CONTROL OF ANIMAL HAEMOPARASITES: CONTINUING SEARCH FOR A 'MAGIC BULLET'

An Inaugural Lecture delivered at the Ahmadu Beuo University, Zaria
on Friday, 31 October 1997

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October 1997

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Praise be to God to whom all praise is due. The Sole Administrator, Other Principal Officers, Distinguished Colleagues, My Dear Students, Ladies and Gentlemen.

Parts of the discourse

This Inaugural Lecture may be divided broadly into 6 parts: (i) inspiration; (ii) prologue; (iii) socio-economic constraints to research in Africa; (iv) importance of livestock, including obstacles to livestock production and health in Africa, and the role of the veterinary profession; (v) my contributions to blood parasitic diseases control, and those of others which are adequately acknowledged; and (vi) concluding remarks - an outlook or glimpse into future challenges.

Inspiration

In preparing this Lecture, I was inspired by three considerations: the first is the recognition that, in the tradition of Inaugural Lectures, one has a platform for uninhibited comment on any subject of one's choice;

the second is the caution to simplify the subject of disease control, and not succumb to the criticism levelled against some of us "*for being or not being high brow professor*";

the third is a sense of history. As I thought of what to say and how to say it, I read a lot of papers, including the following: the Ist Convocation Address of the founder of this great institution, Sir Ahmadu Bello, in 1963. It was a solemn and inspiring trust, summarised in his own words as follows: "Let there be no mistake; the challenges of the future will require the highest academic standards and achievements that we can attain; they cannot be inferior to the standard of any country in the world";

the 1973 Public Lecture delivered, at the invitation of ABU Students Union, by the Rt Hon Dr Nnamdi Azikiwe, on the political analysis of a new Capital for Nigeria, which Prof Ishaya Audu, the then Vice Chancellor described as a "*masterly, lucid and scholarly treatise*", with translations in Hausa (Bayero College), Igbo (UNN) and Yoruba (Lagos University); the long but refreshing 1977 Convocation Speech of Chief Obafemi Awolowo as Chancellor of ABU, delivered in his usual candid style, on why the First Republic failed;

the 1980 blueprint prepared by Prof Adamu Nayaya Mohammed and colleagues of the Nigerian Society for Parasitology on control of communicable diseases including malaria, sleeping sickness and other parasitic infections; the 1974-76 Public Lecture Series delivered by Prof O'Connel on the nature of African States; by Prof Umar Shehu on laying the foundation for rural health care delivery, the precept of the present day primary health care delivery system; by Prof Saka Nuru on the changing role of the veterinary profession, and the extensive discourse by Prof McDonald on aflatoxin in Nigerian groundnuts.

I was particularly struck by the very last one-sentence paragraph of Prof McDonald's disquisition, in which he said: "As research facilities improve in Nigeria I hope that more attention can be paid to the possible importance of aflatoxin and other mycotoxins in human and animal health".

The phrase: "*As research facilities improve in Nigeria...*" kept ringing in my head, given the virtual collapse of research facilities and basic infrastructures in universities and research institutes under the economic structural adjustment programme (SAP) introduced in 1986 with floatation and devaluation of the naira. So, I asked myself: how should this Inaugural Lecture read 20 or 30 years from now - a motivation to do more research on animal diseases, given the importance of livestock to national economy and human health; or a challenge to the younger academics to aspire to a professorial chair and give an Inaugural Lecture, or just another reading material for students?

Prologue

One Nigerian scientist that had intrigued and fascinated me was Professor Sanya Onabamiro. He was a very prolific writer. Few people here would recall that he was a biologist who made significant contribution to our understanding of the life cycle of the guinea worm, *Dracunculus medinensis*, in the mammalian host. The finding was published in 1956 in the *Annals of Tropical Medicine and Parasitology (vol. 50, 157)*, and cited in books on tropical medicine. The Carter Foundation's Global 2000 programme expected world eradication of guinea worm by 1996. Unfortunately in 1997, the disease is still with us. Professor Onabamiro wrote in many subject areas. Some of his writings were serialised in the popular Nigerian weekly, *Sunday Times*, and later published in 1980 in a book form entitled: *"Philosophical Essays"*. In one of such essays titled: *'How scientific theories change'*, Prof Onabamiro said the following about science and scientists: "Science develops in its students a spirit of humility. It stimulates a feeling of doubt. It creates an awareness of incompleteness of data, ... of the possibility of error. But humility has not always been a general characteristic of scientists from early times", said Professor Onabamiro; "it has taken the demolition of several cherished *'scientific'* theories to teach the present generation of scientists that it is dangerous to be over-confident".

This brings me to an experience I had in 1982 as a NORAD Fellow at the Norwegian College of Veterinary Medicine in Oslo. While in Norway, there was an outbreak of a tick-borne virus disease of cattle in the northern part of the country. The attending veterinary surgeon, who trained in Germany, learnt of a Visiting Scientist from Africa working in the field of haemoparasites. So he invited me and my Norwegian host, Professor Erling Søgnen, to come and help solve the problem. A day before we left for northern Norway, Prof Søgnen called me and said: *"Aliu, the expert is not the fellow who knows everything, but the person who does his home work"*. I quickly and tersely retorted that: "*the expert is the experienced, the exposed*, and I possess both qualifications, so there was no way I would not sound like an expert when we visit the farm."

Distinguished colleagues, these axiological ethics or cherished scientific values - *humility, doubt, possibility of error or incompleteness of data, experience, exposure* and of course *home work* have been a source of higher motivation for me, and guided the cautious selection of the title of this Inaugural Lecture - *Control of animal haemoparasites: continuing search for a 'magic bullet'*. In a thanksgiving speech made at the end of the Second World War in 1945, Sir Winston Churchill is famously reported to have told an American audience that the only thing dividing the two great nations of United Kingdom and United States of America was their common language. A similar impossibility can perhaps be said to divide man and his livestock - sickness. Sickness has been man's and his domestic animal's heritage from the beginning of their existence, and search for remedies to combat it is perhaps as equally old. Egypt can boast what is probably the oldest complete medical treatise in existence - the *Ebers Papyrus* - dating back to *ca* 1550 BC. A fragment of the ancient Egyptian veterinary *Papyrus of Kahun* dates back to *ca* 2000 BC, but many paintings and ancient temple carvings clearly depict animal husbandry and treatment of animal ailments at dates even beyond the earliest Chinese and Indian writings on drug folklore, the Chinese *Pen Tsao*, compiled by Emperor Shennug in *ca* 2735 BC, and the *Vedas* of India (*Ayurveda* and *Rigveda*) written *ca* 3000-2500 BC. Some of the agents employed at that time are still in use today, eg, the ancient Egyptians used castor oil as purgative. Nigeria compiled the first National Drug Formulary and Essential Drugs List only in 1989, and essentially for humans.

Socio-economic constraints to research in Africa

In the past two and half decades (since the great African drought of 1968-75 and the oil crisis of 1973), the image of Nigeria and that of the rest of Africa has shifted from great optimism and euphoria of the immediate post-independence era (the 1960s) to one of immense gloom and pessimism (AAS, 1987; Achebe *et al*, 1990). In the minds of many, Africa is now characterised as a continent in crisis, a highly vulnerable and peripheral region of the world, a continent caught in an inevitable downward socio-economic spiral (World Bank, 1989). Internal civil strife and ethnic tensions, high population growth rates, declining agricultural

production, low standard of health and education, repeated cycles of droughts and self-reinforcing process of environmental degradation have rapidly become the most common symbols of African existence. Most African countries are unable to select those areas, especially in agriculture and social services where science can make its greatest development contribution. They cannot mobilise universities, research institutes and industries to choose and develop suitable technologies, and are unable to concentrate resources in a coherent science policy that is reflected in education and training, as well as in research and product development.

The vigour which universities and research institutes in Nigeria displayed during the immediate post-independence era (1960s to 1980s) to maintain a firm tripodal balance of excellence in teaching, research, and professional/community service has shifted to declining quality as evidenced by deteriorating working conditions, under-funding, management problems, and low state of learning and research output.

This persisting negative image of Africa is frustrating African intellectuals, scholars and scientists to doubt their own self-determination to contribute to knowledge conducive to solving socio-economic, livestock and other production problems. African scientists in particular are apprehensive about their critical role as levers of change for a better future. A better future, meaning development, is the most important challenge facing the human race.

The challenge of development

By the year 2025, the world's population is expected to be 8.5 billion, a net increase of over 60% from the current level of 5.3 billion (UNU, 1989). By that date, over 1.1 billion people in the world (dubbed the world's poorest billion, with over 60% in Africa) will lack the basic necessities of life, such as adequate food and water, shelter, health care, good education and job needed to lead healthy productive lives. Development, in its broadest sense, means improved quality of life. As Africa's natural resource base continues to deteriorate, the responsibility for caring for an even larger population tomorrow is equally imperilled. Only *profound changes* in food and water supply, shelter, health care,

education, environmental protection and job creation through science and technology can ensure adequate living standards and, secure for Nigeria or any other African country for that matter, the status of a *developed nation* in the next century. Science and technology have always been the agents of change, whether in the Stone, Bronze, Computer or Space ages. As put properly by the Japanese radical thinker, Shintaro Ishihara (1991), "nations decline when they self-indulgently let life-styles become more important than workmanship, and neglect their [agricultural], industrial and technological base. That is the lesson of history".

Problem of food security

A discussion of strategy for improving livestock production through disease control ought to start by mentioning the problem of hunger and malnutrition in Africa. It is a well-known point of the scientific method that understanding the problem is often much more difficult than finding the answer. In 1960, the human population of Africa was in the order of 200 million; by 1985, this number had risen to 460 million, more than doubling in 25 years. Projections indicate that the African population, which was 612.2 million in 1990, will have reached 730 million by the end of the century, and 1.8 billion by the middle of the next century (World Bank, 1989). This is an average increase of 3% a year. As members of this audience will understand well, achieving a matching 3% increase in agricultural production in Africa to feed this growing population will be a formidable task.

In Nigeria, there is an annual total growth of 1-1.5% in food production, but per capita food production has been on the decline by about 1.2% since 1991 (CBN, 1995). The demand for food and population growth average more than 3% per annum, leaving a short-fall of 1.5-2% in food supply annually. There are two aspects to the problem of food shortage in Nigeria and the rest of Africa. The first, is total food intake, which is essentially inadequate (FOS, 1991). The average daily intake of food, usually staple crops (root crops, cereals and grain legumes) and some meat, is about 2,000 calories (or 1,888 grams) per caput per day. This is below the recommended FAO/WHO minimum of 2,500 calories per

person per day (Table 1: FAO, 1988). The second aspect, is the inadequacy of the protein content of the ingested available food.

Table 1: Food intake per caput per day in Nigeria and other selected countries

Food intake	World average	Nigeria	Libya	Somalia	Cuba	Asia	USA
Total intake[a]	2694	2114	3511	2088	3107	2465	3642
Vegetable products[a]	2274	2044	3007	1450	2427	2274	2914
Animal products[a]	420	70	504	638	680	212	1228
Total protein[b]	70.3	46.6	88.1	65.8	78.9	60.7	106.5
Vegetable protein[b]	46.2	39.8	54.6	27.7	40.5	48.5	35.6
Animal protein[b]	24.1	6.8	33.5	38.1	38.4	12.2	70.9

[a]calories per caput per day; [b]grams per caput per day.
Source: FAO, 1988

It is estimated that the national average supply of protein is about 46.6 grams per caput per day, of which less than 7 grams are from animal sources (meat, fish, milk, eggs). These are far short of the estimated minimum requirements of 86 grams of total protein and 34 grams of animal protein per person per day.

Importance of livestock

The facts about Nigeria are indisputable - a predominantly agricultural country with substantial petroleum and other mineral resources. It has a large expanse of land (910,770 km² in area out of Africa's 22 million km²) with a wide range of agroclimatic conditions and corresponding varieties of vegetation, and a plethora of diseases affecting health and productivity. Agriculture, besides providing food for the nation, plays an important role in expanding industrial and export base, and reducing rural-urban drift. Undoubtedly, livestock play a vital role in the agricultural and rural economies of the developing world, accounting for 7% of Nigeria's gross domestic product (CBN, 1992). Not only do

livestock provide food directly, they provide key inputs to agriculture - manure, fuel, animal traction, etc. For many smallholders, livestock are the only ready source of cash to buy farm inputs (seeds, fertilisers, pesticides) and hire farm labour during the planting season. Income from cropping is highly seasonal, almost all of it coming in just a few weeks after harvest. In contrast, livestock, especially small stock with their high rates of reproduction and growth, can provide a regular source of income from sales. So can milk and milk products like butter and cheese. Larger animals such as cattle are a capital reserve, to be used to pay school fees, dowry, hospital bills, funeral ceremonies, or to undertake the holy pilgrimage. Animals are a crucial link in nutrient cycles, and they add value to resources that would otherwise go to waste. Land that cannot, and indeed should not, be ploughed, crop residues and household wastes, all go to feeding livestock in smallholder systems.

Role of the veterinary profession

The role of the veterinary profession in sustainable agricultural and rural development, in food security of animal origin, in health care, and in the provision of raw materials for the industries (eg, hides and skins, various organs as sources of drugs, lanolin from sheep hair) is clearly defined in the veterinary oath taken on admission to the professional register which requires the: "*... veterinary surgeon to use his or her scientific knowledge and skills for the benefit of society through the protection of animal health, the relief of animal suffering, the conservation and production of livestock resources, the promotion of public health and advancement of veterinary knowledge.*"

These roles are scarcely understood or appreciated by the public. The current veterinary surgeons' population in Nigeria is about 3,000 (Onoviran, 1997). Several years ago, a veterinary surgeon was attending to a dog suspected of suffering from hookworm infection. The lady owner was quite astonished to know that her pet dog, like herself, has a temperature, and was further shocked out of her wits to witness the veterinarian take the temperature of the dog with a thermometer through the rectum and not through the oral cavity or the axilla. The lady shouted: "*doctor, but that is the anus*". This anecdote illustrates the level

of awareness among the general populace about the role of the veterinary profession.

Livestock population

Almost two-thirds of domestic animals in the world are found in developing countries (Table 2: FAO, 1987), but developed nations produce about 70% of the world's animal products. Animals kept in developing countries are far less productive than those kept in developed ones (Table 3: Payne and Smith, 1974). For example, in Nigeria, lactation yields of 500-700 kg per cow are accepted as normal, while in developed countries lactation yields are 3,000-3,500 litres.

Table 2: Population of domestic livestock and man in developing and developed countries in 1987 (millions)

	Cattle	Buffalo	Camels	Sheep	Goats	Pigs	Man
Developed	412.4	0.7	0.3	546.9	28.9	347.1	1,226
Developing	865.3	137.7	16.2	610.8	427.9	492.9	3,069
World	1,277.7	138.4	16.5	1,157.7	501.6	839.8	4,997

Source: FAO, 1987.

Table 3: Estimates of productivity of domestic farm animals in developed and developing countries

Productivity indicator	Sheep	Cow/Steer	Pig
No. of offspring/year			
Developed countries	1.5	0.9	18
Developing countries	0.8	0.4	5
Growth rate (gm liveweight/day)			
Developed countries	100	1,000	500
Developing countries	40	500	40
Milk yield (litres/lactation)			
Developed countries	-	3,500	-
Developing countries	-	500	-

Source: Payne and Smith, 1974

In contrast to crop production, animal production in Nigeria has stagnated or even declined in the last decade (Table 4) in spite of the large expanse of land available for raising livestock. There are 98 million hectares of available land in Nigeria; 70 million hectares are arable, but only 31 million hectares are under cultivation.

Nigeria's livestock population is estimated at: 13.9 million cattle, 34.5 million goats, 22 million sheep, 82 million chickens, 32 million other poultry, 3.5 million pigs, 1.7 million domesticated rabbits, 0.94 million donkeys, 0.21 million horses and 22,000 camels (Table 5: RIM, 1992). About 90% of the cattle and 70-80% of the sheep and goats are found in the semi-arid and subhumid savanna zone, where 80% of the suitable grazing lands lie.

Table 4: Animal products supplies in Nigeria: 1984-94
(in thousand metric tonnes)

Year	Beef	Goat meat	Mutton	Poultry
1984	199	177	65	58
1985	212	186	63	62
1986	223	192	68	64
1987	232	206	79	62
1988	260	209	81	60
1989	275	215	85	54
1990	279	179	84	50
1991	280	182	85	57
1992	281	185	86	52
1993	182	78	91	67
1994	183	80	85	61

Sources: Central Bank of Nigeria Annual Reports, 1980-94;
Federal Office of Statistics Bulletin, 1991-94.

This zone embraces the Southern Guinea, Northern Guinea, Sudan and Sahel with a wide range of climatic conditions which militate against improved animal production, such as seasonal water shortage, heat stress and reduced quality and quantity of natural fodder during the hot dry season (de Leeuw, 1977, Igono and Aliu, 1982a). Although, the climatic condition in the humid zone (with an annual rainfall of about 4000mm, compared to 500mm for the savanna zone) favours the availability of herbage and water all the year round, livestock production, particularly cattle, is hampered by the presence of tsetse flies.

Constraints to livestock production in Nigeria

In spite of Nigeria's potentials in human and physical resource endowments, livestock production in the country is characterised by inadequate investment and back-up technology; by high costs of agricultural inputs, low levels of production systems which vary from predominantly nomadic, transhumance pastoralism to sedentary,

agropastoral systems of all types, including intensive, semi-intensive, extensive, stall feeding and night grazing. The indigenous breeds have poor genetic base with poor growth rates: indigenous cattle, for instance, reach maturity in 2-3 years, and slaughter weight at 4 years, compared to the exotic breeds which reach maturity in 1½-2 years, and slaughter weight in 1-2 years under optimum conditions of hygiene, feeding and water supply. Indigenous animals have poor reproductive capacity, characterised by low calving rate of 44-55% (ie, 44-55 calves are reared per 100 breeding cows each year) compared to 90% for developed countries, and their feed conversion efficiency is low. The animals are also beset by diseases and poor nutrition, particularly during the prolonged dry season. There is poor fodder collection, storage and conservation from the lush pasture growth during the rainy season because we lack the technical know-how to produce the baling twine and, therefore, cannot make hay to supplement dry season grazing.

Table 5: Nigerian livestock population estimates

Species	Pastoral	Village	Urban	Totals
Cattle	11,478,145	2,358,078	49,590	13,885,813
Goats	1,142,154	32,287,589	1,023,981	34,453,724
Sheep	2,678,152	18,356,718	1,057,732	22,092,602
Donkeys	6,872	920,828	8,132	936,832
Horses	3,396	194,706	8,110	206,212
Camels	11,050	76,241	548	87,839
Poultry*	-	97,860,320	6,397,640	104,257,960
Pigs	-	3,352,560	53,821	3,406,381
Rabbits	-	1,475,437	241,409	1,719,846

* includes chickens, 82,400,000; pigeons, ducks, guinea fowl and turkey, 21,900,000.
Source: RIM, 1992.

Attempts to Improve livestock productivity

Improvement of livestock productivity to date has relied on imported animals and husbandry techniques. This approach may have some merit, but studies by Igono and Aliu (1982b) have shown that, on the basis of ability to tolerate heat and maintain good levels of weight gain and milk yield, Zebu calves (*Bos indicus*) with half-Friesian (*Bos taurus*) blood are more adapted to the Guinea Savanna than pure Friesian or those with three-quarter-Friesian blood. However, improved livestock productivity in the tropics is more likely if selection of genotypes and husbandry practices are based on the ability of the animal to survive when faced with inadequate water supply, poor food, tropical diseases and their arthropod vectors.

Nigeria has the potential to meet the growing animal protein needs of its human population of about 104 million, but certain action plans need to be implemented in order to bridge the demand-supply gap. For example, there is need to:

- develop ranches in the humid and subhumid zones which have the greatest potential for mixed crop-livestock farming systems;

- develop year-round feeding strategy including improved pasture (in rangelands and grazing reserves), provision of hay, concentrates (cotton seed cake, maize, etc), fodder trees and shrubs to supplement pasture grazed in the dry season;

- develop peri-urban dairy industry on co-operative basis;

- stimulate intensive poultry production through grandparent stock development and ability to provide alternative feeds (eg, soya cake) and micronutrients;

- organise semi-intensive sheep, goat and pig raising systems;

- improve surveillance and control of animal diseases via the use of readily available and affordable drugs, vaccines and pesticide chemicals;

- introduce selection and breeding of animals through biotechnology for high productivity, and tolerance to diseases, insect pests and environmental stresses;

- encourage cooperation between national and international research institutes, and provide basic infrastructures and adequate funding of research programmes: the minimum threshold which must be crossed for research programmes to make economic impact is 1% of the GNP as recommended by the 1980 Lagos Plan of Action for the Economic Development of Africa. The Egyptian-born Nobel laureate in theoretical physics, Prof Abdus Salam, who is also President of the Third World Academy of Sciences has suggested a minimum of 2%; Nigeria currently invests only 0.2% of its GNP on research.

implement measures that ensure the right of ownership to agricultural land, but which carry an obligation to sustain its productivity through a combination of regulatory and incentive policies, etc (Swallow and Bromley, 1995).

Disease constraints to livestock production

A major study was conducted in 1991 by Winrock International Institute for Agricultural Development (Arkansas, USA, 1992), to assess the future of animal production in sub-Saharan Africa. Topping the lists of animal health constraints on livestock productivity are tsetse-transmitted trypanosomiasis, and tick-borne protozoan and rickettsial diseases. My interest in the chemotherapy of these blood parasitic diseases dates back to 1964 when, after higher school certificate in Government College, Keffi, I was deployed to the Provincial Veterinary Clinic in Jos as Livestock Assistant-in-Training. From there I was posted to Maidon Taro, about 16 kilometers from Bukuru, to participate in the clinical evaluation of *pyrithidium* in the curative and prophylactic treatment of trypanosomiasis. The trials in Nigeria resulted in cattle deaths, but not in East Africa, and the drug was never approved for marketing in west Africa. Trypanosomiasis became my final year student research project at Cornell, and treatment of tick-borne diseases my research topic for a PhD of Texas A&M University. I have since continued to investigate

into the control of these debilitating and fatal diseases. The causative organisms are found in blood, causing red and white blood cell destruction, weight loss, and other disorders that may lead to death.

International and national control efforts

Efforts to control trypanosomiasis and tick-borne diseases continue to occupy national and international research centres and institutions around the world; to cost livestock farmers, governments, international organisations and aid agencies large sums of money annually (McMillan and Meltzer, 1996). These efforts are illustrated by the proceedings of the biennial conference of the OAU/International Scientific Council on Trypanosomiasis Research and Control, the 28th Meeting held in October 1997 in South Africa; the FAO Programme Against African Trypanosomiasis; UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases; the extensive research activities of the International Livestock Research Institute [formerly International Laboratory for Research on Animal Diseases (ILRAD, Kenya) and International Livestock Centre for Africa (ILCA, Ethiopia)]; International Centre for Insect Physiology and Ecology (ICIPE, Kenya); International Trypanotolerant Centre (ITC, Banjul, Gambia), the African Trypanotolerant Livestock Network (ATLN, Kenya), etc.

At the national level, Nigeria established the National Veterinary Research Institute (NVRI, Vom) in 1914 to combat the scourge of rinderpest panzootic which occurred in West Africa between 1885-1890 and 1913-1914, and decimated over 90% of the cattle population. The disease is now kept in check through vaccination and adequate surveillance. In 1928, the present National Animal Production Research Institute (NAPRI) was established as *Shika Stock Farm* with the mandate to develop indigenous livestock breeds suitable for meat, milk and egg production, and develop pastures and other fodder plants as animal feed. The West African (now Nigerian) Institute for Trypanosomiasis Research (NITR, Kaduna) was established in 1951 to curb the ravages of animal and human trypanosomiasis and its tsetse vector in the four British West African colonies of Nigeria, Ghana, Sierra Leone and Gambia. Similar organisations were also established by the French as early as 1926 in their

African colonies (Maurice, 1992). Despite concerted global efforts to curb their impact, blood parasites remain the most common cause of death and production losses in livestock, and the areas occupied by their vectors are even expanding, attesting to their adaptability or being on the "*fast track*" in the evolutionary process, staying ahead of man and his massive chemical onslaught.

The trypanosomiasis problem

Geographic distribution

African Trypanosomiasis is a wasting disease known as *sleeping sickness* in people and '*sammore* or *nagana*' in animals. It occurs across more than a third of Africa. The incidence of tsetse flies and trypanosomiasis has been the single most important determinant of the distribution of livestock on the continent (Moloo, 1993). Approximately 30% of Africa's 173 million cattle are at risk of infection (Adeniji, 1993; Hursey and Slingenbergh, 1995; Shaib *et al*, 1997). Almost all animal species, except poultry, are affected. In addition, 36 out of 52 African countries are endemic for sleeping sickness, with 55 million people at risk of contracting the infection (Cattand, 1995).

Aetiology

One hundred years have elapsed since the discovery, in 1894, by Dr David Bruce of the trypanosome (genus *Trypanosoma*), found in blood and other body fluids, as the causative agent of *nagana*, and the tsetse fly (genus *Glossina*) - a fly slightly bigger than the house fly, but with a taste for blood and a vicious bite - as its transmitter. Tsetse flies occur only in Africa between latitudes 15°N and 30°S, rendering approximately 8.7 million square kilometres of humid and subhumid zones of Africa unsuitable for livestock or mixed agriculture (Jabbar, 1994). Tsetse distribution is assisted by the transhumance and migration of traditional cattle herders into tsetse-infested zones in response to seasonal shortages of water and fodder (Aliu, 1975). Dry season transhumance and cattle migrations also damage the environment by opening large tracts of Africa to deforestation.

While indigenous zebu-type cattle (*Bos indicus*) are generally susceptible to infection, the humpless taurine dwarf cattle, notably the long-horn N'Dama (*Bos taurus longifrons*), the short-horn Muturu and Keteku (*Bos taurus brachyceros*) of central and west Africa, and the West African dwarf sheep and goats are tolerant of the infection. In North Africa, Middle East, parts of Asia and Latin America, camels also suffer from trypanosomiasis.

Transmission

The natural transmission cycles of African trypanosomes involve tsetse flies and wild animals, principally ungulates, which form the major reservoir of infection and are usually symptomless carriers (Vickerman, 1997). The trypanosomes become important when domestic mammals and humans are available as alternative hosts for the tsetse. Domestic livestock and certain wild ungulates can also serve as reservoir for transmission to humans. There are 22 known *Glossina* species, which are broadly classified into forest (*fusca*), riverine (*palpalis*), or savanna (*morsitans*) species according to their preferred habitat. All of them are capable of cyclically transmitting trypanosomes.

Clinical findings

The primary clinical signs of trypanosomiasis are intermittent fever, generalised lymphadenopathy, anaemia, weight loss and reproductive disorders (Ogwu and Nuru, 1981; Jeffcoate and Holmes, 1997). The disease in cattle usually has a chronic course with high mortality. *Trypanosoma simiae* is highly pathogenic for pigs, and infection usually proceeds to death rapidly that it cannot be successfully treated. In humans, nervous symptoms (eg, tremors, headache, apathy, convulsion) later predominate and progress to coma and death.

Current control methods

Much effort has been made to control trypanosomiasis in domestic animals and humans via the use of drugs (Aliu 1981; Brun, 1993), reduction in populations of the tsetse flies (Allsopp, 1994), and the rearing of trypanotolerant livestock (ILCA, 1986). To date, each of the three methods, while remaining very useful, has drawbacks, and vaccine

against the disease is still only a research objective (ILRI, 1996), in spite of the development of a method for the *in vitro* culture of a trypanosome species (Hirumi *et al*, 1977).

Chemotherapy of trypanosomiasis

Towards the end of the 19th century, Paul Ehrlich (1854-1915), a German bacteriologist, observed that some vital dyes, like methylene blue, selectively stained and killed certain bacterial cells. He postulated that chemical substances might be produced that could unite with and destroy parasitic agents of disease without injuring the host cells. He reasoned that these compounds could *"strike the parasites with full force in the manner of magic bullets seeking out the enemy"*.

In 1891, Paul Ehrlich demonstrated the efficacy of methylene blue in the treatment of human malaria caused by the haemoprotozoan parasite, of the genus *Plasmodium*. The first real step forward in the search for *magic bullets* was the preparation, in 1900, of arsphenamine, an organic arsenical, by Ehrlich and co-workers: the compound was of value in treating syphilis and trypanosomiasis. Paul Ehrlich, who is regarded as the father of modern antimicrobial chemotherapy, shared the Nobel Prize for medicine and physiology in 1908 with the Russian bacteriologist and physiologist, Élie Metchnikoff.

Drug treatment and resistance

Drug treatment is the most widely used means of controlling trypanosomiasis. Almost all antitrypanosomal treatments in food animals are administered to cattle (Bida and Aliu, 1981). Because of the nomadic husbandry practised by most cattle rearers in Africa, treatment is on herd basis, each animal being treated with a single dose of the trypanocide. While the single dose regime is usually curative, relapses do occur following treatment. Such relapses are generally attributed to innate parasite resistance or reinvasion of the peripheral circulatory system by trypanosome populations sequestered in sites believed to be inaccessible to the drug, such as the central nervous system (Jennings, 1993). Drug resistance is becoming an increasing constraint to the efficacy of the currently available trypanocides (Ross and Sutherland, 1997).

Furthermore, since many of the compounds are chemically closely related, cross-resistance appears to have compounded the problem.

Existing drugs

During the early part of the 20th century, a major effort was made by the pharmaceutical industry to develop new drugs for the treatment of African trypanosomiasis. The industry's interest, however, began to wane in the 1960s because of the limited market, the increasing R&D (research and development) costs of new products, and the independence movements in Africa. Enormous costs, from US$100 million to over US$350 million, are involved in the development of a single successful new drug. Apart from the difficulty of identifying new active compounds (5,000-10,000 compounds are screened for each successful compound), the need to establish human safety from persistent residues in the face of stringent drug screening regulations is the principal cost constraint.

Since isometamidium was introduced in 1961 (Berg *et al*, 1961), the development of new trypanocidal drugs has made little progress. Only in 1985 was melarsomine (Cymelarsan®), a melaminyl thioarsenite, patented and introduced for the treatment of *Trypanosoma evansi* infection in camels (Raynaud *et al*, 1989). The situation for human sleeping sickness is no better: although one new drug, eflornithine (DFMO) has been developed (Bacchi *et al*, 1980), the treatment time is too long (spread over 35 days), and the cost prohibitively high for African situations where the drug is most needed (WHO, 1995).

Currently, drug treatment of animal trypanosomiasis relies on three closely related compounds that have been widely used for more than 40 years: the phenanthridine, *homidium* (Watkins and Woolfe, 1952); the aromatic diamidine, *diminazene* (Jensch, 1955), and the phenanthridine-aromatic amidine, *isometamidium* (Berg *et al*, 1961). Diminazene, apart from its trypanocidal activity, is also highly effective against *Babesia* infections, an added advantage in veterinary usage in Africa.

Table 6 lists the dosage regimen that should be used for each compound, their spectra of activity, the animal species in which the compounds should be used, and the treatment of cases of relapse.

Quinapyramine (Davey 1950), an aminoquinaldine derivative, was widely used in Nigeria between 1951 and 1963 as a therapeutic and prophylactic agent in cattle, camels, horses, pigs and dogs. However, it ceased to be manufactured in 1974 because of problems of toxicity and the ease with which drug resistance and cross-resistance appeared to develop (Whiteside, 1960; Ndoutamia *et al*, 1993). The withdrawal of quinapyramine compromised control of trypanosomiasis in camels. Thus, in 1984, the compound was reintroduced to the market, but only for use in camels and horses (Schillinger and Röttcher, 1986).

Table 6: Use of curative trypanocides

Drug	Aqueous solution	Dose(mg/kg), Route[1]	Animal activity	Trypanosoma	Treatment of relapse
Diminazene aceturate[2]	7% in cold water	3.5 IM or 7.0 IM or	Cattle, sheep goats Cattle, sheep goats, dog	*vivax, congolense brucei, evansi*	Isometamidium
Homidium chloride[3]	2% in cold water	1.0 IM	Cattle, sheep goats, horses	*vivax, congolense,*	Diminazene, Isometamidium
Isometamidium chloride[3,4]	1 or 2% in cold water	0.25-1.0 IM (deep)	Cattle, sheep goats, horses dogs	*congolense, vivax,* less active on *brucei*	Diminazene
Quinapyramine dimethyl sulphate[5]	10% in cold water	5.0 SC	Camels, pigs, equidae, dogs	*vivax, simiae, congolense, brucei, evansi*	Isometamidium Isometamidium
Melarsomine[6]	cold water	0.25 SC or IM	Camels, buffalo	*evansi*	

[1]IM = intramuscular injection; SC = subcutaneous injection.
[2]Berenil®, Ganaseg® - Farbwerke Hoechst Ag, Frankfurt-am-Main, Germany.
[3]Novidium® - May & Baker, Ltd, Dagenham, England.
[4]Samorin® - May & Baker, Ltd, Dagenham, England.
[5]Trypamidium® - Specia, Paris, France.
[6]Antrycide® - Imperial Chemical Industries (Pharmaceutical) Ltd., Wilmslow, England.
[6]Cymelarsan® - Rhone Merieux, France.

Pharmacokinetics of trypanocides

Properly administered, these drugs have effectively controlled the disease, but reports of drug-resistant trypanosomes are increasing in frequency (Mamman *et al*, 1995). In research aimed at maintaining the long-term efficacy of the compounds now in use, we have developed suitably sensitive analytical techniques to determine the pharmacokinetics (ie, precise drug concentrations in body fluids as a function of time) of diminazene and imidocarb in cattle, sheep and goats (Aliu *et al*, 1977, 1984, 1993; Aliu and Ødegaard, 1983, 1985; Mamman *et al*, 1993a, 1996). The pharmacokinetics of isometamidium and homidium have similarly been determined by other scientists (Gilbert and Newton, 1982; Eisler, 1996). Changes in concentrations of drugs in treated animals over time are predicted using pharmacokinetic data and kinetic modelling computer programmes. Such information is important for the establishment of safe and effective dosage regimen, and for estimation of preslaughter withdrawal period (ie, the time interval which must elapse following last dosing of the drug before the animal product is safe for human consumption).

To overcome the problem of drug resistance in trypanosomiasis, we conducted studies in conjunction with scientists at the Norwegian College of Veterinary Medicine, Oslo, at ILRAD (Kenya), and Sokoine University of Agriculture (Tanzania), on the therapeutic efficacy of diminazene in cattle and goats following two doses given 24 and 48 hours apart (Aliu and Ødegaard, 1985; Silayo, *et al*, 1992). Subsequent study by Mamman and others (1993b) demonstrated that early treatment in the course of the disease and maintaining therapeutic blood levels for a longer period may be more efficacious than 2 repeat doses. Such considerations have forced continuing search for alternative methods of delivering the few available trypanocides (Aliu, 1984; Peregrine, 1994).

Alternative trypanocide delivery systems

Utilising colloidal carriers like dextran, polyvinylpyrrolidone and other nanoparticles, various formulations of the currently available trypanocides have been produced in order to enhance their prophylactic activity and reduce their toxicity. It has been demonstrated that drug-loaded particles

in the colloidal size range follow special routes of absorption and distribution, different from those of molecular solutions of drugs. Most drugs are distributed via partitioning and diffusion, but nanoparticles undergo phagocytosis or, more specifically, endocytosis, and stay in the body longer.

Suramin complexes. The favourite anion for forming complexes with various basic drugs has been *suramin*, which also has trypanocidal activity and has been used in *T. evansi* infection in camels and equidae (Desowitz, 1957). Such suramin salts (eg, *homidium suraminate, quinapyramine suraminate*) have not been used routinely because of poor local and systemic tolerance, and the emergence of drug resistant trypanosomes (Stephen, 1958).

Isometamidium-dextran complex. Isometamidium has both curative and prophylactic properties, and is effective on trypanosomes resistant to other trypanocides. However, it has not been widely used because of its narrow margin of safety and severe local reactions at the site of injection. Only a maximum dose of 1 mg/kg body weight may be administered by deep intramuscular injection. The protection conferred by this dose is variable, lasting 2-22 weeks, due possibly to variation in drug susceptibility between different trypanosome populations, or variation in tsetse challenge.

In an attempt to reduce the local and systemic toxicity of isometamidium, and prolong its prophylactic effect, we prepared a complex of isometamidium with dextran sulphate (molecular weight 500,000). A single subcutaneous dose of the complex equivalent to 2 mg of isometamidium/kg body weight was curative in *T.vivax* infection in cattle and did not produce dermonecrotic effect (Aliu and Sannusi, 1979). In rodents, the complex reduced the local and systemic toxicity of isometamidium ten-fold, and extended its prophylactic activity 4- to 8-fold against challenge with *T. congolense* and *T.vivax* (Aliu and Chineme 1980).

Polymer encapsulation. It is also possible to enhance the prophylactic effect of drugs and reduce their toxicity by encapsulating them either in polymers or in artificial phospholipid membranes (liposomes). De Deken *et al* (1989) produced a slow release polymer that contained 25% (w/w) homidium. Subcutaneous implantation of the device into rabbits resulted in significantly higher serum concentration of homidium compared with non-polymerized homidium. The polymer greatly extended the prophylactic activity of homidium against challenge with *T.congolese* and was not associated with side effects. Trials with the polymer have not been carried out in cattle, but if the ratio of animal body weight to the device's surface area were to remain constant, the required size of the polymeric device would be prohibitively large.

Liposomal formulations. Large multi-lamellar liposomes that contained diminazene, homidium and isometamidium have been prepared (Fluck and Hopkins, 1987). While this resulted in a small increase in the prophylactic activity of diminazene and homidium, a similar effect was not apparent with isometamidium, but its local toxicity was reduced. Liposomal formulations have not been standardized and this has hampered their further evaluation.

Carrier erythrocytes. Homidium has been entrapped in resealed bovine red blood cells (DeLoach 1985), containing sufficient drug for a 100 kg animal. Experimental trials in ruminants have not been reported, but the methodology, as described would be impractical for field use in cattle.

Drug combinations

Various trypanocides have also been used either as 'sanative pairs' or in combination. The danger of selecting drug-resistant organisms by administering potent antimicrobial agents alone has led to the accepted practice of using several compounds together in the treatment of bacterial infections. The accepted procedure for the treatment of human tuberculosis has long been to give, for example, isoniazid in conjunction with rifampin, ethambutol or streptomycin. The use of potentiated sulphonamides (eg, sulphadoxine + pyrimethamine as *Fansidar®*; sulphadimethoxine + trimethoprim as *Septrin®*) is effective in the

treatment of certain strains of falciparum malaria and bacterial infections, respectively, while potentiated penicillins (eg, amoxycillin + clavulanic acid as *Augmentin*®) are used in the treatment of infections with beta-lactamase-producing bacteria, especially respiratory infections with *Haemophilus influenzae*. Such combination therapy, with additive or potentiating effects which help circumvent the development of drug resistant trypanosomes has been evaluated (Aliu, 1977). A combination of isometamidium (0.5 mg) and quinapyramine (0.3 mg)/kg body weight increased the sensitivity of a strain of *T.vivax* which was resistant to either drug used alone; the combination also had wider margin of safety.

In many field sites, 'sanative' drug pairs have been used to prevent the development of drug resistance. Whiteside, in 1960, proposed that homidium and diminazene be used as sanative pair: ie, diminazene is used for one half of the year and homidium for the other half. However, such combinations are often not used. Meanwhile, the high cost of developing new antitrypanosomal drugs suggests that, in the immediate future, there will be greater reliance on strategic combinations of existing agents. Wéry (1994) has shown that combinations based on inhibition of decarboxylase enzymes (eg, ornithine decarboxylase) or exposure to oxidative stress appear promising.

Future antitrypanosomal drug development

The dearth of new drugs, chemically unrelated to those now in use, is stimulating continuing search for new anti-trypanosomal drugs based on biochemical differences between mammalian and parasite cells, and on biochemical pathways that are common amongst, but unique to parasites (Kuzoe, 1996). Trypanosomes and other protozoan parasites are unable to synthesize purines *de novo*. Thus, research on purine metabolism as well as on polyamine biosynthesis, glycolytic enzymes localised in the unique parasite glycosome, trypanothione molecule, and membrane transport point to likely targets in the parasite for chemotherapeutic attack.

New antiparasitic compounds may also be identified as a result of serendipity and research on natural products. *Azadirachtin* extracted from

seeds of the neem plant, *Azadirachta indica*, is reported to have a strong repellent effect against the tsetse fly after coating the ears of the host animal. Scientists at ABU and the Swiss Tropical Institute have confirmed that crude extracts of some African plants (eg, *Annona senegalensis, Cassytha filiformis, Entada abssynica, Securinega virosa, Vernonia subuligera* and *Zimenia americana* have antitrypanosomal activity (Nwude and Ibrahim, 1980; Freiburghaus *et al*, 1996). These plants may provide new chemical leads in designing new types of drugs (Aliu, 1996). Thus, the National Institute for Pharmaceutical Research and Development, established in 1987, should take interest in animal drug development if we are to stay one step ahead of drug resistant strains of trypanosomes and other parasites.

Tsetse Control

The distribution of tsetse flies in Africa has remained virtually unchanged despite considerable control efforts over the last 60 years. Any population reductions have been temporary, with either rapid resurgence or reinvasion from surrounding areas (Barrett, 1997). Deforestation and destruction of wildlife have, however, greatly reduced the natural habitats and wildlife hosts of tsetse fly over much of Nigeria (Bourn, 1983). Current tsetse control methods include ground and aerial application of insecticides; use of impregnated traps and targets, and the sterile insect technique.

Chemical control

At present, there are no practical alternatives to the use of insecticides for large-scale tsetse control. Control of tsetse by application of insecticides from the ground and by aircraft has achieved considerable success in Nigeria. In the 1950s, tsetse control workers began to spray residual organochlorine insecticides, dicophane (DDT, 2.5-3.75% w/v) and dieldrin (2-3% w/v), directly on tree trunks and low branches where tsetse are likely to rest during the hottest and brightest hours of the day. Sequential aerial spraying of infested areas with ultra-low-volume endosulphan (25% w/v), also an organochlorine compound, but with low residual effects, has been widely used. Fixed-wing aircraft and helicopters are used, helicopters being more effective for spraying against riverine

species in dense vegetation. Current opinion holds that aerial spraying should be used only to eradicate an isolated tsetse population or to interrupt parasite transmission during a human sleeping sickness epidemic while longer term control measures are implemented.

Application of pesticide chemicals, especially residual organochlorines, over large areas causes environmental pollution, toxic side effects on non-target species, and leaves undesirable chemical residues in edible animal and plant products (FAO/ WHO, 1996). Future chemical control methods will require compounds that are rapidly biodegradable to ensure minimum accumulation in the environment and in animal tissues.

Tsetse traps and screens

Insecticide-impregnated, odour-baited biconical traps and cloth screens, or so-called targets, strategically placed in fly habitats have been used to reduce fly populations to tolerably low levels. The use of traps was revived in the 1970s with the development of cloth traps, and the discovery that particular colours (royal blue, black or those strongly reflective in the ultraviolet light), and host odours (such as acetone in host breath; various phenols found in cow urine, and octenol) attract tsetse flies. The use of such visual and olfactory attractants has considerably improved the efficacy of tsetse trapping by up to 30 times (Green, 1993; Jordan, 1995; Späth, 1995). Targets upon which the flies alight, may also be impregnated with chemosterilant (eg, bisazir), or growth hormone regulators, juvenile hormone analogues (Graf, 1993), or pyrethroid insecticides (deltamethrin, at 0.6% or 150-200 mg/m² of cloth, or α-cypermethrin, at 300-400 mg/m²).

To date, however, trapping has not been widely used in Nigeria, yet it constitutes an appropriate, non-polluting technology which can be carried out by rural communities. To be effective, the method demands regular target maintenance and the active participation of the livestock-keeping community where the traps and screens are deployed.

Biological control

Biological control of tsetse through predators, parasites and pathogens is still a remote possibility (Na'Isa, 1982). However, an endotoxin derived from *Bacillus thurigiensis* has been reported to be toxic to adult tsetse fly. The gene encoding the endotoxin has been cloned and expressed (Omolo *et al*, 1997).

Applied research on the release of sterile males to seek out wild females and thus, limit tsetse reproduction and population is receiving increasing attention. For efficient use of the sterile insect technique (SIT), sterilisation must result in a male with high survival rate, low fertility and maximum competitiveness. In collaboration with the International Atomic Energy Agency Biological Control (BICOT) programme and NITR, we have studied the effect of various gamma radiation doses from cesium-137 on the survival and fertility of *Glossina palpalis palpalis* (Tenabe *et al*, 1986). Tsetse pupariae irradiated at 25 days or older, with 12 krad cesium-137 in air, or 15 krad in nitrogen, showed normal patterns of emergence and survival, but 97-100% of them were sterile. Based on these laboratory findings, we recommended that these doses be used to sterilize male flies for release into the field.

Perhaps, the next major step will be to understand the physiological basis of the establishment of the parasite in the vector and its maturation into the infective mammalian form (Welburn and Maudlin, 1997). Modern genetic techniques (eg, the polymerase chain reaction, or PCR) may then permit the engineering of tsetse which cannot transmit trypanosomes and are therefore reduced to the level of nuisance flies. The PCR technique allows scientists to produce rapidly (amplify) a billion copies of any given stretch of DNA, the genetic blueprint of life, without needing a living cell. These large quantities are then easily analysed (Nantulya, 1991; Murphy, 1995). For example, tuberculosis cultures require 8 weeks to grow; PCR techniques will confirm the presence of the DNA of tuberculosis organisms in just hours.

Trypanotolerant livestock and biodiversity

The rearing of trypanotolerant livestock is an alternative to tsetse or trypanosomiasis control, particularly in humid and forest areas, for which effective and economic tsetse control methods have yet to be devised. The West and Central African humpless, dwarf cattle breeds such as the hamitic long-horn N'Dama (*Bos taurus longifrons*) and the short-horn Muturu and Keteku (*Bos taurus brachyceros*), as well as the West African dwarf sheep and goats are well adapted to the tropical environment (Rege *et al*, 1994; Baker, 1995). They are able to survive and produce in tsetse-infested areas without trypanocidal drugs due to their long exposure to trypanosomes. They also possess a degree of resistance to ticks and tick-borne diseases, except East Coast Fever, a disease to which they have not been exposed in their natural habitat (Dolan, 1993; ITC,1996). The taurine dwarf cattle breeds were probably introduced to the continent as long as 7,000 years ago (Meghen *et al*, 1994). The larger size and more widespread humped Zebu cattle (*Bos indicus*), which are susceptible to trypanosomiasis, appeared in Africa only about 1,400 years ago. The high producing, genetically improved European cattle breeds (*Bos taurus*), introduced this century, are extremely susceptible to trypanosomiasis, other haemoparasitic and skin diseases. This genetic diversity in animals, which also occurs in crops, is the basis on which future agriculture will be built.

Animal breeding biotechnologies

While the use of trypanotolerant animals can be effective, it is a lengthy process with certain other drawbacks. These animals are typically small in size, and less productive, especially milk production, and not ideal for draught work. Second, they number only 9.8 million, accounting for only 5.7% of the total cattle population in Africa; the dwarf goats and sheep constitute 8% and 9% of the African goat and sheep population of 158 million and 191 million, respectively. However, the advent of genetic markers (which are points of the DNA that can be easily identified), and genome mapping (eg, to locate the specific genes responsible for traits of economic importance), coupled with ability to produce transgenic or cloned animals may accelerate selection and breeding of larger and more productive trypanotolerant cattle (Soller, 1994). The US Congress has

budgeted $3 billion, over a period of 15 years, to a human genome project expected to be completed by the year 2005. The project, described as "*owner's manual*" for the humankind, is to identify all the genetic material in the human species, and will greatly assist a similar global bovine genome project.

Artificial insemination. The application of biotechnologies in animal production will undoubtedly have an effect on food security, and it is in the fields of animal breeding and genetic improvement that the effects are most apparent. Artificial insemination (AI) in livestock, particularly cattle, is one of the most widely utilized biotechnologies in the African agricultural systems. Animal breeding through AI has increased the pace of the genetic gain in livestock. This technology, which has been available for several decades, provides for widespread dissemination of the semen (genes) of small numbers of selected male animals capable of transmitting high productivity and disease resistance to their offspring. In several countries in east and southern Africa, mobile inseminators make their rounds daily and provide AI to cows at insemination points. In Nigeria, AI is limited to crossbreeding at NAPRI and in a few selected farms and not available countrywide.

Multiple ovulation and embryo transfer. Practical technics for multiple ovulation and embryo transfer (MOET) in farm animals were developed about 28 years ago. The technology has now made it possible for animal breeders to increase dissemination of genes of selected females as well as males. In cattle, a selected cow, for example, after gonadotrophic hormone treatment (PMSG and FSH), gonadotropin releasing hormone (GnRH) that results in the recruitment and maturation of numerous oocytes in the ovary, the cow is inseminated with semen from an elite bull. Between 28 and 33 (or 40 and 46) hours following GnRH injection, the resulting fertilized ova (embryos) are harvested from the donor cow and either cryopreserved (freezing and storage in liquid nitrogen) or transferred to surrogate mothers at an appropriate (dioestrus) stage of the reproductive cycle (Jordt *et al*, 1986; Jordt and Lorenzi, 1988). The process can be repeated periodically with the original mating pair, leading to the accumulation of a large number of full-sibling offspring of the

most desirable parents in a relatively short period of time. Embryo transfer technology is not yet in practice within Africa's national agricultural research systems because they are unable to create the basic infrastructural facilities (Chigaru *et al*, 1991).

Transgenic animals

The low productivity and reproductive performance of African livestock provides opportunity for improvement through gene manipulation. Genes are segments of DNA (the hereditary molecule within the cell nuclei) which are subject to crossing over, random segregation and recombination in the production of every mammalian sperm and oocyte. Animal breeders, hitherto, have found it very difficult to predict the outcome of any individual mating. The ability to '*cut and join*' appropriate segments of DNA (*recombinant gene technology*) has opened up the possibility of creating animals which are pure bred for desired traits, including introgression of trypanotolerance from N'Dama to other cattle breeds (Wilmut and Jere, 1991).

Microinjection of engineered DNA into the nuclei of fertilised animal eggs can produce efficient transformation (chromosomal integration). When the injected eggs are introduced into a female and allowed to develop, the new gene is often expressed in some of the newborn animals. By careful breeding, an animal line can be established in which all the animals are homozygous for the new gene (or desired traits). Animals permanently altered in this way are referred to as *transgenic*.

The technology was used to introduce into mice genome the human growth hormone gene under the control of an inducible promoter. When fed a diet including the inducer, some of the mice that developed from injected embryos grew to an unusually large size (Lehninger *et al*, 1993). Introduction of DNA into human and animal cells offers the potential for treating and even curing genetic diseases that have been refractory to traditional therapies. The first commercial product of recombinant DNA technology was human insulin manufactured by Eli Lily and Company by implanting an artificial human insulin gene into *Escherichia coli* cells.

Similarly, human haemoglobin for transfusion is being produced commercially by transgenic pigs, eliminating the need for blood typing.

Animal cloning. The transformation (or chromosomal integration) of animal cells with foreign genetic material offers an important mechanism for advancing knowledge about the structure and function of animal genome, as well as for the generation of animals with desired traits. A clone is a colony of genetically identical molecules of hereditary material, whole cells or organisms. In a broader context, any individual that is the exact genetic copy of another is called a '*clone*'. To make a copy of an organism by non-sexual means is thus referred to as '*cloning*'. Cloning, ie, the creation of a host of individuals with identical genetic make-up, can be achieved through at least 4 different procedures: the most recent involves the implantation of a somatic cell nucleus into an egg cell whose own nucleus has previously been removed. The result is an individual with identical genes, a '*younger identical twin*', so to speak. This process has been carried out successful in clawed frogs, *Xenopus* (Ewe, 1987), and now in mammals - sheep (Campbell *et al*, 1996) and monkeys.

Towards development of antitrypanosomal vaccine

The most cost-effective way of controlling infectious diseases is through immunization. Since the vaccination trials against small pox by the English Physician, Edward Jenner (1749-1823) in 1798, vaccines have been developed for many human and animal diseases, including measles, polio, rabies, rinderpest, anthrax, etc. For smallpox in humans, and rinderpest in cattle, vaccination is the major factor responsible for disease eradication. But scientific obstacles have confounded attempts to develop vaccines against other major afflictions of man and animals such as malaria, trypanosomiasis, tick-borne protozoan and rickettsial diseases. These are relatively complex organisms that have adopted different strategies for evading mammalian host immune responses.

Vaccines exploit the ability of animals to control disease-causing organisms by mounting an immune response to molecules (*antigens* or *antibody generators*) of the parasite. Most vaccines contain one or more

of these accessible molecules purified from the parasite. But the trypanosomes continually change the antigenic nature of their surface molecules, ie, variable antigenic types emerge during an infection to confound and evade the host immune system (Borst *et al*, 1996).

Most animal hosts make immune responses to the first wave of invading trypanosomes, by producing antibodies against antigenic molecules (glycoproteins) exposed on the surface of the parasite. However, before all the parasites can be eliminated, trypanosomes bearing a new surface molecule of the *variable surface glycoproteins* (or VSGs) appear. In susceptible animals, a single trypanosome population is capable of changing its antigenic coat every few days until the host succumbs. It therefore appears unlikely that a conventional vaccine, which primes an animal's immune system against only one or a few antigens, will be broadly effective if based on the trypanosome's variant surface proteins.

Two approaches are currently being pursued to vaccinate animals against trypanosomiasis (Teale, 1993). The first approach focuses on trypanosome components or secreted molecules (eg, proteolytic enzymes, sialidases) that degrade host molecules. It may be possible to use such parasite products as components of vaccines, and thus, prevent the disease process rather than the infection (Esievo, 1983). The second is the study of genetic control of cell division in trypanosomes. This approach complements research on host molecular genetics because it may lead to the identification of host genes whose products can limit parasite division.

Tick-borne diseases of animals

Economic impact

Ticks and tick-borne diseases have long been incriminated as major obstacles to efficient livestock production throughout the tropical regions of the world (Purnell, 1981; Aliu, 1983). In 1990, it was estimated that ticks caused global animal production losses amounting to US$8 billion/annum (Cobbon and Willadsen, 1990). Throughout the tropics, an estimated 600 million cattle are exposed to anaplasmosis and babesiosis, and 200 million to theileriosis. In 1989, 1.1 million head of cattle in

eleven countries of eastern, central and southern Africa died of East Coast Fever (ILRAD, 1991).

Aetiologic agents

In this university, scientists at the Department of Veterinary Parasitology and Entomology have studied the prevalence and importance of tick-borne diseases of domestic animals in northern Nigeria (Leeflang 1977; Leeflang and Ilemobade 1977). They provided historical and research accounts of 26 different tick-borne parasites which occur in livestock and domestic fowl in Nigeria. These pathogens may be classified into three main groups:

- Protozoa (or piroplasms), including *Babesia* which divide in red cells; *Theileria* and *Hepatozoon*, that multiply primarily in white blood cells;

- Rickettsia, including *Anaplasma*, which inhabit red blood cells; *Ehrlichia*, found within phagosomes, and *Cowdria*, that multiply in vascular endothelium, where it causes severe degenerative lesions;

- Bacteria and viruses found in, or associated with, a variety of organs, eg, *Borrelia anserina*, a spirochaete found in plasma and other body fluids.

Clinical infection

Most of these organisms occur as dormant inapparent infections. Only a few occur in uncomplicated apparent infections, such as *Anaplasma marginale* and *Babesia bigemina* in cattle; *Cowdria ruminantium* in cattle, sheep and goats; *Borrelia anserina* in poultry; *Babesia equi* and, to a lesser extent, *Babesia caballi* in horses and donkeys, both often occurring as mixed infections. High parasitaemias of *Theileria mutans* are often found in cattle in Nigeria, but mortality has not been ascribed to the infection. *Theileria parva*, the causative organism of East Coast Fever, causes high mortality in cattle in eastern, central and southern Africa, and *Theileria annulata*, the cause of tropical theileriosis in the Mediterranean littoral, the Middle East and South-East Asia.

Those tick-borne diseases accounting for most of the clinical cases that require treatment in Nigeria include: bovine anaplasmosis (*gall sickness*), babesiosis (*red water or tick fever*) and cowdriosis (*heartwater*) in ruminants; canine babesiosis, ehrlichiosis and hepatozoonosis; babesiosis of horses and donkeys, and avian spirochaetosis. Diseases caused by *Ehrlichia* and *Babesia* species are emerging in different parts of the world as human health problems (Walker and Dumler, 1996; Telford *et al*, 1997).

Indigenous breeds of cattle possess some natural resistance to tick-borne diseases due to their long association with the parasites, creating a state of enzootic stability. The ravages of tick-borne diseases are seen dramatically when exotic *Bos taurus* breeds are involved. In an attempt to improve the livestock industry, developing countries including Nigeria, each year introduce some 70,000 high-quality breeding taurine stock to areas where tick-borne diseases are endemic, and each year more than 50% of these animals die from one or more of these diseases (McCosker, 1981).

Tick control strategies and problems

Piroplasms and rickettsiae are transmitted by hard ticks of the order *Ixodidae*, which occur abundantly in the vegetation and feed on both wild and domestic animals (Mohammed and Aliu, 1973; Mohammed, 1974). The major hard tick genera found in Nigeria are *Boophilus, Hyalomma* and *Rhipicephalus*. A few members of the soft ticks (family *Argasidae*), are serious parasites of livestock and the domestic fowl. *Argas persicus* transmits *Borrelia anserina*, the causative agent of avian spirochaetosis, a very common acute or chronic bacterial disease of free-range and backyard chickens, and Muscovy ducks in Nigeria.

Strategies used to control ticks include spraying or dipping cattle regularly with acaricides (eg, organochlorines, organophosphates, organocarbamates, aromatic diamidines and synthetic pyrethroids); pasture spelling (or rotational grazing); clearing and burning of the vegetation; selection of tick-resistant cattle, and vaccination with crude tick antigens (extracts of tick brain, juvenile and moulting hormones, hormone

antagonists, and pheromone analogues). The Fulani herdsmen also maintain a meticulous hand de-ticking routine, but this has no effect on disease transmission as only engorged ticks are seen and picked.

Reliance on tick control is becoming increasingly difficult in Nigeria and other developing countries for several reasons, among them the high cost of acaricides, growing tick resistance to widely used acaricides, poor management and even absence of cattle dips and spray races (Mitchell, 1996).

Tick vaccine

A subunit vaccine (Tickguard®, Hoechst) against the one-host cattle tick, *Boophilus microplus*, has recently been commercialised in Australia (Tellam *et al*, 1997). Research has shown that crude tick antigens can be divided into unconcealed antigens (to which cattle are normally exposed during tick infestation) and concealed antigens (those to which cattle are not normally exposed during tick infestation) (Willadsen *et al*, 1993). Unconcealed antigens include antigens from the cuticle, salivary glands or salivary gland secretions. Concealed antigens that have been used to date have been proteins located on the gut epithelium of the tick. These proteins have been purified, and their genes used to produce recombinant antigens. The antigens can reduce *B. microplus* feeding success on cattle by 90% (Young, 1991). But considerable time may elapse before a vaccine specific for multihost ticks, as exist in Nigeria, is available.

Control of tick-borne diseases

The clinically important tick-borne diseases of domestic animals differ widely in their characteristics, relative pathogenicities and response to drugs. The carrier state in recovered animals is associated with a well marked co-infectious immunity (or premunition) which plays an important role in their response to therapy. Also, the large *Babesia* species (eg, *B. bigemina, B. caballi, B. canis*) are more responsive to therapy than the small species (eg, *B. bovis, B. equi, B. gibsoni*).

Three major approaches have been used to combat tick-borne diseases: the use of live vaccines coupled with strategic, rather than intensive, tick

control, and the administration of chemotherapeutic drugs. In a 15-month field study on zebu cattle, Sannusi and Aliu (1986) showed that cattle protected by integrated tick and haemoparasite control had superior weight gains than the protective effect of tick control alone and yet, a more superior weight gain with no disease control measures.

Chemotherapy of tick-borne diseases

Until the early 1980s, chemotherapeutic control of tick-borne haemoparasites depended on two groups of drugs: tetracyclines (*oxytetracycline, chlortetracycline* and *rolitetracycline*), and the aromatic diamidines (*diminazene* and *imidocarb*). In 1981, three new compounds were introduced for theileriosis treatment: the hydroxynaphthoquinones (*parvaquone* and *buparvaquone*), and the quinazolinone (*halofuginone*). These drugs are effective, provided they are administered early in the course of the infection before the onset of severe anaemia or nervous system disorders (Aliu, 1983). One drug, imidocarb, holds great promise for the treatment, chemoprophylaxis and chemo-immunization of anaplasmosis, babesiosis, ehrlichiosis and hepatozoonosis (Aliu *et al*, 1976; 1977; Adeyanju and Aliu, 1977). There is also indication that ticks infected with *B. bigemina* lose their infection if fed on imidocarb-treated cattle (Kuttler *et al*, 1975).

The compounds that are currently available for chemotherapy and prophylaxis of tick-borne diseases are summarised in Table 7 (Aliu, 1997), including their spectrum of activity and recommended dose regimen.

Table 7: Chemotherapy of tick-borne diseases

Drug	Activity in field	Animal	Dose/Rout[a] mg/kg	No. of doses	Interval[b]	Use[c]
Oxytetracycline (short-acting)	Anaplasmosis	Cattle	10.0 im	3	24 h	T
	Anaplasmosis	Cattle	11.0 im/v	10-14	24 h	S
	Cowdriosis	Ruminants	5.0 im	2	24 h	T/Cl
	Ehrlichiosis	Dogs	60.0 po	14	24 h	T
			6.5 po	in diet	24 h	P
	Spirochaetosis	Avian	2.0 im	1	-	T
	Theileriosis	Cattle	15.0 im	5	24 h	T
Oxytetracycline[d] (long-acting)	Anaplasmosis	Cattle	20.0 im	1	-	T
	Anaplasmosis	Cattle	20.0 im	2	7 d	S
	Cowdriosis	Ruminants	20.0 im	2	7 d	P
	Theileriosis	Cattle	20.0 im	1	-	T/Cl
Doxycycline implant[e]	Cowdriosis	Ruminants	5-18 sc	1	-	Cl
Diminazene aceturate[f]	Babesiosis	Cattle	3-5 im	1	-	T
		Cattle	1.5 im	1	-	Cl
		Dogs	3-5 im/sc	1	-	T
		Equidae	5-12 im	2	24 h	T
Imidocarb dipropionate[g]	Anaplasmosis	Cattle	3.5 im/sc	2	10-14 d	T
			3.0 im	1	9 d pi	Cl
			4.0 im/sc	2	24 h	S
	Babesiosis	Cattle	1-2 im/sc	1	-	T
			3.0 im/sc	1	9 d pi	Cl
	B. caballi	Dogs	5.0 im/sc	1-2	24 h	T
	B. equi	Equidae	2.0 im	2	-	T
		Donkeys	5.0 im	2	9 d pi	T
		Horses	5.0 im	4	24 h	T
	Ehrlichiosis	Dogs	5-7 im/sc	2	24 h	T
	Hepatozoonosis	Dogs	5.0 im/sc	1	48 h	T
					72 h	T
Parvaquone[i]	Theileriosis	Cattle	10.0 im	2	14 d	T
	T. annulata	Cattle	20.0 im	1		T
Buparvaquone[j]	Theileriosis	Cattle	2.5 im	2	48 h	T
halofuginone[k] lactate[l]	Theileriosis	Cattle	1.2-2 po	2	48-72 h	T
					48 h	T

[a] im = intramuscular; sc = subcutaneous; po = per os; h = hour; d= day; pi = post-inoculation.
[b] T = therapeutic; P = prophylactic; S = sterilization; Cl = chemo-immunization.

Chemo-immunization

On recovery from a primary infection with any of the economically important tick-borne parasites, cattle become immune to homologous challenge. Hence, a vaccination technique has been developed which

involves infecting cattle with controlled amounts of live blood stage parasites and then mitigating the clinical responses (characterized by fever, anaemia, parasitemia and complement-fixing antibody reactions) by chemotherapy. Imidocarb is administered in the case of *Anaplasma marginale* and *Babesia spp*, and oxytetracycline, in the case of *Theileria spp.* and *Cowdria ruminantium*, on the day of stabilate inoculation or as soon as vaccination reactions are observed (Aliu, 1980). This infection-and-treatment method (or *chemo-immunization*) is particularly suitable for introduction of susceptible cattle into enzootic areas alongside adequate tick control programmes.

Towards improved vaccines against tick-borne diseases

The established vaccines against tick-borne protozoan and rickettsial diseases are generally live attenuated vaccines, with concomitant problems of strain instability; possible contamination with other live pathogens; sensitization against blood groups and risk of reactions; poor shelf-life and, therefore, need for cold chain to maintain viability in storage and distribution.

Current vaccines

A strain of *Anaplasma centrale*, a normally non-virulent species, is widely used as a vaccine (Anaplaz®) against the pathogenic species, *Anaplasma marginale*. Strains of *Babesia bigemina* and *Babesia bovis* that have been attenuated (to reduce their virulence) are used as vaccines in Australia and are being exported from there to South-East Asia, Latin America and Africa.

In South Africa, blood infected with *Cowdria ruminantium* is administered to cattle under the cover of tetracycline treatment. A more reliable method described by scientists in ABU (Ilemobade and Blotkamp, 1978) consists of subcutaneous injection of brain (cerebral cortex) homogenate made from infected goats showing a temperature rise of over 40.5°C, or at the terminal phase of heartwater reactions, characterised by opisthotonos and convulsive seizures. Scientists at the Veterinary Research Institute in South Africa have further improved on this ABU

method by developing an endothelial cell culture vaccine for cowdriosis (Bezuidenhout and Brett, 1992).

Future vaccines

Current research around the world on the development of safe, effective, non-living vaccines for tick-borne diseases is directed towards identifying and characterizing molecules of the parasites that will induce protective immune responses in animals.

Proteins located on the cell surface of *Anaplasma marginale* have been found to induce a predominantly antibody-based immunity in cattle (McGuire *et al*, 1991). Scientists at Washington State University and the University of Florida (USA) are exploring the use of combination of these proteins as a vaccine against anaplasmosis. The Washington team has also identified polypeptide complexes located on the surface of the merozoite forms of *Babesia bigemina* that significantly reduce the numbers of parasites in the blood (parasitaemia), although the animals remain susceptible to the anaemia and fever that characterize babesiosis.

Protective recombinant proteins of *Babesia bovis* have been produced in Australia (Gale *et al*, 1991). This followed earlier experiments with crude parasite lysates which were found to confer some protection against the disease in cattle. The Australians are now experimenting with a combination of three recombinant proteins for use in vaccine. Procedures for making vaccines for hepatitis B and influenza, using recombinant DNA, are already in use for nearly 10 years.

Scientists at ILRI, Kenya, have isolated and characterized two major surface proteins of the sporozoite stage of *Theileria parva*, the 67 kilodalton protein (p67) and the polymorphic immunodominant molecule (PIM), that are promising candidates for the development of subunit vaccines against East Coast Fever (ILRI, 1995, 1996). The p67 antigen provides partial protection in cattle against homologous and heterologous challenge. The recombinant PIM antigen provokes a strong antibody response in infected cattle. ILRI scientists are also exploring vaccine delivery systems (Young and Koech, 1994). They have produced recombinant *Salmonella* bacteria and vaccinia viruses that produce p67

antigen and cytokines (chemicals that modulate immune responses). Inoculating cattle with a strain of vaccinia virus that produces both p67 and cytokine, or with the recombinant *Salmonella* resulted in dramatically enhanced antibody responses. To avoid releasing genetically altered organisms, ILRI scientists have made a recombinant capripox virus that incorporates the p67 gene which may work as a dual vaccine against both Lumpy Skin Disease and East Coast Fever. The capripox virus is routinely used to vaccinate cattle against Lumpy Skin Disease.

The protozoan parasites that cause malaria - species of *Plasmodium*, behave in their mammalian host in a similar way as *Theileria parva* causes diseases by damaging white blood cells; *P. falciparum* damages red blood cells. Scientists working on malaria and East Cost Fever are using similar approaches in their search for parasite antigens that will protect people and their domestic livestock against these debilitating and fatal diseases (Hoffman, 1996).

Novel engineered vaccines and antibody therapies hold great promise in our efforts to curb existing and emerging disease threats (Casadevall, 1996). These new vaccines, known as *recombinant DNA vaccines*, are based on subunits of pathogens or introduction of plasmid-DNA (a bacteriophage which can be multiplied inside bacterial host cells) carrying a protein-coding gene that transfects cells *in vivo*, and expresses an antigen causing an immune response. The practical handling of genes - from their isolation and cloning, to their synthesis in gene machines and '*trimming*' for specific purposes, and beyond, to their implantation and mobilisation in host cells - has become an established part of today's scientific and industrial knowledge.

Various animal models of DNA vaccines have been reported (Whalen, 1996), but most of the pathogens studied have been viruses. Since the genes transferred by the plasmid require host cellular machinery to be expressed, DNA-based immunization most resembles a virus infection. However, genes from other organisms (eg, *Leishmania, Mycobacterium, Mycoplasma* and *Schistosoma*) have been used. The types of polypeptide expressed are often the envelope proteins of viruses. It is, however, not

obvious what aspects of a protein produce an effective immune response by this unusual method of antigen delivery. Availability of complete gene sequences (or gene map) for major surface proteins offers several possibilities for construction and testing of recombinant and synthetic vaccines and antibody-based therapies against any existing or emerging pathogens.

DNA vaccines have distinct advantages: they can be manufactured far more easily and cheaply than conventional vaccines. Currently R&D costs for a single vaccine can range from US$50 million to US$200 million. DNA vaccines are also purer and more specific, and cause fewer undesirable side effects, without the risk of acquiring other diseases from blood products. DNA is very stable and resists temperature extremes; consequently, DNA vaccines do not require cold chain to maintain viability.

Concluding remarks - an outlook or futurity

There is no end for a good idea, but I should conclude this Inaugural Lecture by taking a glimpse at future challenges. Scientists knew that atoms could be split. They also knew that such splitting released a great deal of energy. However, until man learned to harness this power, he could not use it for war or peaceful purposes. After 103 years of extensive and costly research, control of haemoparasites and their vectors remains elusive. Animal health care and productivity remain low in Nigeria and much of Africa, due partly to worsening economic situation with loss of regular surveillance and control of animal diseases, and partly to inability to harness developments in science and technology (Nwokolo, 1988) for enhanced livestock production.

Continuing rapid advances in molecular biology and genetic engineering are offering new bio-medical tools for alternative methods of trapping tsetse and vaccinating against ticks; for breeding high-producing, disease-resistant livestock through AI, MOET, transgenesis and cloning; for diagnosing animal diseases using monoclonal antibodies and recombinant DNA; for producing new-generation broad spectrum drugs and rapidly biodegradable chemical pesticides, and even subunit vaccines encoded in

genes that could control most economically important animal parasites. Little, however, can be expected from imported technology (ie, borrowed skills and resources) in the absence of a capability (or a pool of creative and skilled people, and basic infrastructures) to modify and improve it for domestic application (Aliu and Mohammed, 1990; Anya, 1991). As we approach the next millennium, science and technology will be major instruments in the distribution of the wealth of nations as other major factors, such as land, labour, and capital (UNU, 1989).

We must, therefore, seek to improve the effectiveness and sustainability of existing parasite control methods through adaptive research and strict control of veterinary drugs to prevent the spread of resistant strains of parasites (Mohammed *et al*, 1980; Uilenberg, 1996; Barrett, 1997). With regard to availability and control of veterinary drugs, a *Veterinary Medicines Directorate*, similar to the *Narcotics and Controlled Substances Directorate* under the National Agency For Food and Drug Administration and Control (NAFDAC, established by Decree 15 of 1993), should be created to regulate veterinary drugs standards with focus on efficacy, quality, safety and proper usage (Aliu, 1995; Sykes, 1997).

Sustainable rural development requires that tick-borne diseases and trypanosomiasis control campaigns be linked to sustainable land use programmes (Glover and Aitchison, 1967; McKelvey, 1973; Otsyina *et al*, 1996). This in turn requires considerable resources, which the governments of Nigeria have been committing through major agricultural projects: the River Basin Development Authorities; National Agricultural Land Development Authority; World Bank/PTF-assisted National Agricultural Research Project; Fadama Project; Grazing reserves; State Agricultural Development Projects (ADPs); various short-term food supply programmes, such as OFN (Operation Feed the Nation), NAFPP (National Accelerated Food Production Programme), DFRRI (Directorate of Food, Roads and Rural Infrastructure), PTF (Petroleum [Special] Trust Fund) Food Supply Programme, etc. In the same vein, Livestock Development Projects (LDPs) should be established in each State as an integral part of land use development programmes to encourage mixed agriculture and enhance livestock extension service to smallholders (Salmon and Barret, 1994). Livestock Investigation and Breeding Centres

(LIBCs), previously established in different ecological zones, should be rehabilitated with the adoption of the 'open nucleus breeding system' (ONBS), using the sibling test instead of the daughter test, and combined with artificial insemination, multiple ovulation and embryo transfer technologies.

Recognising the importance of biodiversity and indigenous basic research for livestock development, new Livestock Research Institutes or Centres should be established in appropriate ecological zones based on livestock species (poultry, wildlife, swine, and small ruminants) which predominate in the environment and are innately resistant to disease. This is to strengthen the NAPRI Research Stations and complement the International Livestock Research Institute (ILRI, Nairobi) Station in Nigeria. The value of biodiversity and use of natural resources in sustainable development was brought to the attention of the world during the Earth Summit in Brazil in 1992. The Summit resulted in the establishment of the Convention on Biological Diversity, which came into force on 29 December 1994. Nigeria must be part of this global effort to conserve and use biodiversity to feed its rapidly growing human population which is expected to double by the year 2025. Animal products (meat and milk) are vital dietary components, and children who do not get enough meat and milk in their diets may end up physically and mentally compromised. Data from the 1990 National Demographic and Household Survey by the Federal Office of Statistics indicate a serious problem of malnutrition in Nigeria, as 43% of children under five years have stunted growth; 36% are underweight, and 9% are wasted (FOS, 1991).

Nigeria and Nigerian scientists have a lot to contribute towards solving critical research problems in food security, in improved animal health care based on *'magic bullets'*, subunit prophylactic vaccination, and introduction of new genetic variation into indigenous breeds to improve their productivity and disease resistance. To facilitate adoption and widespread application of biotechnology in animal health care and production, Nigerian scientists, in collaboration with International Agricultural Research Centres, must create public awareness of the

importance of biotechnology, and keep government and policy makers well-informed of those technologies that facilitate rapid genetic gains and improve disease control, but which are low in cost and improve economic returns to livestock farmers (Aliu, 1988). Although advances in developed countries can greatly assist this process, they are only feasible if provided in an appropriate form and when comprehensively supported with basic infrastructures.

Presently, Nigerian scientists work under tremendous difficulties in trying to study and solve problems. When General Muhammadu Buhari became Head of State in 1983, he was asked in 1984 about his political programme, and when he would hand over to civilians. He said he did not have time to talk about that; that his first core mission was to rid the country of official corruption and instill discipline. After that he could repair the economy and the politics. Nigerian scientists may not have enough time for research (or to search for '*magic bullets*') if they must grow their own food to supplement their poor salary and severely reduced purchasing power, spend long hours on domestic chores, searching for water and fuel, and awaiting the tantalising electric power supply.

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