born at ILRAD in the last ten years to 100.

Production of the second generation N'Dama-Boran cross-breeds (F₂s) is also going well. The largest family has 39 calves born and 9 confirmed pregnancies, which are due late 1994. The second family has 32 calves born, including one set of identical twins. The other four families number 17, 17, 16 and 8 calves or confirmed pregnancies. This gives a total of 138 F₂s that have been produced from just 6 F₁ heifers.



An embryo from a donor cow.

Embryo transfer is the removal of seven-day-old embryos from the uterus of a donor cow and transfer of these embryos to the uterus of a heat synchronized recipient cow, which carries the embryo/foetus for the remaining nine months of gestation and gives birth to the calf.

To maximize the number of embryos collected, donor cows are 'superovulated' to release several ova at the subsequent heat. These ova are fertilized using artificial insemination and the embryos collected seven days later. A donor cow may be superovulated every eight weeks and so can produce many calves in a relatively short time. An embryo may be bisected to produce identical-twins, which are highly useful for answering research questions.

ILRAD embryo transfer activity from January 1993 through May 1994

	<i>Total number</i>	<i>F₁ generation</i>	<i>Boran</i>	<i>N'Dama</i>
Collections	74	46	16	12
Ova collected	480	353	82	45
Viable embryos	299	203	66	30
Embryos cryopreserved	42	35	7	0
Embryos implanted	224	161	41	22
<i>Pregnancies achieved</i>	<i>169</i>	<i>118</i>	<i>34</i>	<i>17</i>
Embryos split and implanted	26	10	16	0
Split embryos pregnant	24	8	16	0
Embryos per collection	4	4.4	4.1	2.5
Fertilization rate	62%	56%	80%	67%
Pregnancy rate after transfer	75%	73%	83%	77%
Calves per collection	3	3.2	3.4	1.9

P U B L I C A T I O N S

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§ JANUARY 1993 ISSUE: The secre-
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§ APRIL 1993 ISSUE: Estimating the
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Africa · Controlling trypanoso-
miasis by reducing tsetse popula-
tions · A new system for identify-
ing RNA-binding proteins in try-
panosomes · Mitochondrial RNA
editing may help regulate trypano-
some energy production

§ JULY 1993 ISSUE: Biotechnology
in the service of Third World agri-
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§ OCTOBER 1993 ISSUE: Bovine
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calves offer evidence that cyto-
toxic T cells can clear *T. parva*
infections

§ JANUARY-JUNE 1994 ISSUE:
Human nutritional status as a
measure of the impact of livestock
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of trypanosomiasis · Novel vacci-
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parasites · Developing nucleic
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class II MHC in cattle

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Coast fever · ILRAD's links with
global livestock disease research ·
Designer research cows · State of
the bovine genome map

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BOOKS AND BOOK CHAPTERS,
AND PAPERS IN PROCEEDINGS
WRITTEN BY ILRAD STAFF

Note:

Refereed papers presented at scientific meetings and published in special issues of journals are distinguished in this list from non-refereed proceedings papers: titles of non-refereed papers are followed by the word 'In:'.

All the publications in the list below were published in 1993 or in the first half of 1994. The numbers in parentheses are ILRAD Library accession numbers.

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(Below) The world's first artificially produced identical twin N'Dama calves. The calves were produced at ILRAD by splitting an N'Dama embryo in two and implanting the embryos in a foster Boran mother.





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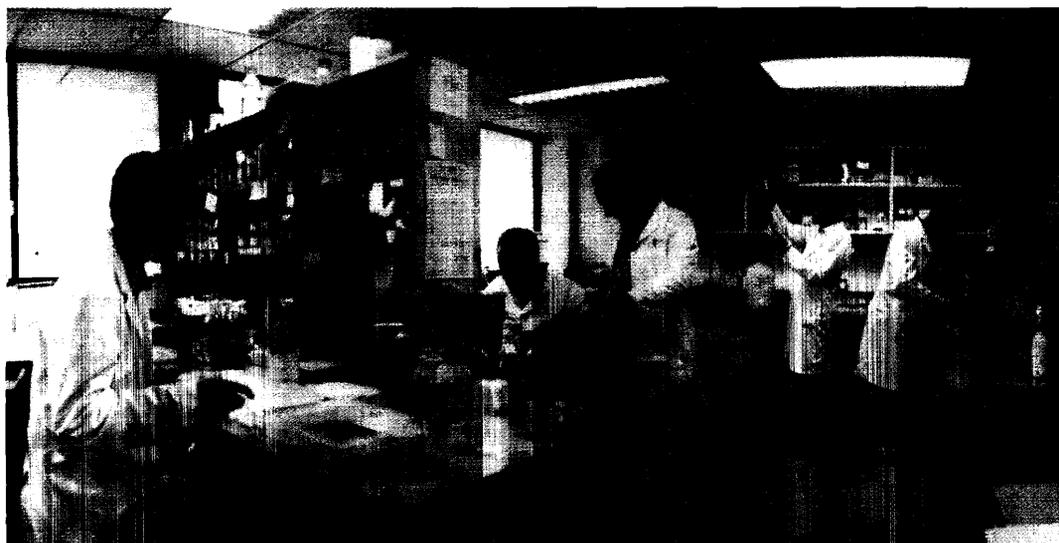
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Laboratory Technician
D. Ndegwa
Laboratory Technician
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K.A. Taylor
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D. Mwangi
Senior Research Fellow
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F. Mucheru
Laboratory Technician
P. Muiya
Laboratory Technician
C. W. Muriuki
Laboratory Technician
D.K. Muteti
Laboratory Technician
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Laboratory Technician
R. Saya
Laboratory Technician
K. Tikolo
Laboratory Technician



The following countries partially supported ILRAD scientists. The numbers are footnotes appended to names in this staff list.

1 Israel	13 Japan
2 USA	14 Belgium
3 UK	15 Belgium
4 Japan	16 France
5 France	17 Japan
6 Belgium	18 USA
7 Belgium	19 USA
8 Italy	20 Canada
9 Canada	21 USA
10 France	22 USA
11 Switzerland	23 USA
12 Japan	

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Theileriosis Program Area Leader: Antigens
S.B. Morzaria
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J. Kiarie
Laboratory Technician
J. Kiundi
Laboratory Technician
D.O. Lugo
Laboratory Technician
T. Ndolo
Laboratory Technician
S. Nduta
Laboratory Technician
J. Ngugi
Laboratory Technician
R. Njamunggeh
Laboratory Technician
T. Njoroge
Laboratory Technician
S. Njuguna
Laboratory Technician
S. Sohanpal
Laboratory Technician
A.K. Tonui
Laboratory Technician
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Laboratory Technician
F. Mbwika
Laboratory Technician
W. Mwangi
Laboratory Technician
D.N. Ngugi
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Laboratory Technician

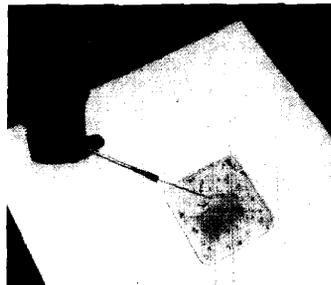
LAB 7 PARASITOLOGY
AND EPIDEMIOLOGY OF
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*Trypanosomiasis Program
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Visiting Scientist
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Research Fellow
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- A. Jaye
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Laboratory Technician
- J.E. Ngatti
Laboratory Technician
- J.T. Njuguna
Laboratory Technician
- M. Ogugo
Laboratory Technician
- M. Omenya
Laboratory Technician
- J.A. Sore
Laboratory Technician
- J.M. Wambugu
Laboratory Technician



LAB 8 SOCIOECONOMICS
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- J.J. Curry
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*Scientist/
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TICK LABORATORY

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- M. Baya
Laboratory Technician
- S. Mwaura
Laboratory Technician
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Laboratory Technician
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Laboratory Technician

CENTRAL CORE UNIT

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COOPERATIVE PROGRAMS,
TRAINING & INFORMATION
DEPARTMENT

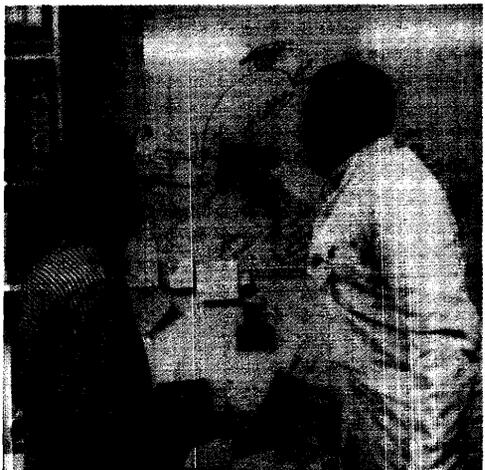
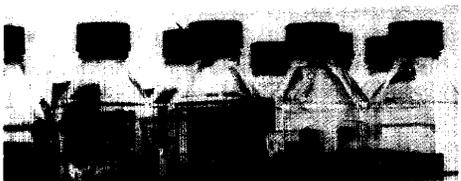
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REPORT TO THE DIRECTORS OF THE INTERNATIONAL
LABORATORY FOR RESEARCH ON ANIMAL DISEASES (ILRAD)

We have reviewed the abridged financial statements set out in Tables A1 to A4, which contain information extracted from the accounting records of ILRAD for the years ended 31 December 1992 and 1993.

We confirm that the information set out in the abridged financial statements is consistent with that contained in the audited financial statements for the years ended 31 December 1992 and 1993, on which we expressed an unqualified opinion.

Price Waterhouse

Certified Public Accountants

PRICE WATERHOUSE
Certified Public Accountants

8 September 1994

Table A1. Summary costs by program and activity (US\$ thousands)

	1993	1992
COSTS OF OPERATIONS		
Research		
Parasitology—Trypanosomiasis	444	664
Biochemistry	713	799
Cell Biology	462	501
Immunobiology	890	916
Parasitology—Theileriosis	823	877
Pathology	767	731
Immunoparasitology	829	842
Tsetse Laboratory	233	267
Tick Laboratory	244	248
Electron Microscopy	167	167
Epidemiology and Socioeconomics	446	475
<i>Research subtotals</i>	<u>6,018</u>	<u>6,487</u>
Research Support		
Research Support	615	719
Farm Animal Production	333	453
Laboratory Animal Production	162	191
Radioisotope and Central Core Services	644	713
<i>Research Support subtotals</i>	<u>1,754</u>	<u>2,076</u>
Training and Conferences	657	771
Library and Information Services	489	493
Administration		
Board of Directors	171	178
Office of the Director General	591	655
Finance	316	378
Personnel	106	131
Purchasing	368	487
<i>Administration subtotals</i>	<u>1,552</u>	<u>1,829</u>
General Operations		
Engineering	817	1,022
Transport	235	294
Services	284	346
Food and Housing	(72)	20
Stores	45	65
<i>General Operations subtotals</i>	<u>1,309</u>	<u>1,747</u>
Quinquennial Review Costs	—	324
TOTAL OPERATIONS AFTER DEPRECIATION	<u><u>11,779</u></u>	<u><u>13,727</u></u>

Table A2. Summary of core operating funds from donors (US\$ thousands)

	1993	1992
UNRESTRICTED AND RESTRICTED FUNDS FROM DONORS		
Unrestricted Funds from Donors		
World Bank	2,050	3,240
United States Agency for International Development	1,675	1,975
United Kingdom	860	1,132
Canadian International Development Agency	685	839
Japan	654	519
Switzerland	438	670
BMZ Germany	430	664
Sweden	388	544
Norway	287	336
Belgium	250	290
Denmark	154	174
Netherlands	136	147
France	117	120
Italy	100	74
African Development Bank	163	—
Finland	—	49
<i>Unrestricted Funds from Donors subtotals</i>	<u>8,387</u>	<u>10,773</u>
Restricted Funds from Donors		
United Nations Development Programme	1,058	932
Italy	200	500
Belgium	250	290
Japan	150	150
Australia	112	116
Ireland	149	—
<i>Restricted Funds from Donors subtotals</i>	<u>1,919</u>	<u>1,988</u>
TOTAL UNRESTRICTED AND RESTRICTED FUNDS FROM DONORS	<u>10,306</u>	<u>12,761</u>

Table A3. Summary of sources and application of funds (US\$ thousands)

	1993	1992
SOURCES OF FUNDS		
Core Operating Funds		
Unrestricted Funds from Donors	8,387	10,798
Restricted Funds from Donors	1,919	1,963
Earned Income Applied in the Year	392	1,059
Exchange Loss on Donations	(13)	(253)
Unexpended Balance from Previous Year	293	453
Transfer from Working Capital Fund	801	—
TOTAL SOURCES	<u>11,779</u>	<u>14,020</u>
APPLICATIONS OF FUNDS		
Core Operations before Depreciation	10,708	12,581
Capital Expenditure	344	588
Transfer to Capital Replacement Fund	727	558
Unexpended Balance Carried Forward	—	293
TOTAL APPLICATIONS	<u>11,779</u>	<u>14,020</u>

Table A4. Balance sheet as at 31 December 1993 (US\$ thousands)

	1993	1992
ASSETS		
Fixed Assets		
Land and Buildings	7,380	7,608
Research & Operating Equipment	2,033	2,484
Other Assets	282	371
Subsidiary Company		
Investment	1,786	1,786
Long-Term Loan	30	30
<i>Fixed Assets subtotal</i>	11,511	12,279
Net Current Assets	4,854	5,074
TOTAL ASSETS EMPLOYED	16,365	17,353
FUND BALANCES		
Capital Fund	11,511	12,279
Working Capital	2,012	2,813
Unrestricted Core Surplus	—	293
Revolving Fund	100	100
Capital Replacement Fund	2,742	1,868
TOTAL FUNDS	16,365	17,353

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With end-of-the-year reports and critical readings from ILRAD scientists, particularly: Tom Dolan, Head of the Tickborne Diseases Research Program; Alan Teale, Head of the Trypanosomiasis Research Program, Brian Perry, Head of the Socioeconomics and Environmental Impact Program, and Ross Gray, Director General.

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