THE ROLE OF BRUCELLOSIS AS A CAUSE OF HUMAN ILLNESS IN THE PASTORAL NAROK DISTRICT, KENYA

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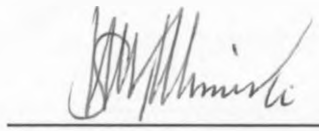
DECLARATION

This report is my original work and has not been presented for a degree in any other university



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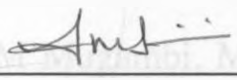

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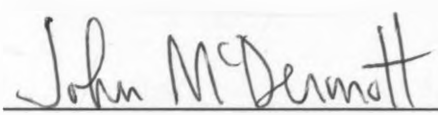

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To my late father M'Mugambi, Mama Regina and uncle Obadiah

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ABSTRACT

Brucellosis is a common disease among pastoralists, who live in close association with their animals. A retrospective study of medical records was undertaken to investigate the extent of brucellosis in causing ill-health among the pastoralists of Narok District in Kenya. Morbidity data for the past seven years (1986-92) covering over 1 million cases and detailed case records involving 2077 patients over the past two years (1991-92), from reporting and testing health units in the district were evaluated. Two main objectives were investigated; first, morbidity data was used to describe the occurrence, seasonal pattern and age distribution of human brucellosis and other diseases presenting with "flu-like" symptoms in Narok and second, to use data from detailed case records to investigate associations between diagnosis of brucellosis and malaria and potential clinical predictors. All brucellosis diagnosis was based on a positive Rose-Bengal (RB) test but most malaria diagnosis was based on clinical findings only.

Diseases with flu-like symptoms constituted the majority (52%) of reported cases. Of these, malaria was the most commonly diagnosed (79%). Brucellosis accounted for 0.8%, pyrexia of unknown origin (PUO) 2.4% and rheumatism 7.1%. However, only a small fraction (4/60) of clinics diagnosed any brucellosis cases. If only clinics regularly testing for brucellosis (Rose-Bengal test) were considered, the proportional morbidity of brucellosis among the cases with flu-like symptoms increased to 13.7%, while malaria, rheumatism and PUO accounted for 69.3%, 16.1% and 1% respectively. In my opinion, the higher proportional morbidity of brucellosis in testing dispensaries is a better estimate. Although testing dispensaries might be considered as

"referral" centres, each time a new dispensary begins testing for brucellosis a large number of "new" cases are uncovered without decreasing cases at dispensaries already testing for brucellosis. Considering all attendances reported at the four testing dispensaries, brucellosis accounted for 5.5% of all illnesses, rheumatism 6.4%, PUO 0.4% and malaria 27.7%, against 0.4%, 3.7%, 1.3% and 41.1% considering all health facilities in Narok District. It appears that brucellosis is grossly under-reported in the district due to lack of testing (diagnosis) by most health facilities.

Brucellosis and malaria were responsible for 21.2% and 55% of patients with flu-like symptoms in the detailed study of records. For brucellosis, clinical diagnosis was not relied on but was always supported by laboratory tests. In fact, patients visiting health facilities with flu-like symptoms in Narok were invariably considered to have malaria on the initial visit. Brucellosis was only suspected after malaria therapy failed. This diagnostic pattern created the impression that brucellosis was mainly associated with a long duration of illness; however, in logistic regression models of clinical signs among patients tested for brucellosis, patients positive to the RB test had shorter duration of illness than negative patients ($p = 0.003$). Statistically, in patients tested for brucellosis, a positive RB test was significantly associated with joint pain ($OR = 4.3$; $p = 0.009$), headache ($OR = 19.8$; $p = 0.004$), duration class ($p = 0.003$), and interactions between joint pain-headache ($OR = 0.05$; $p = 0.004$) and lameness-headache ($OR = 8.38$; $p = 0.074$). The stepwise logistic regression model with these clinical signs correctly predicted the RB test result 62.3% of the time with a sensitivity (Se) of 66.6% and specificity (Sp) of 52.2% if a 0.290 cutpoint was used.

Malaria was more common, easier to diagnose clinically and affected younger people than brucellosis. For patients subjected to blood smear examination,

identification of malarial parasites was statistically associated with age class ($p = 0.041$), headache (OR = 2.2; $p = 0.070$), joint pain (OR = 7.7; $p < 0.0001$) and interactions between emesis and pale mucous membranes (OR = 12.0; $p = 0.058$), pale mucous membranes and headache (OR = 0.02; $p = 0.002$) and headache and joint pain (OR = 0.315; $p = 0.018$). The stepwise logistic regression model correctly predicted the blood smear test result 67.2% of the time with a Se of 62.1% and Sp of 77.4% if a 0.350 cutpoint was used.

For both diseases, the value of routine laboratory testing or standard clinical symptoms in differential diagnosis of these and other flu-like diseases could not be established. The patients tested by either the RB test for brucellosis or the blood smear examination for malaria were likely unrepresentative of all potential patients. Given the high levels of brucellosis uncovered, further prospective studies in both human and animal populations are currently underway. For humans, clinical and laboratory diagnosis will be evaluated in all patients presented with flu-like symptoms. Most importantly the high rate of human brucellosis in Narok is due to brucellosis in the cattle, sheep and goat reservoirs. To effectively protect humans, a study to better estimate the incidence and economic effects of brucellosis in these species is being undertaken. Finally, it was observed that many patients in Narok considered brucellosis treatment too costly, too long and too painful. Because of poor acceptance of current treatments, clinical trials to identify a less costly, shorter, and better accepted treatment regimen should be considered.

CHAPTER ONE

1.0 INTRODUCTION

Brucellosis is a direct bacterial zoonosis of cosmopolitan distribution. The disease is commonest in people in close contact with animals, which are the main sources of human infection. Subsequently, pastoralist peoples like the Maasai of Narok are at high risk. Cattle kept under nomadic pastoralism have a higher prevalence of brucellosis than those kept on farms (Hussein *et al.*, 1978), thus constituting a larger reservoir for human infection. Brucellosis can be transmitted by contact and oral exposure, making it a health risk to people in direct or indirect contact with infected livestock.

Brucellosis has both public health and economic significance (McDermott *et al.*, 1987, Nicoletti, 1989). Its public health significance arises from the organism's ability to infect and cause disease in humans. In humans brucellosis is characterized by fever, chills, headache, weakness, joint pains, night sweats and weight loss. These symptoms are non-specific, highly variable and common to a number of other diseases like malaria, Q-fever (Coxiellosis), Rift-Valley fever, rheumatism, leptospirosis, psittacosis and influenza. This protean nature makes it difficult to arrive at a clinical diagnosis of brucellosis. Patients presenting with the above symptoms are often treated for malaria to the exclusion of other possible differential conditions. Only in a few of the health units in Narok, are persistent cases tested for brucellosis.

In animals, the disease causes economic losses through foetal losses, lowered fertility and reduced production. It is characterized by abortion, retained afterbirth, orchitis, epididymitis, impaired fertility and hygromas. Some infected animals may remain asymptomatic.

Brucellosis in Kenya has been documented in both animals and human beings (Wright *et al.*, 1953; Cox, 1966, 1968; Fazil, 1975; Oomen, 1975; Kagunya, 1977; Paling *et al.*, 1988). The relative importance of brucellosis as a cause of human illness has, however, not been determined, although the disease is highlighted in the Ministry of Health Annual Reports (Anon, 1992) and by the work of Oomen in Machakos District (Oomen, 1975, 1976). It is likely that many cases of brucellosis in humans are not recognized, and that it occurs rather frequently among livestock owners and other occupationally predisposed groups. Literature exists to support this view. Schwabe (1984) noted that clinical diagnoses of malaria obscure the occurrence of many febrile diseases in Africa. In Narok and other pastoral areas, the absence of diagnosis rather than the disease (brucellosis) is likely to be the problem. The differential diagnosis especially of febrile conditions needs emphasis. Roy *et al.* (1965) reported that 21 out of 351 Indian patients with unspecific fevers had diagnostic titres of brucellosis.

Many people attend dispensaries (health units) with fever related ailments and a proportion of such people are often wrongly treated repeatedly for malaria which is a better known and potentially fatal disease. The awareness of other diseases with similar clinical presentations is scanty and often lacking in pastoral areas. Some of the cases which do not respond to malaria therapy could be brucellosis patients. Human brucellosis was rarely diagnosed in Egypt (though animal brucellosis was well known) until it was discovered that a large proportion of patients with unspecific fevers were actually suffering from brucellosis (Schwabe, 1984). Studies on the prevalence of brucellosis conducted in pastoral areas elsewhere in Africa suggest that the rate of infection is high among pastoralists. Collard (1962) reported a 26.4% brucellosis prevalence in Nigeria and Gidel *et al.* (1976) 10% in Burkina Faso. McDermott *et al.*

(1987) drew attention to the economic and public health importance of brucellosis in Southern Sudan where they reported a 20% prevalence in cattle. In Kenya, Gomen (1975) reported 146 cases in Machakos District and in recent years, 359 out of a total of 1,112 human serum samples from Narok and Turkana Districts submitted for brucellosis testing at the Veterinary Research Laboratories, were found to have anti-brucella antibodies (Mugambi, personal communication). The presence of brucellosis in the major domestic animal species in Kenya (Philpott and Auko, 1972; Waghela and Gathuma, 1975; Kagunya, 1977; Waghela *et al.*, 1978) and some wildlife species (FAO/WHO, 1971; Paling *et al.*, 1988) indicates an abundant source of infection for man. This is especially probable in the pastoral areas where livestock, wild animals and people live in close proximity, a situation favouring transmission between animals and humans.

Under pastoralism, the risk of brucellosis is both occupational and food-borne. The large herds of stock pose an increased risk of infection through wide-ranging contact, frequent additions from unproven sources and improper sanitation. Pastoralists live in close contact with animals and rely almost exclusively on their products for subsistence. The low standards of hygiene and lack of adequate cooking facilities increase the risk of infection through animal foods. Poor environmental sanitation due to poor disposal of aborted foetuses, foetal membranes, dead animals and the accumulation of animal wastes increase the probability of infection. There is also a slight possibility of vector transmission through bites and contact (FAO/WHO, 1971).

The incidence, prevalence and risk factors for brucellosis in Kenya have not been specifically studied. The few studies carried out so far have only been based on selected case follow-ups rather than population based samples. They, however, indicate

that the disease is widespread. Zoonotic infections tend to be poorly diagnosed and little suspected even in areas with big case loads of fevers of unknown origin and other broad and unspecific diagnoses. This is a particular problem in areas where resources are severely limited. Laboratory facilities, qualified personnel and general physical infrastructure are lacking. Thus, pastoralists in their unique lifestyle have unique problems requiring unique approaches.

The present study was conducted to assess the frequency of occurrence and predictive symptoms for brucellosis among Maasai pastoralists in Narok District with the overall goal of attempting to assess the relative importance and differential diagnosis of brucellosis in the District. Since malaria is common in Narok and the main rule-out for brucellosis, specific data on the occurrence and clinical features of malaria was also collected.

1.1 SPECIFIC STUDY OBJECTIVES

1 To conduct a retrospective study of patient records at reporting health units in Narok District to determine the proportion of patients complaining of flu-like ailments consistent with brucellosis and malaria.

2 To determine the proportional morbidity and other epidemiologic features of both diseases in the District.

3 To investigate associations between clinical signs and symptoms with positive laboratory tests for brucellosis and malaria.

4 To establish an index of suspicion for either disease based on the symptoms to suggest when laboratory tests should be considered for definitive diagnoses at dispensaries with laboratory facilities, and to assist clinical diagnoses at those without.

5. Describe the present treatment of human brucellosis in Narok District.

CHAPTER TWO

2.0 LITERATURE REVIEW

Brucellosis is an infectious bacterial disease of animals and man. In animals it is characterized by abortion, retained afterbirth, orchitis, epididymitis, impaired fertility and hygromas (Blood and Henderson, 1989). In humans, brucellosis is characterized by fever, chills, sweating, joint pains, body aches, weakness and weight loss. Domestic animals, primarily cattle, sheep, goats and swine are the reservoirs of human brucellosis. Occasionally, fowls (Angus *et al.*, 1972), dogs (Carmichael, 1979) and horses (Denny, 1972) have been reported to transmit the disease to humans.

2.1 THE CAUSAL ORGANISMS

Brucellosis is caused by bacteria in the genus *Brucella*. There are six recognized species in this genus, four of which are zoonotic (Huddleson, 1943). According to the Bergey's Manual of Systematic Bacteriology (1984, Vol.1), they include *B. abortus*, *B. melitensis* (Meyer and Shaw, 1920), *B. suis* (Huddleson, 1929) and *B. canis* (Carmichael and Bruner, 1968) which are zoonotic and *B. ovis* (Buddle, 1956) and *B. neotomae* (Stoenner and Lackman, 1957) which are not zoonotic. The *Brucellae* display a wide host range though showing obvious host preferences. *Brucella abortus* (9 biotypes) prefers cattle, *B. melitensis* (3 biotypes) goats, *B. suis* (4 biotypes) swine, *B. canis* dogs, *B.ovis* sheep and *B. neotomae* the desert wood rat (*Neotoma lepida*). These are the primary hosts of the various *Brucella* organisms.

Inter-species transmission of *Brucella*, however, occurs readily. *Brucella abortus* has been reported to infect cattle, sheep and goats (Van der Hoeden, 1933),

horses (Denny, 1972), dogs (Bicknell *et al.*, 1975; Taylor *et al.*, 1975). It has also been reported in swine (Blood and Henderson, 1989), fowls (Angus *et al.*, 1972), camels (Kagunya, 1977), man and a number of wild animals (FAO/WHO, 1971; Paling *et al.*, 1988). *B. melitensis* infects sheep and goats (Meyer, 1964), cattle, camels and buffalos (FAO/WHO, 1971), impalas (Thorpe *et al.*, 1967), rabbits, swine, poultry and humans (FAO/WHO, 1971). *Brucella suis* infects swine, cattle, sheep and goats, humans, dogs and probably other species (Carter and Chengappa, 1991). *B. canis* infects dogs (Carmichael, 1967; Henderson *et al.*, 1974;), foxes (Pickerill, 1970), monkeys (Percy, 1972), and man (Morriset and Spink, 1969; Swenson *et al.*,1972; Blankenship and Sanford, 1975; Munford *et al.*,1975). *B. ovis* and *B. neotomae* do not seem to infect other species besides sheep and the desert wood rat respectively (Meyer, 1979).

Brucella organisms have been isolated from animals since 1887 but it was not until 1914 that the first *Brucella* of human origin were identified by Bruce (Carter and Chengappa, 1991). They are gram-negative, non-motile, and non-spore forming small rods. They are not capsulated and usually occur singly but occasionally in small groups. In culture they form smooth and rough colonies which show characteristic dissociation after the fourth day of growth (Huddleson *et al.*, 1952). This dissociation is associated with loss of virulence and the antigens responsible for agglutination. There is a resultant increase in auto-agglutination. They have a closely related antigenic structure which makes their differentiation in serologic studies difficult. *Brucellae* have been classified into different biotypes based on metabolic reactions, cultural requirements and susceptibility to the *Brucella* phage (Alton *et al.*, 1975).

They are generally aerobic and carboxyphilic, catalase and urease positive and do not produce acid in conventional peptone media fermentations.

A number of *Brucella* spp. have been isolated in Kenya since 1968. Cameron (1971) reported the isolation of *B. ovis* from rams in the Rift Valley province. In 1971, Philpott and Auko (1972) isolated all three biotypes of *B. melitensis* from sheep and goats. The organism has also been isolated from a bovine foetus (Waghela, 1976, 1977) and human patients (Oomen, 1975). *Brucella abortus* biotypes 1, 3 and 9 have been isolated from Kenyan cattle (Waghela, 1976). *Brucella suis* has so far only been isolated from rodents (Heisch *et al.*, 1963). No isolation from wildlife has been achieved although serologic evidence of infection has been adduced (Waghela, 1976; Paling *et al.*, 1988). Isolation of *B. melitensis* and *B. abortus* from humans has been documented (Wright *et al.*, 1953; Manson-Bahr, 1956; Oomen, 1975).

2.2 SURVIVAL OF *BRUCELLAE*

Within the host, *Brucellae* are protected from host defence by localizing and proliferating within the cytoplasm of monocytes and reticulo-endothelial cells (Jubb *et al.*, 1985). They may remain in the host for life. It has been observed that this constitutes an increased risk of spread through environmental contamination especially by the female animals when the number of organisms peak cyclically during pregnancy and delivery, both normal and premature (Brinley Morgan, 1970). Such shedders are a serious source of danger to other animals and man as they are clinically unaffected.

Brucellae are very sensitive to sunlight. They can, however, survive for up to six months in necrotic or foetal tissues and for two to three months in dry soil that is

protected from sunlight (Flores-Castro and Baer, 1979). Drying slowly in the presence of organic matter prolongs their survival. This condition is of interest in pastoral areas where people share huts with animals, because any contamination occurring within the house remains a source of infection for a long time. In frozen secretions, urine, milk and water, *Brucellae* may survive for up to two or more years. *Brucellae* survive well at temperatures below freezing point, at 4 to 8^0 C in a moist environment and in the absence of direct sunlight.

Brucella are, however, readily killed by freeze-thaw conditions, heat, phenol, formaldehyde, quaternary ammonium compounds and pasteurization at 62.7^0 C for 30 minutes or 71.6^0 C for 15 seconds (Flores-Castro and Baer, 1979). *Brucellae* are inhibited by fermentation products but are only killed after prolonged fermentation (FAO/WHO, 1971), usually too long for normal processing. A study carried out among the Fulani pastoralists of Nigeria showed that traditional souring of milk for 24 hours did not kill *Brucellae* (Ezeh, 1978), making it a public health hazard to the consumers. In dairy processing, *Brucellae* tend to concentrate in the cream fraction of the products thereby making them a common source of human infections (FAO/WHO, 1971; Flores-Castro and Baer, 1979).

2.3 EPIDEMIOLOGY OF BRUCELLOSIS

2.3.1 Distribution of brucellosis

Brucellosis is a cosmopolitan problem of livestock except in a few countries where eradication has been achieved. *Brucella abortus* is probably the most widespread due to the universal distribution of cattle, but *B. melitensis* has been the most

frequently isolated as a cause of human illness (Wright *et al.*, 1953; Manson-Bahr, 1956; Cox, 1966, 1968). *Brucella melitensis* infection in humans is common wherever goats are raised, but it is especially prevalent in developing countries (OIE, 1976). The same applies to *B. abortus* and *B. suis* in cattle and pig raising areas respectively.

Brucella melitensis may have originated in the Middle East where small ruminants were first domesticated, but is now known to occur widely throughout the world (Alton, 1987). The development of large-scale livestock production (for example, sheep in the Middle East) has led to serious epidemics, sometimes in areas where the disease has not been common (Radwan *et al.*, 1984). *Brucella suis* is also commonly isolated from humans (Glosser, 1972). In all instances, the primary livestock hosts are the main reservoirs of human brucellosis.

Brucellosis is not new to Africa. Since it was first reported in animals in Kenya in 1914 (Anon, 1914), it has been documented in most countries studied (Chukwu, 1985). Reports on biotyping show that *B. melitensis* biotypes 1, 2 and 3 occur in Kenya (Philpott and Auko, 1972). Most *B. abortus* biotypes occur in Africa (Chukwu, 1985). *Brucella abortus* biotype 1 occurs in Kenya (Waghela, 1976), Nigeria (Ezeh, 1978) and Senegal (Verger *et al.*, 1979: quoted by Chukwu). Biotype 2 has been reported in Nigeria (Ezeh, 1978) and biotype 3 in Kenya (Waghela, 1976), Nigeria (Ezeh, 1978), Uganda (Elliott and Christiansen, 1977), Tanzania (Hummel and Staak, 1974) and Senegal (Chukwu, 1985). Biotype 4 has been reported in Nigeria and biotype 6 in Somalia (Andreani *et al.*, 1983: quoted by chukwu). Biotype 7 has been reported in Egypt, South Africa and Ivory Coast (Cote D'Ivore), while biotypes 8 and 9 have been reported in Uganda (Chukwu, 1985). Other species of *Brucella* found in

Africa are: *B. canis* in Nigeria (Okoh *et al.*, 1978), B. ovis in Kenya (Cameron, 1971) and South Africa (Van Rensburg *et al.*, 1958). *B. suis* has been isolated in rodents in Kenya (Heisch *et al.*, 1963).

In many African countries, brucellosis has only been diagnosed by serology. Human and animal brucellosis has also been reported in Zimbabwe, Botswana (Cooper and Carmichael, 1974), Sudan (Ibrahim, 1975), Sierra Leone (Opitz, 1969), Tunisia (El Fourgi, 1973) and Zambia (D' Cruz, 1976). In Nigeria, human brucellosis has been documented (Collard, 1962). Gidel *et al.* (1976) found a 10% apparent prevalence among the pastoralist peoples of Upper Volta (Burkina Fasso). In 1962, Collard found that 26.4% of human serum samples from the Fulani of Nigeria contained *B. abortus* agglutinins. Ovine and caprine brucellosis (Anon, 1985) and human brucellosis (Boargob and Muhammed, 1985) occur in Libya.

In Kenya, animal and human brucellosis has been reported in practically every district surveyed (Waghela, 1976, 1977; Oomen, 1975). The first report dates back to 1914 (Anon, 1914), followed by widespread abortions in 1923, which were suspected to have been due to brucellosis. A Milk Ring Test survey at Kenya Co-operative Creameries branches gave an overall reactor rate of 19% with a range of 12 to 38.3% (Anon, 1955). Shortly before this, Wright *et al.*, (1953) had described the first cases of human brucellosis. Manson-Bahr (1956) then described the clinical aspects of brucellosis, while Cox (1966, 1968) observed many cases in the north where he performed serologic tests under rural conditions. Heisch *et al.*, (1963) isolated *B. suis* from rodents at the coast, while Waghela and Gathuma (1975) reported serologic evidence of porcine brucellosis in Kenya. Nagy and Sorheim (1969: quoted by

Waghela, 1976) working at Kenya Meat Commission (Athi River) examined sera from cattle. The highest reactor rate was found in cattle from Nyanza Province (15.78%) and the lowest in those from Central Province (1.67%). Clinical cases of human brucellosis have also been described by Fazil (1975) from Machakos District and North Eastern (N.E) Province. This was further demonstrated by Kagunya (1977) in a study based on the N.E province, where the presence of anti-*Brucella abortus* agglutinins in cattle and camels and those against *B. melitensis* in sheep and goats were reported. Wildlife species have similarly been reported to have anti-*Brucella* agglutinins although no isolation have been made in Kenya so far (Paling *et al.*, 1988). *Brucella melitensis* has been isolated from the Impala in northern Tanzania (Schiemann and Staak, 1971). The prevalence of brucellosis in animals and man is undoubtedly higher in the pastoral areas of Kenya where large numbers of livestock are kept in close contact with the people (Oomen and Wegener, 1982). Kagumba and Nandokha (1978) reported higher prevalences in cattle from Maasai-land and other semi-arid areas of East Africa.

2.3.2 Environmental Contamination With *Brucellae*

Domestic animals are the main contaminants of the human environment with *Brucella* organisms. *Brucellae* are facultative intracellular pathogens with a predilection for the reticuloendothelial system (RES) and reproductive organs. They cannot live outside their hosts (Carter and Chengappa, 1991). Involvement of the urogenital system of infected hosts is of great epidemiologic importance. It is the principal route of escape for the organism leading to environmental contamination that is essential for its spread. Massive numbers of the organism are present in the uterine discharges of

infected animals from about a week before parturition or abortion, to about a month after. This is because organisms tend to concentrate in the uterus due to high levels of erythritol in the gravid uterus. This fact may preclude *Brucellae* in the uterine discharges of women because erythritol, the growth stimulator for *Brucelia* species in animal placentae, is absent in women (Porreco and Haverkamp, 1974). This is further supported by the observation that abortion rates in pregnant women with brucellosis does not exceed the spontaneous rate in healthy pregnant women (Porreco and Haverkamp, 1974; Panjarathinam, 1984). The organism has, however, been isolated from the cervical mucosa of a post-parturient infected mother (Singer *et al.*, 1991).

The uterus should ideally be negative for bacteria after involution, but some animals may shed the organism for weeks or even months (Stableforth, 1959). Animals shedding the organism in this manner contaminate the environment. Discharges falling on water, food or household objects can lead to infection through the oral, respiratory or percutaneous routes. Some animals shed the organisms even after healthy delivery. Such animals constitute a subtle source of infection for both humans and animals.

The second major route of escape for *Brucellae* is the mammary route. Nearly all infected lactating animals develop a *Brucella* induced mastitis and discharge the organism either continuously or intermittently throughout the lactation period and sometimes continue to discharge the organism in subsequent lactations (Morgan, 1970). The milk looks normal but it has an increased somatic cell count (Jubb *et al.*, 1985), and a chronic suppurative inflammation of the mammary gland is observed on microscopic examination. *Brucella* organisms have been isolated from the milk of cattle and goats in Kenya (Anon, 1934; Philpott and Auko, 1972). Isolation has also

been achieved from animal semen, uterine discharges, aborted foetuses, and human blood (Oomen and Wegener, 1974; Oomen, 1975). Other modes of environmental contamination are through infected carcasses, aborted foetuses and foetal membranes, and the faeces of some infected animals.

2.4 BRUCELLOSIS IN HUMANS

2.4.1 Main Risk Groups

The main risk groups for human brucellosis are people who consume unpasteurized animal products and all those in contact (direct or indirect) with animals and their products. These include veterinarians, butchers and abattoir workers, farmers, livestock market employees, animal attendants, meat inspectors, processing plant workers for animal products like dairy plant workers and wool industry workers (CDC, 1976). Laboratory workers are at risk of infection from contact, accidental inoculation or aerosolization of cultures or infected laboratory materials. Travellers are also exposed to brucellosis (Arnow, 1984) through food and contact. Also at risk are housewives and children who work and play in close contact with domestic animals. Another category of people predisposed to *Brucella* infection are herdsmen. These are especially close to their animals thereby providing repeated opportunities for infection. Given these occupational risks, adult working age males are most commonly affected (CDC, 1976). Among herdsmen, nomadic pastoralists are at even higher risk because of their closer association with animals and complete reliance on animal products for subsistence.

2.4.2 Modes of Transmission

Brucella organisms are very invasive. They are capable of penetrating the mucus membranes of the nose, throat, conjunctiva, urogenital tract, epithelium of the teat canal, parenchyma of the mammary glands and testis, and normal and abraded skin (Jubb *et al.*, 1985). Human infection with *Brucellae* depends upon contact with infected animals or their products or materials contaminated with animal discharges (Hendricks and Meyer, 1975). Consumption of unpasteurized raw milk and dairy products is a common method of transmission (Young, 1983; Cooper, 1992). Raw, semi-cooked or pickled meat is also a source of human infections (Saddler, 1960). The widespread adoption of pasteurization of milk and heat treatment of meats have reduced brucellosis to an occupational hazard in most developed countries. However, in pastoral areas people have not adopted these practices, thus increasing their risk of food-borne brucellosis.

The most common mode of transmission of brucellosis is through foods of animal origin. There is a direct relationship between the level of brucellosis in animals and the incidence of human infection which has been shown to be influenced by methods of animal husbandry, standards of hygiene and food customs (Escalante and Held, 1969). Milk from cattle, sheep, goats, camels, water buffaloes and other domesticated animals is the most common source. *Brucella abortus* is, however, less likely to be transmitted this way, compared with *B. melitensis* which is more infective (Flores-Castro and Baer, 1979). Dairy products like cheese, cream, butter, chocolate and yoghurt can be a source of infection if they are prepared from unpasteurized milk (CDC, 1976). The isolation of *Brucella* organisms from goat milk in Kenya (Philpott

and Auko, 1972), suggests that raw milk may be a medium of transmission. The cream fraction of milk is more heavily laden with the organism than the skimmed fraction (FAO/WHO, 1971) and requires more heating to kill the organisms.

Besides primary infections, secondary contamination of carcasses with *Brucella* may occur through milk when the udder is cut. *Brucella* can survive pickling, smoking and freezing of meats. Occasional exposure may result from vegetables or water which have been contaminated with infected discharges, secretions or animal excreta (FAO/WHO, 1971; Ray, 1979).

Pastoralists have more frequent direct contact with infected animals or contaminated materials (eg. foetuses, placentas, urine, carcasses, manure etc.) and may be infected via respiratory, conjunctival or dermal routes. Direct contact is a common mode of exposure for occupational infections, usually through minor cuts and abrasions. Inhalation of infected dried materials of animal origin in houses, laboratories, abattoirs, railway tracks and lorries that have been used to transport infected animals, and farm premises used for housing animals may lead to infections through the respiratory system and conjunctiva (FAO\WHO, 1971; Olle-Goig and Canela-Soler, 1987). Inhalation is nevertheless not felt to be a major route of infection with *Brucella* organisms (Report of Sub-Commitee on Public Health, 1972).

Brucella melitensis has been isolated from the vaginal mucosa, urine and milk of infected women (Singar *et al.*, 1991) and the semen of infected men (Vandercamb *et al.*, 1990). *Brucella* have also been isolated from the vaginal swabs of Maltese prostitutes (Report of the Committee for the Investigation of Mediterranean Fever, 1907; quoted by Ruben *et al.*, 1991). These instances, however, do not constitute

sufficient evidence to implicate venereal transmission, though suggesting that it can occur under some circumstances. Ruben *et al.* (1991) observed the transmission of *B. melitensis* between spouses in what they suggested to be person to person transmission through coitus, while Goosens *et al.* (1983) also suggested that brucellosis may be sexually transmitted in humans. There are also isolated reports of cases occurring after blood transfusion (Wood, 1955), bone marrow transplantation (Naparstek *et al.*, 1983) and to nursing babies through the mothers' milk (McCullough, 1970). Luban *et al.* (1988) reported brucellosis in three newborns in Kuwait and implicated trans-mammary infection although milk cultures were negative. Trans-placental transmission is another potential mode of transmission but seems unlikely because the human placenta lacks erythritol (Porreco and Haverkamp, 1974).

Blood sucking arthropods have been mentioned as possible *Brucella* transmitters (FAO\WHO, 1971). *Brucellae* have been shown to multiply and persist in both ticks and insects and maintain their virulence to mammals. Arthropods may transmit *Brucella* through bites but ticks can also cause transmission by contact because they excrete the organisms in coxal fluid (Spink, 1956; Stableforth, 1959); but, there is little evidence of their direct role in natural transmission.

2.4.3 The Clinical Importance of Human Brucellosis

The pathogenesis of human brucellosis is similar to that in animals. Clinically, the disease may be rapid or insidious in onset or remain asymptomatic (Henderson and Hill, 1972). The manifestations of brucellosis tend to be protean and nonspecific (Young, 1989) though they could be limited to specific organs or systems, thus,

leading to localized brucellosis or complications of brucellosis. Fever and chills usually characterize acute brucellosis, with the more insidious disease presenting with mild symptoms. Incubation varies from a few weeks in acute and subacute disease to months in the chronic infection (Sacks and Rensburg, 1976). The onset may be very dramatic followed by an apparent recovery in the acute disease. Fever and bacteraemia are often present with the former tending to persist in the majority of cases. Most patients with chronic and subacute brucellosis may not develop a bacteraemia though they may harbour the organism for years in localized foci. Sometimes sero-converted patients may have never developed symptoms, showing that exposure to *Brucella* may cause antibody production without producing clinical disease. This is especially true in occupationally exposed groups (Henderson and Hill, 1972).

The clinical signs observed depend on the nature of infection (Sacks and Rensburg, 1976) and may sometimes relate to the route of infection. Pneumonia and gastro-intestinal complications may occur following aerosol inhalation and ingestion of contaminated food respectively (Patrella and Young, 1988). Chronic brucellosis commonly occurs in patients with mild attacks because they rarely seek medical attention (Young, 1983). Diurnal pyrexia with body temperature rising in the afternoons accompanied by chills and fatigue are the most frequent symptoms reported. Other symptoms are weakness, myalgia, arthralgia, profuse nocturnal sweating (Simpson and Frazier, 1928), anorexia with rapid weight loss, severe frontal headache and backache (Young, 1983). Depending on where the organisms localize, other symptoms may be observed. These are poly-arthritis, spondylitis, pharyngitis, abdominal pain due to enlargements of the liver, spleen, and mesenteric lymph nodes, renal damage, orchitis, epididymitis, and endocarditis (Percy and Belter, 1960). An

estimated rate of osteo-articular complications of 10-70% has been reported depending on the study population and diagnostic criteria used (Young, 1983). The majority of osteo-articular complications in brucellosis involve the spine (Lifeso *et al.*, 1985) and the sacro-iliac joint with or without involving other joints (Steinberg, 1948; Gotuzzo *et al.*, 1982). Bone and joint involvement tend to be the most common lesions associated with chronic localized brucellosis (Kelly *et al.*, 1960; Martin *et al.*, 1961).

There is formation of granulomas in most affected tissues. In the liver, *Brucella* associated granulomatous lesions have been described in both experimental animals and patients (Braude, 1951; Cervantes *et al.*, 1982). Cirrhosis may take place and sometimes cause jaundice. Death occurs almost invariably in persons with subacute endocarditis (Percy and Belter, 1960). All Brucella species have been shown to cause endocarditis but *B. abortus* is the most frequent (Hart *et al.*, 1951).

Some brucellosis patients experience nonspecific symptoms referable to the nervous system. These include headache, lassitude, mental inattention and depression, but direct invasion of the nervous tissue is rare. An estimated 10% of patients with brucellosis suffer debilitating neuro-psychiatric complications (Spink, 1956). More recent reports however indicate a lower incidence of 3-5% (Shakir *et al.*, 1987). The best defined syndrome of neuro-brucellosis is meningitis with or without alteration of consciousness, caused by invasion of the central nervous system by *Brucella* (Bouza *et al.*, 1987). Neurological symptoms like headache, nuchal rigidity, nausea, vomiting and altered consciousness have been reported in brucellosis patients (Mousa *et al.*, 1986), but psychiatric disturbances like depression, amnesia, psychoses and personality disturbances are more common (Bashir *et al.*, 1985). Spinal cord involvement may

occur leading to spastic paralysis or paresis of the lower extremities with some sensory and bladder impairment. Rare cases may resemble acute anterior poliomyelitis (Debono, 1964). Other disturbances including neuro-muscular affections, epistaxis, osteomyelitis, thrombosis, sore throat and gastro-enteritis also occur (Huddleson, 1943; McCullough, 1964; Mousa *et al.*, 1986).

Brucellosis has also been reported to localize and cause pathology in organs of the urogenital system. In men it localizes in the testicle and causes orchitis (Simpson and Frazier, 1958). Renal lesions may occur characterized mainly by pyelonephritis or localized lesions indistinguishable from renal tuberculosis (Dunea *et al.*, 1969). Case reports have documented abortion in women with brucellosis (Young, 1983; Kelly and Ribbins, 1987) and *Brucellae* isolated on occasion from maternal and foetal tissues (Poole, 1972; Schreyer *et al.*, 1980), but the abortion rates in brucellosis cases and controls are the same (Criscuolo and Dicarlo, 1954). Febrile episodes could have been the cause of abortion in brucellosis patients.

Brucella organisms have been isolated from respiratory secretions (McDonald, 1939; Harris, 1943) and lung tissue (Weed *et al.*, 1952) although respiratory manifestations are infrequent (Samra *et al.*, 1983). Non-specific gastro-intestinal (GIT) symptoms, including diarrhoea and abdominal pain have been described in patients who had ingested unpasteurized goat cheese (Thapar and Young, 1986). They include anorexia, nausea, vomiting, constipation and lower quadrant abdominal pain that mimics acute appendicitis (Huddleson, 1943; Young, 1989). Acute ileitis has been associated with brucellosis in a patient who had ingested contaminated food (Patrella and Young, 1988; Ho *et al.*, 1986). Brucellosis patients may also develop non-specific

lesions in other systems, such as the skin, eye and ears (Berger *et al.*, 1981; Young, 1983) but these are rare.

2.4.4 Diagnosis of Human Brucellosis

Diagnosis based purely on clinical signs is not easy because brucellosis is a multi-system infection presenting with a wide variety of nonspecific symptoms (Young, 1983). A clinical diagnosis requires a high index of suspicion. A presumptive diagnosis can, however, be made based on symptoms consistent with the disease and epidemiologic findings suggestive of exposure to Brucella. Such a diagnosis is best confirmed by isolation or serologic tests if possible.

2.4.4.1 Clinical Diagnosis

A clinical diagnosis of brucellosis should be established by taking a detailed patient history giving due regard to the occupation (Williams, 1973; Young, 1983), patient's history of travel (Arnow *et al.*, 1984), types of food eaten and exposure to animals. These are useful in establishing an index of suspicion. About 50% of patients with brucellosis experience an insidious onset of symptoms occurring over weeks to months, with an average of 3 weeks (Young, 1989).

2.4.4.2 Bacteriologic Diagnosis

Isolation of the causal organism is the most specific diagnosis of brucellosis but is both hazardous and tedious, and cultures from infected patients are not always positive (Young, 1989). The blood broth culture in 10% carbon dioxide is the simplest and most commonly used method (Castaneda, 1961), but other laboratory media can be

used. Isolation should preferably be attempted during the febrile phase of the disease (Robertson *et al.*, 1980). Tonsillar swabs, blood, cerebrospinal fluid, peritoneal and synovial fluids, vaginal swabs, seminal serum, and tissues especially the liver, spleen, and lymph nodes are the clinical specimens used (Kelly *et al.*, 1960). The majority of cultures are positive between the 7th and 21st days, but cultures should not be declared negative until the 45th day of incubation (Rodriguez-Torres *et al.*, 1983). Suspect colonies can be identified provisionally using the Gram stain and slide agglutination test using high titre anti-Brucella serum. Isolation of *Brucellae* is, however, both dangerous and difficult, thus favouring the less hazardous use of serologic testing as a diagnostic tool.

2.4.4.3 Animal Inoculation

Animal inoculation is another method of isolation of *Brucella* from specimens, especially if they are contaminated (Robertson *et al.*, 1980). Because *Brucellae* are intracellular parasites, the buffy coat from centrifuged blood can be inoculated intra-peritoneally into guinea-pigs, which are then bled by cardiac puncture at monthly intervals for three months and the blood cultured to isolate the organisms (Robertson *et al.*, 1980). This method, however, takes too long to be useful for diagnosis.

2.4.4.4 Serologic Diagnosis

Serologic methods based on the detection of antibodies against *Brucella*, are used as indirect proof of infection. There is widespread use of almost all available tests, suggesting the possible absence of an ideal test (Ramon and Ignacio, 1989).

The immune response in brucellosis involves all the three main immunoglobulin groups; IgG, IgM and IgA. IgM appears first followed almost immediately by IgG. IgG antibodies persist while IgM and IgA decrease rapidly to undetectable levels. Given its persistence and higher levels, IgG detection is used for serologic diagnosis. IgG is an indication of active infection or continuous exposure. *Brucellae* are covered by a lipopolysaccharide (LPS) molecule which is responsible for occasional cross-reactions with other Gram negative bacteria (Diaz *et al.*, 1968). The LPS elicits a vigorous antibody response (Jones and Berman, 1976) but soluble fractions and several outer membrane also do (Riezu-Boj *et al.*, 1978).

Serologic methods have been classified into those that use whole smooth cells as antigens and those using soluble antigens. SAT, RB test, CFT, Coomb's test and immuno-fluorescent tests use whole cells while ELISA, RIA and gel precipitation tests use soluble antigens (Parratt *et al.*, 1977; Gilbert and Hawes, 1981).

i) The Serum Agglutination Test (SAT)

This test detects both IgG and IgM, and is the most commonly used test in both animals and man. Suspensions of the killed *Brucella* are used as the antigen. Agglutination is the positive reaction and is expressed in international units (iu). Results are interpreted according to the WHO guidelines of 1971. In humans, a high or rising antibody titre is presumptive evidence for *Brucella* infection though a low titre does not expressly exclude it. Patients showing doubtful results should be retested after two weeks to ascertain the outcome. Specificity of the agglutination reaction has been criticized, but it is now known that non-specific agglutination is caused by the use of

rough rather than smooth *Brucella* (Ramon and Ignacio, 1989).

ii) The Mercapto-Ethanol Test (MET).

This is an agglutination test performed in the presence of 2-mercapto-ethanol which inactivates IgM leading primarily to the detection of IgG. The test is performed in the same way as the tube agglutination test. IgG is generally associated with active infection therefore making MET an important test for assessing the infection status of patients. Its use in the diagnosis of human brucellosis is, however, controversial and needs further evaluation (Buchanan and Faber, 1980; Ramon and Ignacio, 1989).

iii) The Complement Fixation Test (CFT)

In this test, dilutions of the inactivated suspect serum are incubated with the antigen and complement at 37^0 C for 30 minutes. Then a mixture of sheep red blood cells and haemolytic serum are incubated at 37^0 C for another 30 minutes. Reactions are read as the degree of haemolysis and recorded. The test is laborious but very sensitive and unlikely to give false negative results. It can best demonstrate active infection because IgG is by far the most active complement fixing antibody.

iv) The Coomb's Anti-human Globulin Test

This test is used to demonstrate non-agglutinating antibodies in brucellosis (Coombs et al., 1945), being preferred for patients with clinical histories suggestive of brucellosis, but who have tested negative to the SAT. It utilizes the Coomb's reagent which causes agglutination in sera with antibodies that are normally incapable of causing agglutination (incomplete antibodies). Incomplete antibodies occupy sites on

the antigen, thereby preventing agglutinins from causing agglutination. The Coomb's reagent is a specific antiserum which blocks these incomplete antibodies thus allowing agglutination to occur. This test is frequently used in sheep. It is performed by exposing *Brucella* to the patients' serum that has been heated to 70^0 C. Coomb's test has been found to be a sensitive procedure (Hall and Manion, 1953) although showing higher titres than SAT (Otero *et al.*, 1982).

v) Indirect Fluorescent Antibody Test

The test employs fluorescein labelled antigens to detect specific antibodies in the patients' sera. It is probably more sensitive than SAT and CFT but more expensive, thus limiting its application in diagnosis (Morgan, 1967).

vi) Skin (allergic) Test (ST)

This makes use of hypersensitivity to *Brucella* antigens acquired through infection or vaccination. The reaction may be due to immediate (humoral) or delayed (cell mediated) hypersensitivity. A wide variety of allergens: killed bacteria, cell walls, *Brucella* products of sonication, broth culture filtrates, *Brucella* hydrolysates, lipopolysaccharide and nucleoproteins are used (Parnas, 1956). The test is performed by intradermal injection of 0.1 ml of the allergen and the reaction is read within 24-48 hours. Allergic tests are not considered reliable for individual diagnosis (Kerr *et al.*, 1968). Disadvantages include non-specific reactions and positive reactions in patients long after recovery.

vii) The Rose Bengal Agglutination Test (RB test).

The potential usefulness of the RB test for the diagnosis of human brucellosis was suggested by the FAO/WHO committee (FAO/WHO, 1971) and has more or less replaced the rapid slide test which was prone to false negative results (Cernyseva *et al.*, 1977). It has since been found a useful screening tool in the serodiagnosis of human brucellosis (Hossain *et al.*, 1991). The test has a low rate of false negatives, but it can give false positive results with sera from patients with *Y. enterocolitica* 0:9 infection or healthy patients exposed to smooth Brucella (Russell *et al.*, 1978). The suspect serum is placed in a well and thoroughly mixed with an equal volume of the RB antigen. Results are read after rocking the mixture for two minutes.

viii) Enzyme Linked Immuno-sorbent assay (ELISA)

Indirect ELISA has been described as the method of choice for the diagnosis of human brucellosis (Ramon and Ignacio, 1989). The commonly used antigens are a suspension of the smooth bacteria or extracts of LPS (Saj *et al.*, 1987; Jimenez *et al.*, 1992). Several authors have concluded that ELISA is both specific and sensitive (Diaz *et al.*, 1976; Magee, 1980; Sippel *et al.*, 1982; Saj *et al.*, 1987).

ix) Other Diagnostic Tests

Numerous additional tests are available for the diagnosis of brucellosis in humans. They are radio-immuno assay, gel immuno-diffusion, immuno-blotting, rivanol and latex agglutination tests.

2.4.5 TREATMENT OF HUMAN BRUCELLOSIS

The treatment of brucellosis in humans should pay due regard to the clinical nature of the infection. Patients with acute and subacute brucellosis may need supportive therapy, including bed rest and adequate feeding. In spite of the health risk brucellosis constitutes to man, there is still no completely effective treatment or easy method of control (Cisneros *et al.*, 1990). Antibiotic treatment using different regimes and preparations has been used for a long time. Tetracyclines have been used at a rate of 1-2 grams daily for up to three or more weeks. Relapses may, however, occur following treatment, thus, necessitating extension for another 2-3 weeks. Tetracyclines treatment has also been used parenterally. Streptomycin at a rate of 1g/day has been preferred especially in cases where localized lesions occur or in severe disease.

The use of single drugs has generally proved to be less efficacious than drug combinations. *Al* Sibai *et al.* (1992) reported that ciprofloxacin alone was effective in alleviating acute symptoms, but was associated with a high rate of relapses. Thus, they proposed that it should be used together with other agents. This observation supports experimental results that quinolones failed to cure murine brucellosis (Shasha *et al.*, 1992). They reported better results with a combination of doxycycline-rifampin. In humans, synergism exists between tetracyclines and streptomycin in brucellosis therapy (Herrell and Barber, 1952; Feitz *et al.*, 1973; Salala and Ravdin, 1985). This was further emphasized by Zancada Diaz de Entre Sotos *et al.* (1992) who reported good efficacy in treatments using a streptomycin-tetracyclines and doxycycline-rifampin combinations respectively. This is consistent with treatment results in animals. The use of tetracyclines-streptomycin combination was initiated in the 1950s (Magill and

Killough, 1953). A 21 day regime of this combination is commonly used. This has been found effective in relieving the initial symptoms (Feitz *et al.*, 1973) but is frequently associated with relapses. A combination of doxycycline-rifampin is currently recommended as the treatment of choice by the World Health Organisation (FAO/WHO, 1986). Formerly the tetracycline-streptomycin combination was the recommended treatment (FAO/WHO, 1971). The current regimen has, however, been reported to be inferior to both the tetracycline-streptomycin and doxycycline-streptomycin (Colmenero *et al.*, 1989; Cisneros *et al.*, 1990) combinations. While fewer relapses occur when more than one antibiotic is used (Feitz *et al.*, 1973; Kambal *et al.*, 1983), no regimen has so far had none. Tetracycline-streptomycin therapy has a relapse rate of 15-26% (Feitz *et al.*, 1973), but prolonging treatment from 21 to 30, or even 45 days reduces the number of relapses to between 2.8 and 8.4% (Colmenero *et al.*, 1989). Studies employing rifampin combined with doxycycline have reported a relapse rate ranging from 0 to 38% (Kosmidis *et al.*, 1982; Colmenero *et al.*, 1989). A recent study on doxycycline-streptomycin has reported a relapse rate of 3.9% and the authors have recommended a 6 week course of doxycycline plus 2 weeks of streptomycin injections (Cisneros *et al.*, 1990). However, since streptomycin is injectable, treatment compliance is reduced. Doxycycline-rifampin is an all-oral dosage and for this reason has been suggested as the primary treatment for human brucellosis (Sande *et al.*, 1990).

The use of trimethoprim-methoxazole with or without gentamycin for the first five days, has also been suggested as treatment for human brucellosis (Hassan *et al.*, 1971). At a dosage rate of 800mg/160mg, three times a day for three weeks, this

combination had a relapse rate of 4% (Hassan *et al.*, 1971). Relapses can be reduced by extending the treatment period. In cases where septicaemia occurs, corticosteroids and other anti-inflammatory agents may be used together with antibiotics, but this may not be necessary in ordinary cases. In chronic brucellosis, antibiotics with physiotherapy and sometimes surgical interventions are inevitable. This is particularly true in valvular endocarditis, liver abscess, osteo-arthral complications and many other pathologic processes accompanied by structural changes (Colmenero *et al.*, 1991; 1992; Delvecchio *et al.*, 1991). Treatment in early infection has a much higher complete recovery rate than when treatment is initiated later in the course of disease. Better treatment results in human versus animal brucellosis have been attributed to a higher cell membrane permeability to antibiotics in humans (Feitz *et al.*, 1973).

2.4.6 PREVENTION AND CONTROL OF HUMAN BRUCELLOSIS

Control and the eventual eradication of brucellosis in animals is the only means by which human brucellosis can be eliminated. As in animals, vaccination may be used as a protective tool against human brucellosis. However, this is usually considered only a temporary measure until the more recommended application of sanitary and hygiene measures can be implemented. A vaccine prepared from the *Brucella abortus* strain 19-BA has been widely used in the Commonwealth of Independent states (CIS) (former Soviet Union) (FAO/WHO, 1971). Vaccination is usually targeted at groups of people occupationally exposed to *Brucella* infection. Vaccination of other high risk groups, such as pastoralists, could be considered depending on the risk level.

Both inactivated and live vaccines produce immunity and persistent antibodies which cannot be distinguished from those due to infection. The use of 19-BA vaccine has been shown to protect against *B. melitensis* infection (FAO/WHO, 1971). However, in large doses 19-BA vaccine can cause infection. A single immunization by dermal scarification (epicutaneous) with the live 19-BA vaccine provokes sensitization without causing illness. Annual boosters are not necessary except in the occupational groups that are highly exposed to *B. melitensis* and only when the intradermal allergic test is negative. Vaccination of humans using 19-BA vaccine has not been conducted widely outside CIS and no other vaccine types have been used.

In most countries, environmental sanitation, household and personal hygiene are the primary methods for the control and prevention of human brucellosis. Milk, meat and other animal or vegetable products contaminated with animal wastes, secretions and excretions should be adequately heated before consumption. The target control population should be educated on aspects of primary health, hygiene, sanitation and the risk factors for brucellosis. This will enable them to avoid getting infected (Gubina, 1982). People should always use protective attire when working with animals or in animal premises. Most of these measures are not easy to apply in pastoral areas.

2.5 BRUCELLOSIS IN ANIMALS

2.5.1 Main Reservoir Species

Animals are the reservoirs of human brucellosis. Man is infected accidentally through contact with infected animals and their products, or ingestion of infected animal products. *Brucellae* have both true (primary) and alternative (secondary) animal

hosts. Cattle are the true host species of *B. abortus* but infection by this organism is reported in other *Bovidae* like the domestic buffalo in Asia and Middle East, the African buffalo (*Syncerus caffer*), the North American bison and the yak which is highly susceptible. Other *Bovidae* reportedly infected with *B. abortus* are the waterbuck, eland, impalas, gazelles, topi and wildebeest (FAO/WHO, 1971). The one-humped and two-humped camels (FAO/WHO, 1971), horses (Denny, 1972), donkeys, swine, sheep (FAO/WHO,1971) dogs (Carmichael, 1966) and poultry (Felsenfeld *et al.*, 1951; Angus *et al.*, 1972), a wide variety of other mammals, and a few species of arthropods like mosquitos, flies and ticks have developed infection from natural exposure (Ray, 1979). Some reptiles, amphibians, other species of insects, rodents and other small mammals have been experimentally infected with *Brucellae* (Ray, 1979).

The epidemiologic importance of such an extensive potential host range is not clear, but fragmentary evidence suggests that most of these animals can be sources of human infection. The bulk of available evidence, however, implies that *Brucella* infection in alternative hosts is incidental and of minor epidemiologic importance (Ray, 1979).

Brucella melitensis is mainly transmitted to man by goats but alternative hosts like sheep, cattle, donkeys and camels in pastoral areas, and swine, poultry, domestic carnivores and wild animals can be sources of human infection. *Brucella suis* which has a smaller host range than either *B. abortus* or *B. melitensis* has swine as the dominant primary hosts. Other animal species that have been reported to harbour the organism are the European hare, reindeer, cattle, sheep, goats and dogs that are in contact with infected swine. Human infection with *B. suis* is fairly common in

occupationally exposed groups (CDC, 1976).

Usually, it is not easy to differentiate between the various species of *Brucella* because most of the available host range information is derived from serologic surveys. The organisms are very close antigenically.

The animal sources of *Brucellae* in Kenya are cattle, sheep, goats and rodents as determined by isolation. Wild animals have been shown to have *Brucella* agglutinins but isolation has not been achieved so far (Paling *et al.*, 1988).

2.5.2 Modes of Transmission of Animal Brucellosis

Most animals are infected by ingesting materials contaminated by other infected animals (Manthei and Deyoe, 1970; Flores-Castro and Baer, 1979). Transmission from humans to animals is rare. Exposure occurs by the licking or muzzling of newborns and external genitalia of infected animals, ingestion of feed and water contaminated with secretions, excretions, or tissues especially when aborted animals shed Brucella organisms on vegetation and water sources. Contact infection through the skin and mucus membranes may occur from heavily contaminated bedding while aerosols and droplets generated by tail switching and during parturition facilitate infection through the airways and conjunctiva (FAO/WHO, 1971).

Intra-mammary exposure through the teat canal can occur during hand milking (Morgan, 1970; Olitzki, 1970) due to cross-contamination. Infected females may transmit infection to the conceptus in-utero or through milk post-natally (Renoux and Alton, 1955). Although the organisms localize in the male and female genital tracts, venereal transmission is thought to be insignificant (Arthur *et al.*, 1989) probably

because the number of *Brucellae* in semen is much lower than the number required for infection per-vaginum. Female animals can, however, be easily infected during artificial insemination with semen from infected males when it is introduced directly into the uterus (Arthur *et al.*, 1989).

Transmission by ticks and biting insects has been demonstrated experimentally, but their role in natural transmission has not been documented (Spink, 1956; Stableforth, 1959). *Brucellae* have been shown to multiply and persist in ticks and other insects and to maintain their virulence to mammals (FAO/WHO, 1971). Insects transmit infection through bites and ticks excrete *Brucella* in coxal fluid making contact transmission possible. Other modes of transmission such as waterways, air currents, contaminated equipment and scavengers are remote possibilities when other modes of transmission are eliminated (FAO/WHO, 1971; Ray, 1979).

A number of features of pastoralist herds (large herds, free movement and mixing of nomadic herds) enhance the transmission of brucellosis (Kellar *et al.*, 1976).

2.5.3 Pathogenesis and the Clinical Disease

After infection of the host, *Brucella* organisms are subjected to non-specific host defence through engulfment by leucocytes. In the leucocyte they multiply within the cytoplasm leading to the eventual rupture and death of the leucocyte. The *Brucellae* are then released into the host system. Their ingestion by monocytes then takes place leading to the transportation of *Brucella* to regional lymph nodes where an immune response characterized by granuloma formation may take place (Jubb *et al.*, 1985). Invasion of the lymphatics and the blood stream ensues through the thoracic duct

leading to a bacteraemia and generalized infection occurring from 14 days to several months. Bacteraemias are of variable durations and may last in excess of five months. However, lysis by macrophages especially after cell mediated immunity has been activated, may stop further development of the disease. Localization of the organisms may occur in organs, especially those of the reticuloendothelial system: liver, spleen, bone marrow and lymph nodes, as well as the mammary glands, testes and uterus. There the organisms may persist for years.

Necrosis and abscessation commonly occur in swine and man, but also in sheep, goats and cattle with very virulent strains. Many *Brucellae* disintegrate or are lysed in the tissues with the subsequent release of endotoxins which have harmful effects on various tissues, including nervous tissue. Hypersensitivity is manifested by an intradermal reaction. The enterotoxin can cause fever, hypercalcemia and leucocyte variability in small amounts and anaphylactic shock in large amounts. It can also induce abortion in pregnant animals and women (Davis *et al.*, 1973). Pathology occurs in all the organs where localization has taken place, but the most serious tissue damage occurs in the gravid uterus. Proliferation of *Brucellae* results in necrosis and the destruction of maternal and foetal placental membranes, leading to foetal death and expulsion. Uterine damage may be permanent, thus, impairing fertility. These processes which lead to the establishment of *Brucella* organisms in the host and clinical disease, are responsible for the eventual shedding of Brucellae which culminates in the infection of new hosts.

Clinically, the incubation period varies from a few days to several months depending on host factors and the parasite characteristics. The bacteraemia may persist

for more than two months and cause death if very severe. An abortion storm with retention of foetal membranes due to an inflammatory enlargement of the maternal villi, are the initial signs of the introduction of brucellosis in a herd. Abortion may occur at any stage of pregnancy, but most occur in the third trimester.

Most affected animals usually abort only once but subsequent infertility develops in some animals due to chronic endometritis and caruncular fibrosis. In male animals, organisms localize in the reproductive organs and associated lymph nodes. This leads to orchitis, epididymitis, seminal vesiculitis, and inflammation of the ampullae of the ductus deferens. These lesions lead to impaired sperm production and deformities resulting in reduced fertility. *Brucellae* may be excreted continuously or intermittently in semen during the course of infection. Other signs observed in brucellosis are arthritis and hygromas especially in pastoral areas (Domenech *et al.*, 1980). Occasional lameness, weight loss and bronchitis characterized by short honking coughs also occur in brucellosis. Young animals infected *in utero* or post-natally tend to recover spontaneously before reaching sexual maturity. Some, however may remain infected until maturity when the disease manifests during pregnancy. The presence of brucellosis in animals is a potential threat to the health of people in direct or indirect contact with them.

2.5.4 Diagnosis of Animal Brucellosis

The diagnosis of animals brucellosis is of both public health and economic importance. It signifies a potential source of human infection besides threatening livestock production. The absence of pathognomonic signs in brucellosis may lead to

unreliable clinical diagnosis (Hendricks and Meyer, 1975). Abortion storms in animal populations and individual animals may signify brucellosis (Arthur *et al.*, 1989), and is therefore useful in clinical diagnosis. Definitive diagnosis is based on laboratory isolation and identification of the causal organism. Presumptive clinical diagnosis is based on clinical history, clinical signs and physical examination, and indirectly on demonstrating *Brucella* antibodies by serology. While most diagnosticians may use only one of these methods, a combination of epidemiology, serology, clinical and bacteriologic evidence would be the best approach (Romano and Ignacio, 1989). The laboratory techniques used to arrive at a diagnosis of brucellosis in animals are generally the same as those used for human diagnosis.

2.5.5 Treatment of Animal Brucellosis

The treatment of brucellosis in animals is not routinely done since it is generally and frequently not successful and contrary to public health and eradication principles. In countries attempting eradication, where treatment is not allowed, brucellosis positive animals are slaughtered. Brucellosis treatment is tedious, prolonged and costly but in countries not attempting eradication, some animals may be of sufficient economic and genetic value to warrant treatment.

Different therapeutic regimes have been evaluated for brucellosis in cattle and other species with varying successes (Bunnel *et al.*, 1953; Kuppaswany, 1954; Denny, 1972; Milward *et al.*, 1984; Nicolleti *et al.*, 1985; Clara *et al.*, 1989; Martin *et al.*, 1989). Therapeutic failures in the treatment of animal brucellosis are common, probably due to the persistence of *Brucellae* within phagocytic cells of the reticulo-

endothelial system, into which antibiotics do not permeate (Collins and Campbell, 1982). Prolonged therapy and drug combinations have generally shown superior efficacies and should be preferred to conventional one drug therapy (Milward *et al.*, 1984). Antibiotics should, however, be discouraged in recently vaccinated animals because they tend to interfere with the development of immunity (Smith *et al.*, 1983).

2.5.6 Control, Eradication and Prevention of Animal Brucellosis

The control of brucellosis in domestic animals has been successful in some countries, but remains widespread in developing countries where human infection reaches epidemic levels in some areas (Kolar, 1987: quoted by Alton, 1987). For success in the management of a brucellosis outbreak, education of the people is essential in order to gain the widest possible support for the program. Programs for control must locate the infection, contain it and eliminate infected animals. A testing scheme is an essential first step in such a program in order to identify infected herds. Serology using pooled serum or testing the pooled milk are common approaches.

A conventional brucellosis control program may involve mass testing, quarantine, environmental hygiene, mass immunization, mass chemotherapy as well as epidemiological and laboratory diagnoses. Positive reactors should be removed from the general herd, while negative reactors should be retested two or three times after 1-2 months so that those still negative can be declared Brucella free. These must then be protected from infection through improved hygiene and segregation measures. This is necessary even where animals are vaccinated because the protection conferred is by no means absolute. In areas where rigorous hygiene measures can be enforced, control

and even eradication can be achieved without recourse to vaccination (Arthur *et al.*, 1989). In herds with high reactor rates all animals may be slaughtered or failing this all reactors should be completely separated from non-reactors during parturition and immediately disposed of. This should be followed by rigorous cleansing and disinfection, and disposal of infective material. Aborting or parturient animals should be isolated from at least 4 days prior to and 14 days after delivery (Arthur *et al.*, 1989). Other measures capable of reducing the rate of infection in a herd are: i). Improved hygiene at milking to prevent spread from udder to udder through the milkers' hands. ii). Providing the best accommodation possible where animals are housed. iii). Weaning newborns at the earliest possible and rearing them in a Brucella free environment. iv). The exclusion of arthropod vectors as far as possible from the animal premises.

In a region or country, once the incidence has been successfully reduced, a more radical approach such as total eradication can be attempted. Eradication involves test and slaughter of all positive reactors or herds. Eradication may not be feasible in areas with a prevalence of more than 2%. It can not work in the absence of adequate veterinary organisation for surveillance and testing, and administrative support for program implementation. This is an expensive venture that demands a strong political, financial, technical and social backing. Movement controls are also required and owners of slaughtered animals must be adequately compensated. Negative reactors are retested after 1-2 months and only certified free after three consecutive negative tests (Arthur *et al.*, 1989).

Given all these requirements, control and eradication measures are difficult to

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Given all these requirements, control and eradication measures are difficult to

execute in pastoral areas. Here brucellosis remains a problem, compounded by communal grazing, indiscriminate herd expansions (additions), transhumance nomadism, low levels of hygiene and poor standards of living. These areas have poor basic sanitary installations and scanty water supply. In addition, close interaction between domestic and wild animals, man and domestic animals may make it difficult to stop the transmission cycle. These factors make control programme planning and implementation daunting.

Vaccination has been applied to control the spread of animal brucellosis. This may be helpful from an animal husbandry point of view but is less than satisfactory from a public health standpoint. It does not eliminate infection and therefore constitutes a perpetual infection risk to consumers of raw animal products (Arthur *et al.*, 1989). To satisfy both needs, a dual approach should be adapted. This should preferably begin with widespread vaccination in order to reduce losses due to abortion and other sequelae of *Brucella* infection in animals followed by eradication at a later stage.

Live, attenuated or inactivated vaccines have been used against brucellosis. The strain 19 *B. abortus* attenuated vaccine is widely used in cattle. This strain is of low pathogenicity, capable of causing abortion in pregnant cows but unable to spread from animal to animal. The vaccine is best used in heifers 3-9 months old. It is not recommended for use in bulls because it can cause orchitis and epididymitis. When used in adult animals, strain 19 confuses serologic diagnosis during normal surveys. When used in already infected animals, the vaccine does not alter the course of disease. Killed vaccines such as strain 45/20 and H38 are available in adjuvant form (FAO/WHO, 1971). The *Brucella abortus* vaccines are widely used in other animal

species such as small ruminants (Alton, 1987), horses, camels, and buffaloes (FAO/WHO, 1971).

Vaccination in small ruminants is more commonly done using the Rev 1 strain of *B. melitensis* which is a live attenuated vaccine (Entasser *et al.*, 1963). Immunity resulting from vaccination is lifelong with agglutination titters remaining positive for many years, but should not be used in pregnant ewes or does and at least one month should be allowed between vaccination and breeding. Vaccination is recommended to be restricted to lambs and kids. The Rev.1 is preferred for small ruminants (Verger and Plommet, 1985) with the inactivated *B. melitensis* H38 adjuvant vaccine being little used (Alton, 1987). In swine, a live *B. suis* strain of reduced virulence is used which produces immunity for about 1 year. Live vaccines have been found to provide more prolonged immunity compared to inactivated vaccines (FAO/WHO, 1971).

A combination of these measures has achieved success in places like Denmark where the incidence of animal brucellosis was reduced from 25% in 1946 to 2.4% in 1954 (Nielsen, 1955: quoted by Arthur *et al.*, 1989) and the number of human cases from 325 to 35. In the United States, the number of human cases was reduced from 2000 in 1947 to 248 in 1967 by similar measures. Other countries where brucellosis control has been achieved include Britain, Norway, Sweden and Canada (Arthur *et al.*, 1989).

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1. THE STUDY AREA

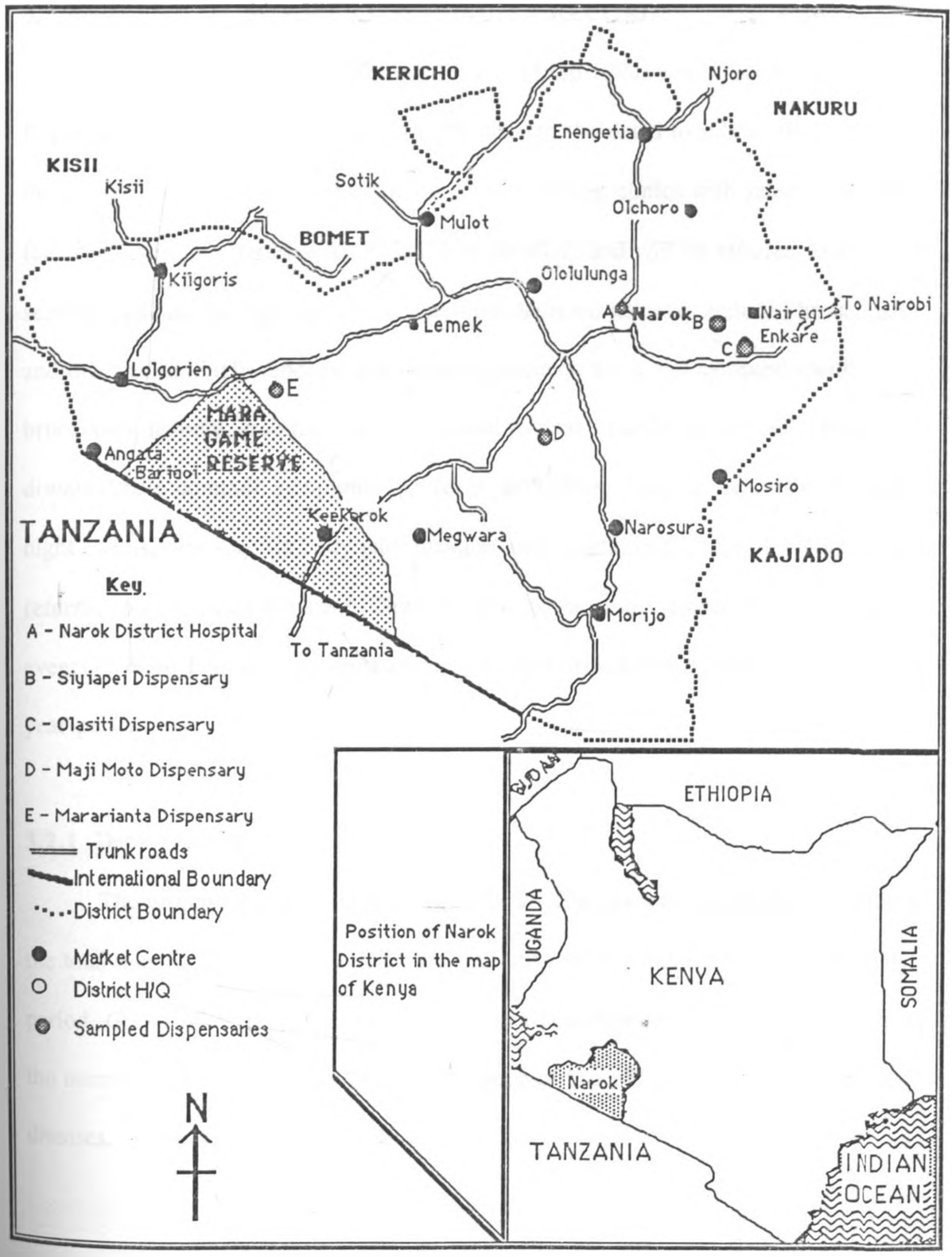
This study was conducted in Narok district, Rift Valley Province, Kenya. Narok was chosen since a large proportion of serum samples sent for brucellosis testing to the Veterinary Research Laboratories, Kabete, from this district were positive. Most of Narok district is a typical pastoral setting where brucellosis can ideally be passed from livestock to man. Narok is in the southern part of Kenya (Figure 1) and covers approximately 16,000 square kilometres, with a human population of about 400,000 persons (Central Bureau of Statistics (CBS, 1983). The livestock population in the district is estimated at 1.05 million (K.R.E.M.U., 1993) comprising about 60% cattle and 40% sheep and goats. The altitude ranges from 1700-2300 meters above sea level in the pastoralist area of the District, but parts of the northern agricultural zone rise to 3,000 meters. The pastoralist area receives 500-750 milimeters (mm) of rainfall on average, with the agricultural areas receiving 750-1250mm. The vegetation cover is predominantly savanna, characterized by open and wooded grasslands. Narok is the seat of the Maasai-Mara game reserve which houses a great variety of game species. Economic activities are dominated by nomadic pastoralism, tourism and wheat farming. The inhabitants are predominantly of the Maasai ethnic group.

Four local dispensaries that regularly tested for brucellosis were selected for data collection. Two, Siyiapei and Olasiti, are located in relatively well settled areas bordering the agricultural zone (Figure 1). Siyiapei was the first health unit to begin

testing for brucellosis in the district. Suspected brucellosis patients have been referred to Siyiapei from other clinics and dispensaries. Maji Moto is located south of Narok town in an unsettled pastoralist area. The fourth dispensary, Mararianta is located on the north-eastern edge of Maasai-Mara game reserve. It receives patients from both Kenya and Tanzania. Mararianta is purely pastoral with no settlements, save for small villages adjacent to tourist lodges.

These data collection sites (dispensaries) were distantly separated and probably difficult to reach (Figure 1). The detailed case (patient) records for these dispensaries were obtained from individual dispensary patients' record books. Morbidity records for each dispensary were obtained from the Narok district Hospital (NDH) where monthly reports are submitted by all dispensaries. NDH is the central health unit in the district, located within the municipality (Figure 1).

Fig.:1 Map of Narok showing the data collection sites (dispensaries) and main market centres: Inset, map of Kenya showing the location of Narok District.



3.2 ANALYSIS OF SUMMARY MORBIDITY RECORDS

Morbidity data for the previous 7 years (1986-1992) were obtained from the Narok District Hospital, where all dispensaries are mandated to submit monthly morbidity reports. All the patients visiting the reporting clinics with selected diseases (or syndromes) of interest were included in the study and will be referred to as the selected patients[1] through out this dissertation. Selected diseases included brucellosis and diseases routinely reported and showing common signs and symptoms with brucellosis, namely; malaria, rheumatism and pyrexia of unknown origin. These diseases share common symptoms like fever, arthralgia, myalgia, headache, backache, night sweats, non-specific body pain, malaise and weight loss, and will subsequently be referred to as selected diseases[2]. Thus, the data considered included all morbidity events of these four selected diseases reported to Narok District Hospital during the 7 year period.

3.2.1 Data Analysis

The proportional morbidity of the selected diseases was calculated by dividing the total number of cases of each by the total number of patients seen over the study period. Graphs were prepared (Freelance, Lotus Development Corp., 1988) to display the monthly and annual trends in the occurrence of brucellosis and the other selected diseases.

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[1] Patients presenting with the symptoms of interest who were included in the study.

[2] Diseases included as differentials for brucellosis by virtue of sharing common signs and symptoms

3.3 THE STUDY OF DETAILED CASE RECORDS

3.3.1 Study Population and study of detailed patient records from brucellosis testing dispensaries

To better investigate clinical signs and symptoms associated with brucellosis and malaria diagnosis, a more detailed study of patient records from four selected health units that routinely tested for brucellosis, namely, Siyiapei, Olasiti, Maji Moto and Mararianta were studied for the two year period (1991-92). All patient records listing symptoms of fever, arthralgia, myalgia, headache, backache, night sweats, non-specific body pain, malaise and weight loss were selected. Any combination of these symptoms will be labelled as flu-like[3] signs and symptoms and will be referred to as such throughout the dissertation.

In addition to clinical signs and symptoms, details of date seen, name, age, sex, residence, duration of illness, complaints (symptoms), diagnosis (clinical and or laboratory) and treatment were extracted from each selected record. Patients of all age groups from both sexes were considered. Information on the occupation of patients was not available from the records.

3.3.2 Data Analysis

The data was entered into a data base (Dbase IV) package for handling. Descriptive statistics of the clinical symptoms, duration of illness and age for brucellosis and malaria patients (listed in Table 1) were estimated in SAS (Statistical

[3] Non-specific signs and symptoms common to brucellosis and the diseases selected as its differentials

Analysis System Institute, 1988). Malaria and brucellosis cases were graphed by age class in the Freelance (Lotus Development Corp., 1988). The proportional morbidity of brucellosis and malaria among flu-like patients was calculated by dividing the number of test positive patients by the total number of records examined.

For the subsets of patients tested for brucellosis or malaria, associations between test positive outcome and clinical features (Table 1) were investigated using logistic regression. The stepwise procedure of BMDP-LR (BMDP Software Inc. Release 7, 1992) was used. Variables were allowed to enter and exit the model one at a time at a 90% level of significance. The hierarchy principle whereby simple linear terms were retained in the model for all interacting variables even when the latter did not meet the selection criteria (Bishop *et al.*, 1975) was followed. A goodness-of-fit was assessed by comparing the observed versus predicted values provided in the cost matrix of BMDP-LR.

Table 1. The clinical features of patients tested for brucellosis or malaria that were considered for inclusion in logistic regression models.

	Description
Abdomen	Non-specific abdominal pain reported by the patient
Age	Age at time of treatment (divided into classes).
Blood changes	Haematological changes; jaundice and pale mucous membranes observed by the clinician
Bone pain	Pain felt in the bone (according to patients)
Chills	Cold spells sometimes accompanied with shivering experienced by patients in the course of illness
Duration	Duration of illness prior to visit (divided into classes: >1 week, < 1 week, >2 weeks <=2 months and > 2 months.
Emesis	Spells of vomiting experienced by patients in the course of illness
Fever	Body temperature above normal at time of attendance measured by the clinician
Headache	Atraumatic ache in the head reported by the patient
Joint	Joint swelling observed by the clinician
Malaise	Generalized body weakness reported by the patient
Lameness	Impaired walking ability observed at time of attendance
Nervous	Disturbed neurological integrity observed by the clinician
Pain	Joint pain reported by the patient
Sex	Male or female
Sore-throat	Throat pain or sore throat or recurrent tonsillitis reported at time of attendance
Sweat	Night sweat reported by the patient

CHAPTER FOUR.

RESULTS

4.1 SUMMARY MORBIDITY DATA

A total of 2731 monthly reports comprising a total of 1,037,875 cases from all health units reporting to the Narok District Hospital over the previous seven year period (1986-92) were studied. Of these, 538,182 (51.9%) had flu-like symptoms consistent with the diseases of interest for this study (brucellosis and its main differentials). Brucellosis was diagnosed in 4,211 (0.8%), rheumatism in 38,339 (7.1%), pyrexia of unknown origin (PUO) in 12,980 (2.4%) and malaria in 426,652 (79.3%) of flu-like cases. The estimate for brucellosis was considered unrepresentative because only four out of sixty reporting dispensaries were testing and consistently reporting brucellosis. The records of one of the dispensaries considered in the detailed study of records (Mararianta) had not been submitted to the District Hospital consistently and thus, were not included in the morbidity statistics (Appendix 1).

A total of 44,062 patients were seen at the four testing dispensaries (mean of 6295 patients per year) over the study period (1986-92). Of these, 17,601 (an average of 2514 per year) had flu-like symptoms consistent with brucellosis. Brucellosis was diagnosed in 2,404 (343 per year, about 13.7%) of those showing the symptoms of interest. The rest were diagnosed as follows; rheumatism 2,840 (16.1%), pyrexia of unknown origin (PUO) 167 (1.0%) and malaria 12190 (69.3%). The overall proportional morbidity of brucellosis (among all the attendances) over the period of study in the four dispensaries[4] was 5.5%. Rheumatism and PUO had 6.4 and 0.4%

[4] Four dispensaries contributing detailed case records, viz: Siyiapei, Olasiti, Maji Moto and Mararianta.

while malaria had 27.7% proportional morbidities respectively. Figure 2 shows the variation in case loads of brucellosis and selected differential diseases at the testing dispensaries.

Using the detailed data collected from 1991-92, 178 patients from the testing health units had a tentative diagnosis of rheumatic joint pain. Seventy-seven (43.3%) of these were tested for brucellosis and 39 (50.7%) were positive to the RB test. Assuming that 50.7% of those with a diagnosis of rheumatism could test positive for brucellosis, the overall proportional morbidity of brucellosis in all patients with flu-like symptoms would rise to 8.7%.

Brucellosis and malaria were diagnosed throughout the year with malaria showing seasonal peaks during the rains (Figure 3) with an increase in its reporting over the years (Figure 5). Brucellosis showed minor peaks in March and October. The yearly and monthly trends of brucellosis and other diseases with flu-like symptoms are displayed graphically for the testing and all dispensaries (Figures 3, 4).

The pattern and mean monthly cases of unspecific fevers (rheumatism and PUO) (Figure 6) were different considering all reporting dispensaries (Figure 5) and those testing for brucellosis separately (Figure 4). The mean monthly reported cases of rheumatism and PUO was higher for dispensaries not testing for brucellosis (Figure 6).

Figure 2: The case frequency (load) of selected diseases with flu-like symptoms reported by three of the dispensaries testing for human brucellosis in Narok district, 1986-92.

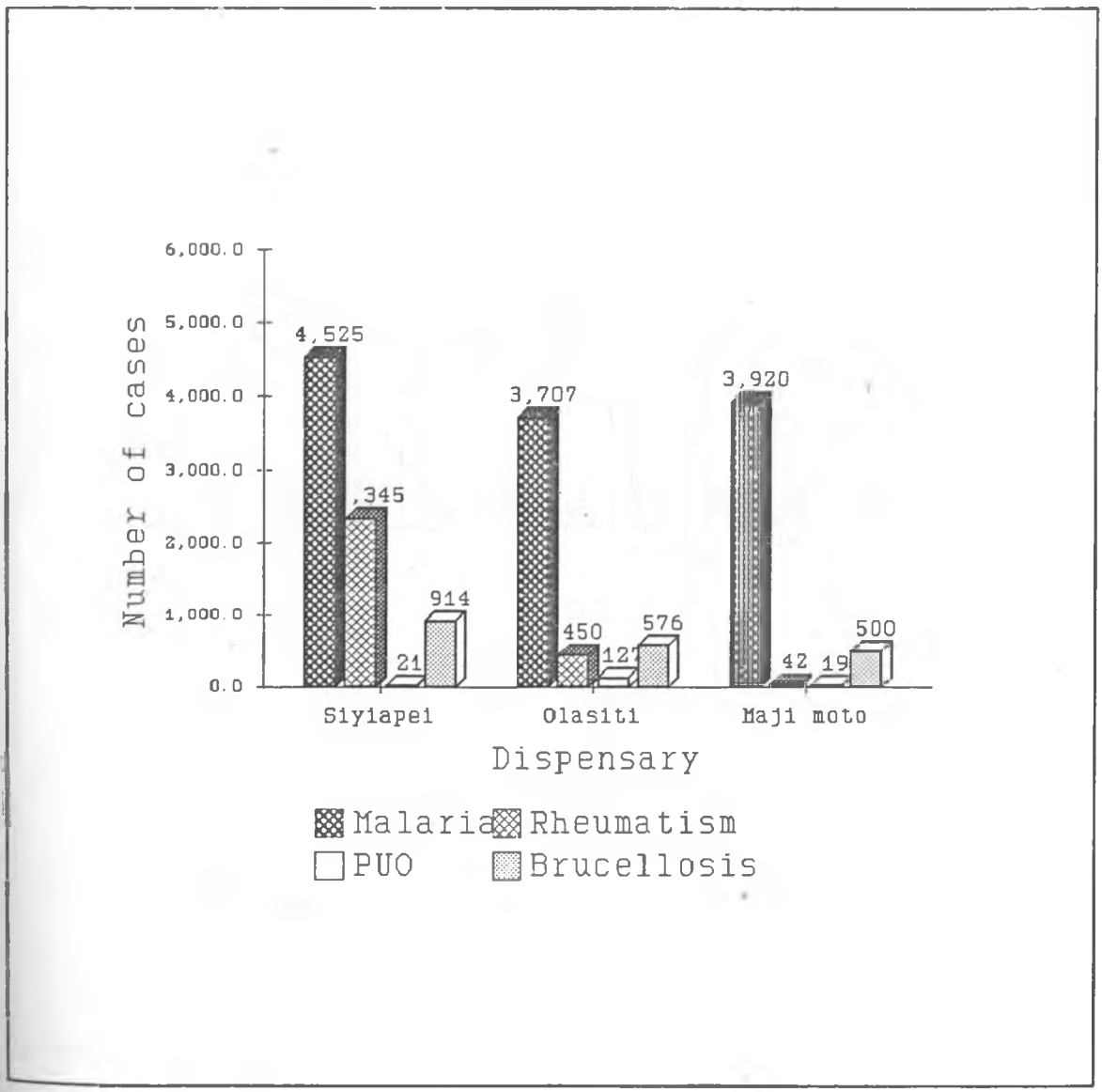


Figure 3: Monthly (January-December) reported occurrence of human brucellosis and malaria in Narok District, 1986-1992.

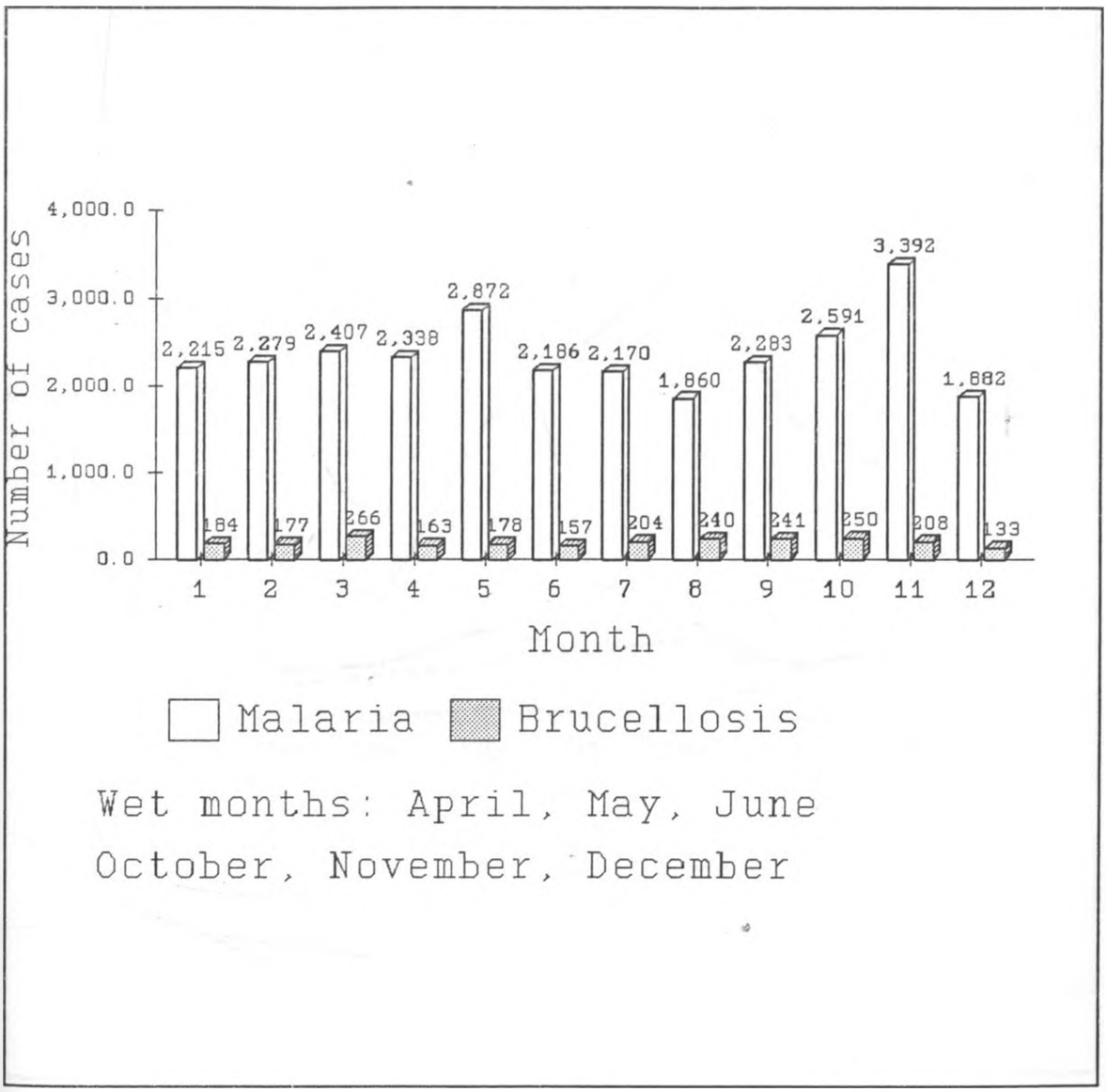


Figure 4: Annual trends of human brucellosis and selected diseases with flu-like symptoms at the brucellosis testing dispensaries in Narok, Kenya, 1986-92.

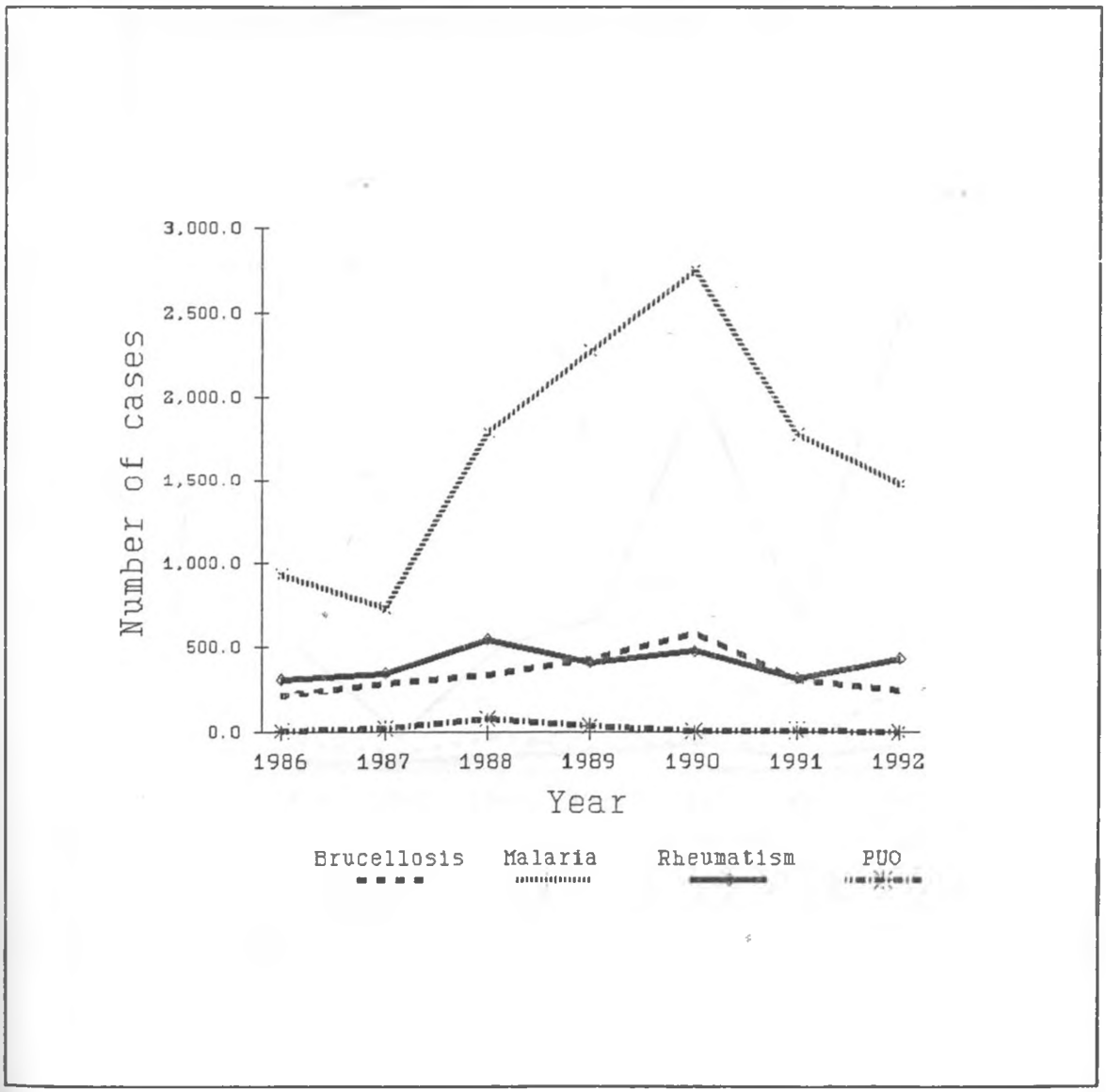


Figure 5: Yearly trends of selected diseases with flu-like symptoms at all the dispensaries reporting to the district hospital in Narok, Kenya. 1986-92.

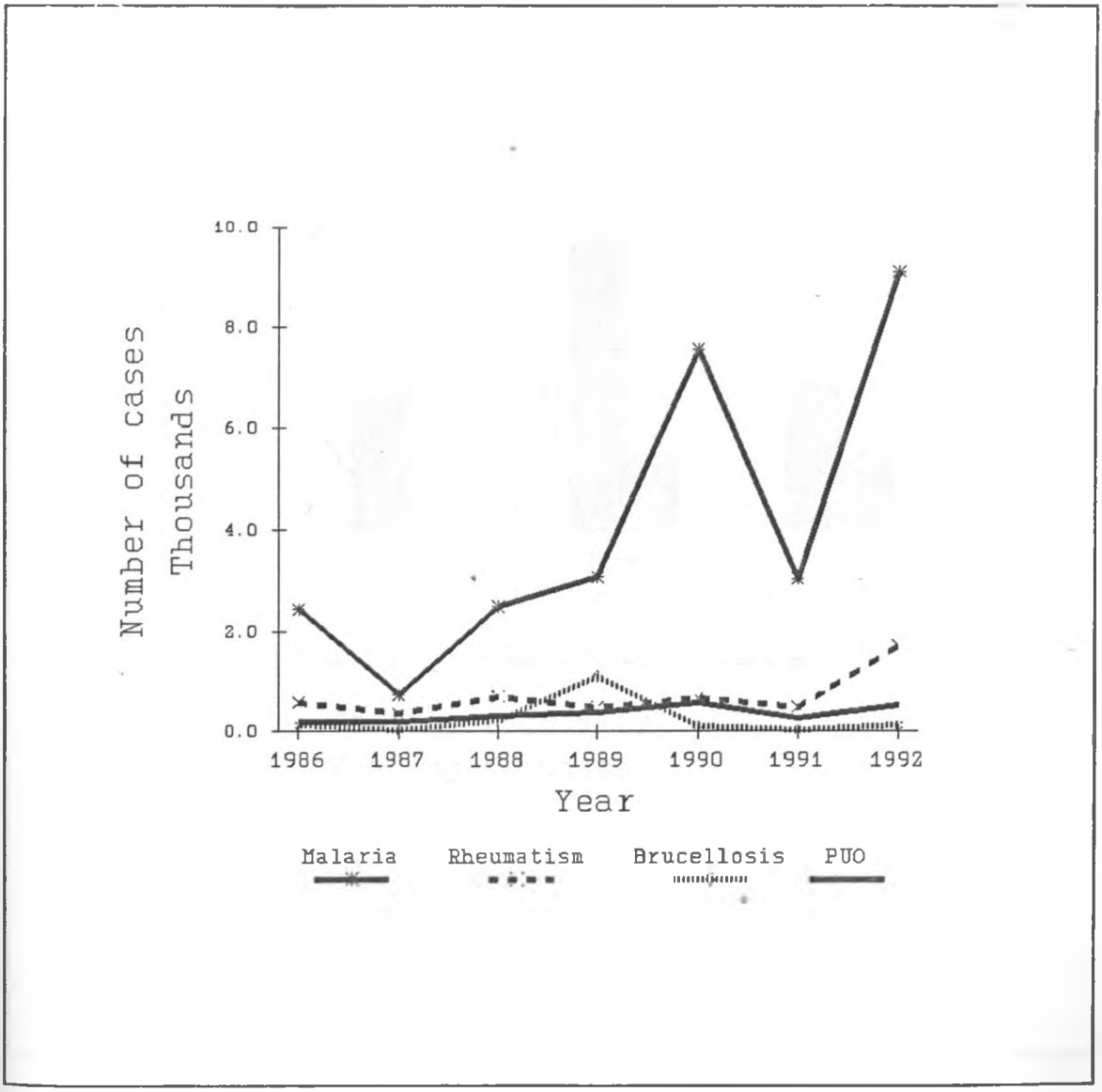
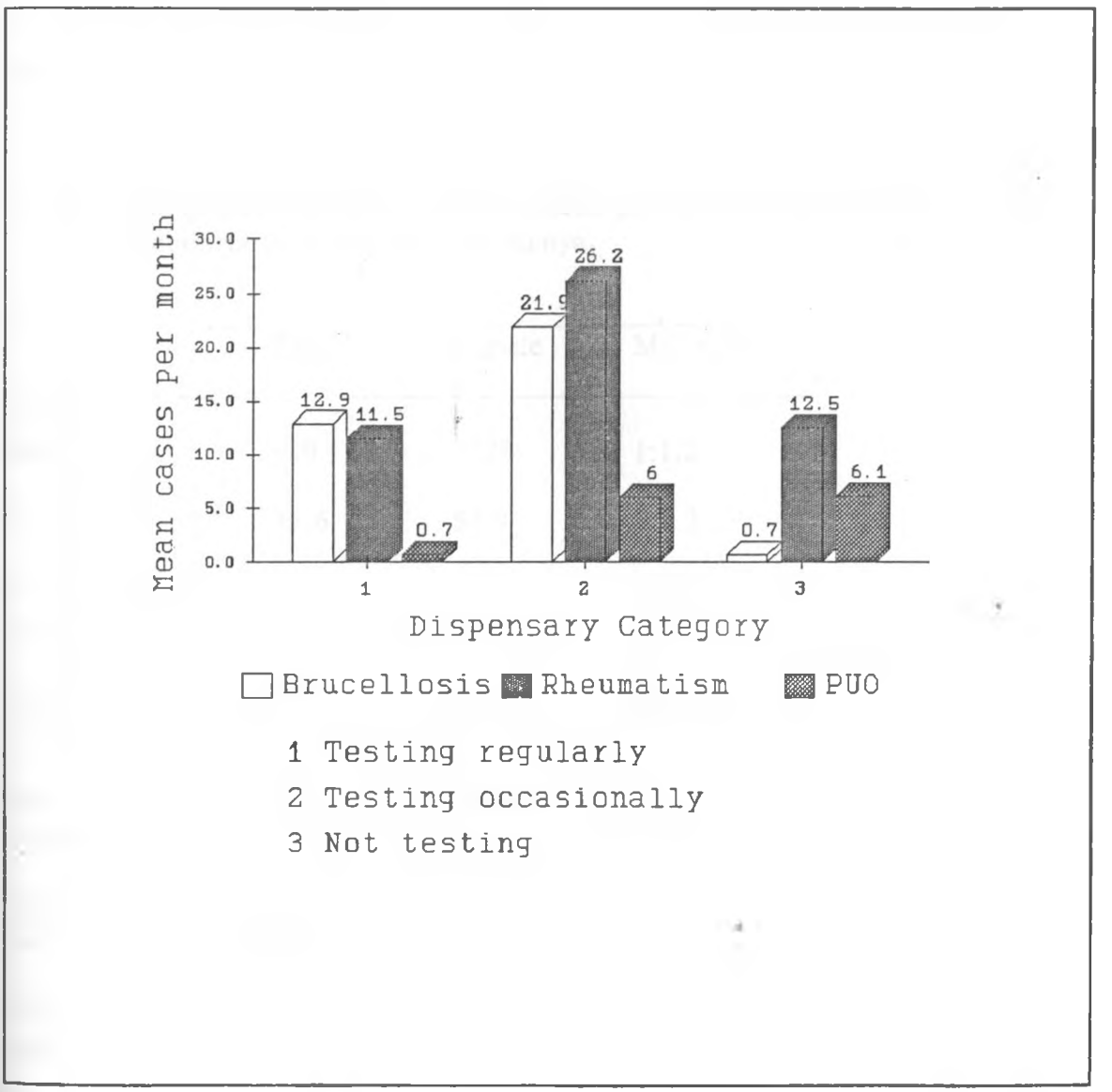


Figure 6: Comparison of the reporting rate of human brucellosis, rheumatism and PUO among the different categories of brucellosis testing dispensaries in Narok district, Kenya, 1986-1992.



4.2 DESCRIPTION OF INDIVIDUAL PATIENTS' RECORDS

A total of 2077 patient records from four health units that routinely tested for brucellosis were examined. Malaria had an equal (balanced) gender distribution (χ^2 = 2.5, p = 0.115), but brucellosis diagnosis was more common in females (χ^2 = 3.24, p = 0.072) (Table 2). The males tested, however, had a higher reactor rate to the RB test.

Table 2. The gender attributes of 2077 febrile patients examined for brucellosis and malaria in Narok District, Kenya.

	Male	Female	M:F ratio
Total Number seen	949	1128	1:1.2
Percent of total	45.6	54.9	1:1.2
Number tested for brucellosis	264	361	1:1.4
Number positive for brucellosis	196	244	1:1.3**
Percent positive for brucellosis	74.2	67.6	1.1:1
Number tested for malaria	219	246	1:1.1
Number tested for malaria	154	156	1:1*
Percent positive for malaria	70.3	63.3	1.1:1

Key: M = male, F = female.
** = Significant difference between sexes
* = No significant difference between sexes

The age distribution of brucellosis and malaria patients is presented in Figure 7. Brucellosis patients were aged between 1 and 80 years with an average of 27 years (95% CI 25-28). Malaria patients were aged between 1 month and 87 years with a mean of 21 years (95% CI 20-23). The age distribution of brucellosis showed a peak at the 11-15 year age category while malaria peaked at the 1-5 year old category (Figure 7). Brucellosis seemed to occur relatively more frequently in older patients (past 30 years of age) than malaria.

The symptoms recorded for the selected patients were joint pains (68.2%), fever (58.3%), headache (43.4%), malaise (23.2%), joint swelling (9.0%) and chills (8.2%). Other symptoms recorded included night sweats, lameness, bone pains, sore throat, abdominal pain, emesis, insomnia and other nervous disturbances among others. A summary of reported clinical features is presented in Tables 3 a and b.

The duration[5] of illness for test positive patients showed that brucellosis patients had a longer pre-visit duration of illness than malaria patients (Table 3 a and b). Majority of patients with a diagnosis of malaria (53.2%) were sick for less than one week before seeking medical attention, but most of those with a diagnosis of brucellosis (65.2%) were sick for more than two weeks (Table 3 a). The mean pre-visit duration of illness for malaria patients (test positive) was 47.9 days (95% CI 31.9-63.9 days) if 25 patients with a duration of five or more months (Table 4) were included. Among these 25, 75% (6/8) of those tested for brucellosis were positive. On ignoring patients with a duration greater than 150 days, the mean duration for malaria decreased to 13.5 days (95% CI 11-15.9 days). Brucellosis patients had a mean

[5] Recorded time period over which the patient had been unwell before visiting the health facility for treatment

duration of illness of 204.3 days (95% CI 162.8-245.8 days). Only 20.5% of brucellosis cases were diagnosed within 2 weeks of onset. The vast majority were only diagnosed as long standing (subacute or chronic) brucellosis. The duration of illness was unknown for 63 (14.3%) test positive brucellosis and 28 (9%) test positive malaria patients respectively (Table 3 a and b).

The diagnosis of malaria was mostly based on clinical symptoms (55%) with laboratory confirmation being used on only (22.4%) of these. The majority of those tested were positive for plasmodium parasites (67%). All the suspected brucellosis patients were tested and about 71% were positive.

The proportion of test positive malaria and brucellosis among the detailed study patients was 14.9% and 21.2% and that from summary morbidity data 41% and 5.5% respectively. For rheumatism, it was 3.7% and PUO 1.3%.

Table 3 a: Description of the clinical features and assessment of their predictive ability and that of duration, age and sex of 625 patients tested for brucellosis using the Rose-Bengal plate test in Narok district, 1991-1992.

Symptom	Number with symptom	% patients with symptom	% test +ve with symptom	% test -ve with symptom
Joint pain	576	92.2	90.9	95.1
Fever	188	30.1	28.9	33.0
Headache	151	24.2	22.3	28.7
Joint swelling	142	22.7	22.1	24.3
Malaise	68	10.9	10.0	13.0
Lameness	57	9.1	11.1	4.3
Sore throat	42	6.7	7.5	4.9
Abdominal pain	32	5.1	5.2	4.9
Bone pain	25	4.0	3.6	4.9
Chills	15	2.4	2.1	3.2
Emesis	14	2.2	1.8	3.2
Night sweat	10	1.6	1.6	1.6
Blood changes	8	1.3	1.1	1.6
Nervous	2	0.3	0.5	0.0
DURATION (In days)				
1 - 6	59	9.4	7.3	14.6
6 - 14	79	12.6	13.2	11.4
15 - 60	171	27.4	28.4	24.9
61 - 120	97	15.5	18.4	8.7
> 120	130	20.8	18.4	26.5
Unknown	89	14.2	14.3	14.1
AGE (years)				
0-5	24	3.8	4.6	2.2
6-20	244	39.0	43.2	29.2
21-55	289	46.2	41.8	56.8
>55	48	7.7	7.5	8.1
Unknown	20	3.2	3.0	3.8
SEX				
Male	264	42.2	44.6	36.8
Female	361	57.8	55.5	63.2

NB: Features with a bigger difference between the percent test positive with symptom and percent test negative with symptom were considered better predictors of the positive test result and vice versa.

Table 3 b: Description of the clinical features and assessment of their predictive ability and that of duration, age and sex of 465 patients tested for malaria using the Blood Smear test in Narok District, 1991 to 1992.

Symptom	Number with symptom	% patients with symptom	% test +ve with symptom	% test -ve with symptom
Fever	334	71.8	77.1	61.3
Joint pain	245	52.7	40.7	76.8
Headache	234	50.3	47.7	55.5
Malaise	167	35.9	34.5	38.7
Emesis	78	16.8	18.4	13.6
Abdominal pain	76	16.3	16.5	16.1
Chills	65	14.0	14.2	13.6
Nervous	40	8.6	9.4	7.1
Blood changes	24	5.2	5.8	3.9
Night sweat	13	2.8	2.3	3.9
Joint swelling	10	2.2	0.3	5.8
Sore throat	9	1.9	2.6	0.7
Bone pain	3	0.7	0.7	0.7
Lameness	1	0.2	0.3	0.0
DURATION (days)				
1-6	220	47.3	53.2	35.5
6-14	100	21.5	22.6	19.4
15-60	55	11.8	9.4	16.8
61-120	12	2.6	2.3	3.2
>120	27	5.8	3.6	10.3
Unknown	51	11.0	9.0	14.8
AGE (years)				
0-5	104	22.4	29.0	9.0
6-20	105	22.6	22.9	21.9
21-55	212	45.6	40.3	56.1
>55	10	2.2	1.6	3.2
Unknown	37	8.0	6.8	10.3
SEX				
Male	220	47.3	49.7	42.6
Female	245	52.7	50.3	57.4

NB: Features with a bigger difference between the percent test positive with symptom and percent test negative with symptom were considered better predictors of the positive test result and vice versa.

Table 4: The Brucellosis Test Response in suspected malaria patients who had a duration (in days) of illness of more than five months

No.	AGE	SEX	DURATION	DIAGNOSIS	BS	BSRESULT	BT	BTRESULT
1	30	F	365	BMa	1	-	1	+
2	38	M	730	Ma	1	-	0	-
3	20	F	365	Ma	1	-	0	-
4	15	M	1460	BMa	1	-	1	+
5	42	F	365	Ma	1	-	0	-
6	35	F	448	BMa	1	-	1	-
7	40	F	730	R	1	+	0	-
8	27	F	180	B	1	-	0	-
9	20	F	365	Ma	1	+	0	-
10	43	M	730	MaO	1	+	0	-
11	60	F	365	Ma	1	-	0	-
12	23	F	1095	Ma	1	-	0	-
13	23	F	1095	Ma	1	+	0	-
14	34	M	730	BMa	1	-	1	+
15	23	F	365	Ma	1	+	0	-
16	22	M	1095	MaO	1	-	0	-
17	13	M	365	BR	1	+	1	+
18	12	M	180	Ma	1	-	0	-
19	14	M	180	Ma	1	+	0	-
20	19	M	525	MaO	1	+	0	-
21	30	M	730	BMa	1	-	1	+
22	35	F	210	Ma	1	+	0	-
23	30	M	210	BMa	1	-	1	-
24	38	M	180	BMa	1	-	1	+
25	2.5	M	365	MaO	1	+	0	-

KEY:

<u>Test symbols</u>
BS = Blood Smear test (1 = done, 0 = not done)
BSResult = BS result (+ = positive, - = negative)
BT = Brucellosis Test (1 = done, 0 = not done)
BTResult = BT result (+ = positive, - = negative)

<u>Sex symbols</u>
M = male, F = female

<u>Diagnosis Code</u>
B = Brucellosis
Ma = Malaria
BMa = Brucellosis/Malaria
R = Rheumatism
BR = Brucellosis/Rheumatism
O = Other condition eg pneumonia

4.3 TREATMENT OF CASES

4.3.1 Brucellosis Patients

The proportion of patients who tested positive for brucellosis by therapeutic regimen is reported in (Table 5). According to WHO guidelines, only those treated with tetracycline-streptomycin or doxycycline-rifampin received adequate therapy.

Table 5: The reported treatment of four hundred and forty cases of human brucellosis in Narok, Kenya 1991-1992.

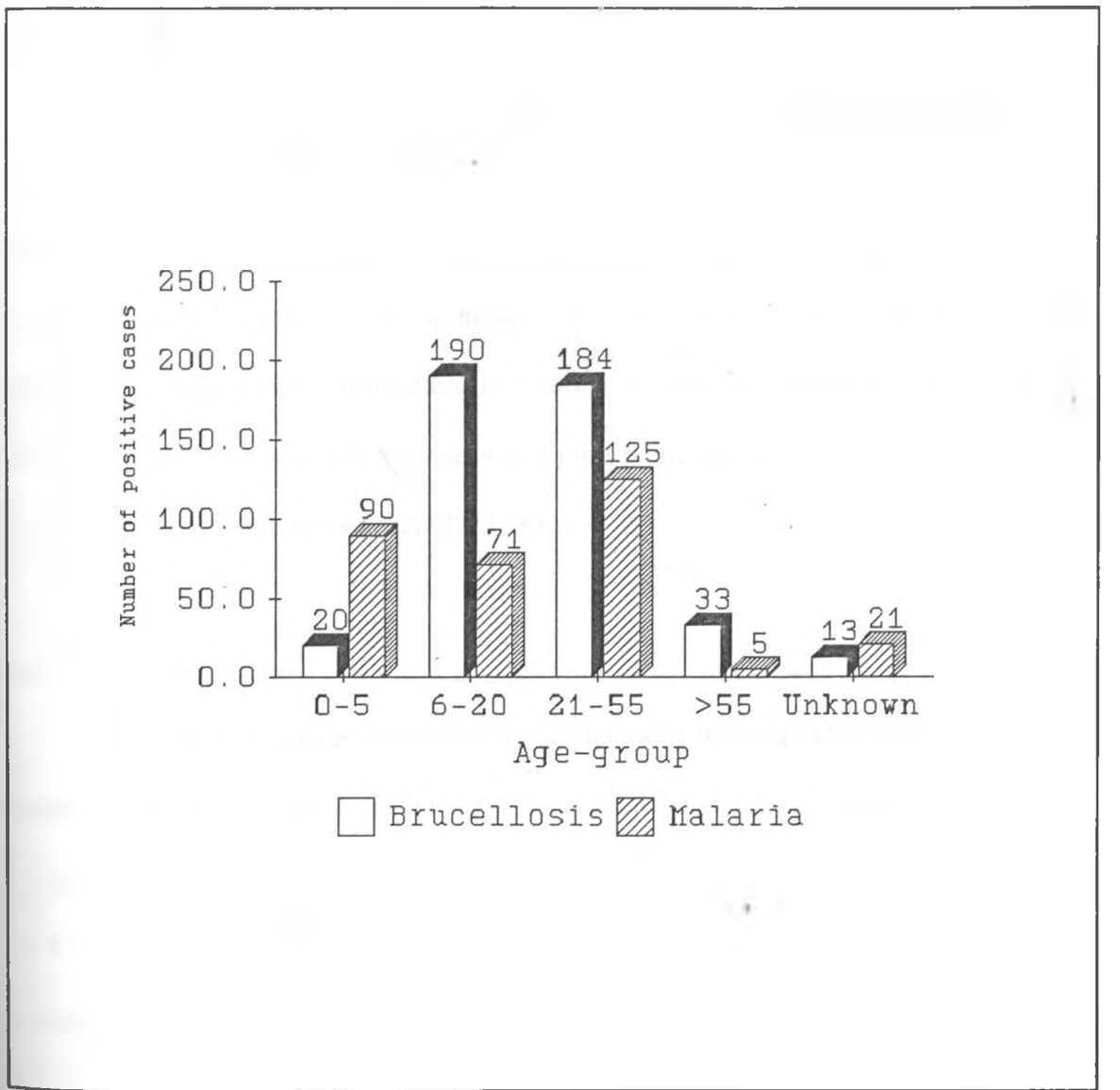
DRUGS USED	Number Treated	Percent of all patients
Tetracyclines and streptomycin	175[a]	39.8
Tetracyclines, Streptomycin, and Sulphonamide*	172[a]	39.1
Others	265	60.2
Total	440	100

NB: [a]-Represents adequate treatment (inclusive of each other)
*-Sulphamethoxazole + Trimethoprim (Potentiated sulphonamide).

4.3.2 Malarial Patients

Most of the people diagnosed positive for malaria were treated using chloroquin (80.6%). Fansidar^{R} and quinine were used in 13.2% and 4.8% of malarial patients respectively. Eleven patients (3.5%) were not given any antimalarial agents in their treatment. One got only iron tablets, six got painkillers, three got nothing at all and one was given a combination of painkillers and multivitamins. Painkillers were administered to 212 (68.4%) of the patients. Of these about 81% patients got a combination of painkillers and chloroquin, 14% fansidar^{R} and 5% quinine. Multivitamins, iron tablets, valium and indocin were administered to 9.7%, 6.4%, 7.1% and 5.5% of all malarial patients respectively.

Figure 7: Occurrence of human brucellosis and malaria by age-group (years) from among 2077 patients seen at brucellosis testing dispensaries in Narok District, Kenya 1991-1992



4.4 STATISTICAL MODELS OF CLINICAL SYMPTOMS FOR TEST REACTORS

4.4.1 Brucellosis

A model for clinical symptoms associated with positive reactions among patients clinically suspected to have brucellosis and subjected to a confirmatory Rose-Bengal test is presented in Table 6.

In brucellosis patients, headache (OR = 19.8, p = 0.0041), joint pain (OR = 4.26, p = 0.0093), duration (OR = < 1, p = 0.0029), lameness and their interaction terms were significant (Table 6). At a 0.29 cut-point, about 62% of brucellosis patients could be correctly predicted by the model, with a sensitivity of 67% and specificity of about 52% (Appendix 5). Joint pain, increasing duration and headache, and the interactions of lameness with headache and joint pain, significantly increased the odds of testing positive for brucellosis (Table 6).

4.4.2 Malaria

A model for clinical symptoms associated with malaria detection on blood smear examination is presented in Table 7. For malarial patients tested using blood smears, joint pain (OR = 7.7, p = 0.0001), headache (OR = 2.2, p = 0.07), age (p = 0.04), emesis (p = 0.2) and blood changes (OR = 1.6, p = o.6) and their interaction terms were significantly associated with a positive blood smear result (Table 7).

The model for malaria correctly predicted 67% of the test result with a sensitivity of 64% and specificity of about 73% at a 0.41 cutpoint respectively (Appendix 5). Age class (young), headache, joint pain, abdominal pain and blood

changes singly, and the interactions between nervous signs and fever, emesis and blood changes, emesis and sex (being male) and chills and decreasing age (class), increased the odds of a positive test significantly (Table 7).

Table 6: The final stepwise Logistic regression model of brucellosis test result (BTR) for brucellosis patients considering the main effects and interactions.

VARIABLE		β	SE(β)	OR	P-VALUE[a]
Intercept		-1.476	0.602	0.23	0.007
Duration class[b]	6-14	-0.885	0.378	0.41	0.003
	15-60	-0.900	0.326	0.41	
	61-120	-1.418	0.393	0.24	
	>120	-0.431	0.332	0.65	
	Unknown	-0.589	0.369	0.56	
Joint pain		1.449	0.558	4.26	0.009
Lameness		-1.308	0.457	0.27	0.004
Headache		2.985	1.040	19.80	0.004
Joint pain* headache		-2.969	1.060	0.05	0.004
Lameness*headache		2.125	1.140	8.38	0.074

[a] p-value of likelihood ratio test
[b] compared to the 1-5 day duration class
* -Interaction symbol.

Table 7. The final stepwise logistic regression model for blood smear result (BSR) in malaria patients considering the main effects and interactions.

VARIABLE		β	SE(β)	OR	P-VALUE[a]
Intercept		-2.372	0.390	0.09	0.000
Ageclass[b]	6-20	0.380	0.443	1.46	0.041
	21-55	0.621	0.411	1.86	
	>55	1.324	0.819	3.76	
	Unknown	1.431	0.514	4.18	
Headache		0.774	0.428	2.17	0.070
Joint pain		2.039	0.391	7.68	0.000
Emesis		-0.341	0.287	0.71	0.234
Blood changes (anaemia and jaundice)		0.490	0.827	1.63	0.554
Emesis*blood changes		2.481	1.390	12.0	0.058
Blood changes* headache		-3.716	1.440	0.02	0.002
Headache*joint pain		-1.157	0.492	0.32	0.018

[a] -p value of likelihood ratio test
[b] -Compared to the 1-5 year age class
* -Interaction symbol.

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[a] -p value of likelihood ratio test
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* -Interaction symbol.

CHAPTER FIVE

DISCUSSION

With a human population of about 400,000 and over 1 million head of livestock, there are about 2.5 potential livestock sources per person for human infection with brucellosis in Narok. This, enhanced by free interaction between a large wildlife population with humans and livestock, favours cross-infection and therefore makes brucellosis a potentially important zoonosis in Narok.

The retrospective case-records approach was chosen mainly because of its merits of ease and economic feasibility. While it is difficult to ensure the correctness of all data collected, this study allows for a qualitative assessment of the brucellosis situation in Narok using existing resources. In addition, inferences about the association of clinical signs and the occurrence of both brucellosis and malaria are useful guides in planning follow-up studies. Overall, despite the possible limitations in collecting health clinic data retrospectively, the observation of Kelsey *et al.* (1984) that plausible causal inferences can be expected from retrospective studies is considered true in this study.

5.1 EXTENT OF THE PROBLEM

From the findings of this study, it is difficult to arrive at an exact estimate of brucellosis occurrence in Narok District. A large proportion (52%) of people seeking treatment at health units in Narok suffer from flu-like ailments, suggesting that these form the bulk of cases in dispensaries. Malaria was the most important cause of flu-like symptoms, comprising about 79% of the cases, though, only 22% of these were

confirmed by blood smear examination. Thus, laboratory tests are rarely used for malaria diagnosis. From this data, it could not be determined whether the malaria suspect patients whose blood smears were examined were representative of all malaria patients or were just the less obvious clinical cases. Clinicians may not need to rely on blood smear examinations since the predictive value of a clinical diagnosis of malaria may be relatively high due to its high prevalence. One suggestion might be to reserve differential laboratory diagnosis of the various causes of flu-like diseases to patients with long (> 14 days) duration of illness (Table 3).

Other causes of flu-like illnesses were less frequently diagnosed. Brucellosis was the least reported (0.8%) cause. This low rate of reporting was due to lack of awareness and diagnosis, as only 4 out of 60 reporting dispensaries tested for brucellosis consistently. Broad (syndrome) clinically-based diagnoses of diseases with flu-like symptoms such as rheumatism (7.1%) and PUO (2.4%) were more commonly reported than brucellosis. However, if data from dispensaries that test for brucellosis is used, brucellosis is much more commonly diagnosed with a proportional morbidity of (13.7%) among patients with flu-like symptoms. Unlike malaria, brucellosis diagnosis in Narok relies on both clinical and laboratory diagnosis (Rose-Bengal test) rather than clinical evidence. The strategy is to test patients with prolonged 'unresolved malaria' for brucellosis. This suggests that little effort is made to diagnose brucellosis clinically in the acute stage. This reliance on laboratory testing may be wise given the low sensitivity, specificity and predictive values of clinical signs in brucellosis diagnosis (Table 6, Appendix 5).

The summary morbidity data obtained in this study gave different estimates of brucellosis occurrence from the detailed case reports. The summary data is likely a

gross underestimate of the true situation since most dispensaries do not consider and test for brucellosis (Appendix 1). If the proportional morbidity of brucellosis is estimated only from the summary morbidity data of the four testing dispensaries, brucellosis accounted for 5.5% (55 per 1000) and malaria 27.7% (277 per 1000) of total cases, and 13.7% (137 per 1000) and 69.3% (693 per 1000) of flu-like cases respectively. The proportional morbidity of brucellosis increased to 21.2% if only detailed case records from the two year (1991-92) period were used. These estimates are probably more realistic. Although it can be argued that the four testing clinics were actually "referral" centres for brucellosis, the history has been that each time a new clinic begins to test for brucellosis, a large number of "new" cases are uncovered without decreasing the number of cases in the old clinics. Thus, there is probably more brucellosis in Narok District than is presently reported.

It is suspected that clinics not testing for brucellosis were misdiagnosing brucellosis cases as either malaria, rheumatism or pyrexia of unknown origin (PUO). As support to this hypothesis, in the 4 dispensaries testing for brucellosis, 51% (39/77) of patients, diagnosed clinically as rheumatism and tested at a later visit for brucellosis, were positive. Also, non-testing clinics had a much higher proportion of rheumatism and PUO cases than brucellosis testing clinics (Figure 2) and showed a concomitant variation suggestive of mistaken diagnosis (Table 5). Seventy-five percent (6/8) of suspected malaria patients with a long duration of illness tested positive for brucellosis (Table 4), implying that long standing malaria-like symptoms are caused by brucellosis.

Malaria has been documented as the main disease obscuring the diagnosis of other febrile ailments in Africa (Schwabe, 1984). Other diseases such as Q-fever

(Vanek and Thimm, 1976), Rift-Valley fever (Kilelu and Kirui, 1993), visceral leishmaniasis (Mutero *et al.*, 1992) and other zoonotic infections, need to be considered in some areas, but in most pastoralist areas brucellosis is an important cause of flu-like symptoms (Schwabe, 1984; Roy *et al.*, 1965). Based on results from this study, malaria accounted for 41% (410 per 1000) of all the ailments and 52%-55% of flu-like cases, slightly higher than Brinkmann and Brinkmann's (1991) estimate that malaria causes about 40% of fever cases in Africa.

The preponderance of human brucellosis among the Maasai of Narok is attributable to a number of factors that favour its spread and high-level endemicity. The Maasai culture of keeping large herds of often untended animals, presence of animal brucellosis and absence of a control program, close association between people and animals, low level of sanitation and hygiene, consumption of raw animal products and low public health awareness and facilities, all contribute to human infection with *Brucella*. In addition to public health problems, animal productivity of sheep, goats and cattle is also likely to be affected by brucellosis infection. For these reasons, further studies to establish the actual incidence and prevalence of brucellosis in livestock and humans, and evaluate the effect of brucellosis on animal production in Narok District are required.

5.2 SPECIFIC DISEASE SYMPTOMS AND DIAGNOSIS

The basis of any clinical diagnosis is the symptoms expressed by the patient and signs observed by the clinician. In brucellosis, the clinical presentation is variable due to its multi-system involvement. Many of the signs and symptoms resemble those of malaria, Q-fever and Rift-valley fever among others. The clinical features of the

positive brucellosis and malaria patients were generally indistinguishable save for the age class and duration of illness and the proportion of patients involved for each disease (Table 3 a&b and Appendix 3&4).

In Narok, clinicians use an elimination approach for patients presenting with flu-like symptoms. These patients are initially treated for malaria. Brucellosis is only considered if the patients do not respond to the initial treatment. This approach, may be reasonable for many classes of patient (since malaria is much more prevalent). However, in other patients with a higher pre-test probability of brucellosis (eg. older patients who are lame), brucellosis deserves early consideration. The current pattern of clinical diagnosis and treatment for patients with flu-like symptoms may be partly responsible for the chronicity of brucellosis in most patients. A more strategic approach encompassing patient history, epidemiology, physical examination and selective laboratory testing could lead to more rapid diagnosis of brucellosis with only minimal added cost.

While common symptoms were recorded for both malaria and brucellosis positive patients, symptoms differed in importance between the two diseases (Table 3). Joint pain, joint swelling and long duration of illness (Table 3a) were more common in brucellosis patients in Narok. Similar observations were reported by Oomen (1976) in a prospective study of brucellosis in Machakos District. The brucellosis logistic regression model shows that a short duration of illness was significantly associated with a positive Rose-Bengal test (Table 6), although the diagnostic strategy used by the clinicians in Narok District did not consider early diagnosis. Brucellosis had a higher morbidity in females than males ($\chi^2 = 3.24$, $p = 0.072$) tending to disagree with workers who have reported higher rates in males. This higher morbidity of brucellosis

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in females in Narok District can be explained by low attendance rate of men at health units (far away tending to animals) and their unwillingness to seek treatment for "minor illnesses".

In patients with a diagnosis of malaria, fever, headache and malaise occurred more frequently than in brucellosis patients. Malaria cases were characterized by a short duration (<15 days) and occurred in younger patients (Table 3b and 7) than brucellosis cases. Empirically, fever, joint pain and headache are suggestive of malaria when they occur over a short period of time (< 7 days), especially in young patients (Table 3b, Figure 7). The preponderance of fever in patients with a diagnosis of malaria, corresponding with its high frequency in young people (Figure 7) suggests that, this age-group is more susceptible to malarial parasites. This is supported by the work of Rougemont *et al.* (1991), who concluded that young patients (2-9 years) presenting with fever in West Africa were most likely to be suffering from malaria.

The value of routine (low-cost blood smear examination and Rose-Bengal plate test) malarial and brucellosis testing for patients with flu-like symptoms could not be established in this study. Of the patients with blood smears examined for malaria parasites, 67% were positive. However, it is not known whether patients with doubtful clinical presentations were more likely to be tested. The logistic regression model of clinical symptoms for malaria (Table 7) also predicted 67.2% of malaria cases (with a sensitivity of 62.1% and specificity of 77.4%) if a 0.35 cut-point was used (Appendix 5 ii).

Brucellosis was only diagnosed based on a positive Rose-Bengal test. Clinical diagnosis alone was never relied upon. This diagnostic strategy is due to the lower rate of occurrence and perceived lack of a classic clinical picture for brucellosis. However,

only highly suspect patients were tested for brucellosis, making the tested population unrepresentative of the population at risk in Narok District. Seventy percent of patients tested for brucellosis were positive. The logistic regression model of clinical symptoms correctly predicted test results 62.3% of the time (with a sensitivity of 66.6% and specificity of 52.2%) at a cut-point of 0.29 (Appendix 5 i).

Given the selection biases under which patients were tested for brucellosis and malaria in this study, it is not possible to establish clinical patterns (combinations of symptoms) by which only clinical diagnosis can be relied on and patterns in which ancillary laboratory tests (eg. blood smears and Rose-Bengal plate test) would be necessary adjuncts. These questions are being addressed in an on-going prospective study of patients with flu-like symptoms in Narok District.

5.3 TREATMENT

The current WHO recommended standard treatment for human brucellosis is a combination of doxycycline and rifampin (FAO/WHO, 1986). Dispensaries in Narok use the previously recommended combination of streptomycin and tetracycline (FAO/WHO, 1971) plus sulphonamide (Bactrim^{R} or septrim^{R}) (Table 5). The current treatment of human brucellosis in Narok was considered to be too costly (over Kshs. 1,500 per case), too long and too painful, by both patients and clinicians. Many instances were reported in which patients refused or cut-short brucellosis treatment. Clinicians are encouraged and provide a "standard" mode of treatment (Table 5). This has been recommended since no therapeutic regime has been found to be completely effective (Feitz et al., 1973; Colmenero et al., 1989, Hassan et al., 1971). Although not systematically recorded, it was reported that herbal medicines are commonly used

to treat brucellosis in Narok District. Clearly, many patients and clinicians are unhappy with current brucellosis treatment regimes, although, this should be expected since brucellosis is a difficult disease to treat. Further efficacy trials on alternative therapies deserve attention in future.

CHAPTER SIX

CONCLUSIONS AND RECOMMENDATIONS

6.1 CONCLUSIONS

Based on the findings of this study, several conclusions concerning brucellosis and malaria were drawn.

1. Brucellosis and malaria are prevalent in Narok district, although prevalence and incidence could not be precisely estimated in this study.
2. The proportional morbidity of brucellosis among "flu-like" diseases estimated from records of the four dispensaries testing for brucellosis is probably more accurate than the estimate based on records from all dispensaries in the district.
3. Both brucellosis and malaria have a seasonal pattern in their occurrence, but this is more pronounced for malaria.
4. Brucellosis is more commonly diagnosed in older patients. In younger patients ($\leq$ 5 years) brucellosis is rarely diagnosed while malaria is frequently diagnosed.
5. Brucellosis was rarely diagnosed in patients with a short duration of illness. The usual strategy for diagnosing and treating patients presenting with flu-like symptoms is to initially treat for malaria and to consider other differentials in non-responsive cases.
6. The differential diagnosis of diseases with flu-like symptoms is inadequate in most health facilities in Narok District. Brucellosis, while relatively common in Narok, is not considered at all in most dispensaries.

7. The diagnosis of both brucellosis and malaria could not be solely predicted using clinical signs. The clinical diagnosis of malaria will more often be correct since malaria is very common. However, the most appropriate application of laboratory tests to assist in the differential diagnosis of patients with flu-like symptoms requires further research (eg. testing the hypothesis that routine RB test and blood smear examinations for older patients might be valuable while young children could simply be treated as malarial patients on the initial visit).

8. The common occurrence of human brucellosis detected in Narok is associated with the lifestyle of the Maasai pastoralists. The specific highest-risk practices require further study. However, it is likely that given the close association between the Maasai and their animals, control of brucellosis in animals will be required.

6.2 RECOMMENDATIONS

Based on the results of this study a number of recommendations for future follow-up are indicated.

1. That public health information on the modes of transmission of brucellosis be disseminated to help reduce human infection.

2. Given the close association between Maasai and their animals and the potential of important economic losses due to brucellosis infection in animals, more detailed studies on the incidence and economic impact of brucellosis in animals are required. This information should be collected with the purpose of investigating whether vaccination or other measures to control brucellosis in the animal population are economically justified and feasible.

3. Since the differential diagnosis of diseases with flu-like symptoms is inadequate in almost all health facilities in Narok, information on bruceilosis and RB test kits should be supplied to all health facilities in the district.

4. Strategies for improved differential diagnosis of diseases with flu-like symptoms are required. A prospective study on patients with flu-like symptoms to estimate probabilities for specific diseases based on various combinations of patient history, clinical signs and other data is required. This information combined with a knowledge of the sensitivity and specificity of potential laboratory tests can then be used to design improved protocols for the differential diagnosis of diseases with flu-like symptoms.

5. The current treatment for brucellosis (particularly Streptomycin injections daily for 21-30 days) is not well accepted. Therapeutic trials to assess potential shorter, less costly and thus potentially better accepted treatments for brucellosis would be very useful.

REFERENCES

ALTON G.G., JONES, L.M., AND PIETZ, D.E., 1975. In: Laboratory techniques in brucellosis. 2nd Ed. WHO monograph series No. 55.

ALTON G. G., 1987. Control of *Brucella melitensis* in sheep and goats: A review. Trop. Anim. Hlth. Prod. **19:** 65.

ALTON G.G., JONES L.M. AND PIETZ D.E., 1975. Laboratory techniques in brucellosis, 2nd edition, W.H.O. Geneva.

AL-SIBAI M. B., HALIM M. A., EL SHAKER M.M., KHAN B.A. AND QUDRI S. M., 1992. efficacy of ciprofloxacin for treatment of *Brucella melitensis* infections, Antimicrob. Agents chemother., **36 (1):** 150.

ANGUS R.D, BROWN G.M, GUE C.S Jr., 1972. Avian Brucellosis. A case report of transmission from cattle. Am. J. Vet. Res. **32 (I0):** 1609.

ANON, 1914. Dept. Agric. British East African Ann. Rept. 1913-1914.

ANON, 1934. Department of Veterinary Services, Colony and Protectorate of Kenya, Annual Report.

ANON, 1955. Department of Veterinary Services, Colony and Protectorate of Kenya, Annual Report.

ANON, 1976. Quarterly epizootic circular list B, Office International des Epizootics (OIE), Paris, October-December.

ANON, 1985. Animal Health Year book, FAO animal production series, No. 25.

ANON, 1992. Ministry of Health annual report for 1992, Kenya.

ARNOW P.M., SMARON M. AND ORMISTE V., 1984. Brucellosis in a group of travellers to Spain, J. Am. Vet. Med. Assoc., **251**: 505.

ARTHUR G.H, NOAKES D.E, AND PEARSON H, 1989. In: Veterinary reproduction and obstetrics, 6th Ed. pp 395-99.

BASHIR R., AL-KAWI Z., HARDER E.J. AND JINKINS J., 1985. Nervous system brucellosis: diagnosis and treatment, Neurology **35**: 1576.

BERGER T.G., GUILLE A.A., GOETTE D.K., 1981. Cutaneous lesions in brucellosis, Arch. Dermatol., **117**: 40.

BERGEY'S MANUAL OF SYSTEMATIC BACTERIOLOGY, 1984. Vol.1, ed. Noel R. Krieg, ed. in chief, Holt J.G. pp 377-388.

BICKNELL S.R., BELL R.A., AND RICHARDS P.A, 1975. *B. Abortus* in the bitch, Vet. Rec. **199**: 85-86.

BISHOP Y.M.M., FIENBERG S.E.AND HOLLAND P.W., 1975. Discrete multivariate analysis: Theory and practice, Cambridge, MA, MIT press

BLANKENSHIP R.M. AND SANFORD J.P., 1975. *B. canis*; a cause of undulant fever, Am. J. Med. **59**: 424.

BLOOD D.C. AND HENDERSON J. A., 1989. Diseases caused by *Brucella* species. In: Veterinary medicine. Diseases of cattle, sheep, goats, pigs and horses, 7th Ed, pp 677-97.

BMDP-LR, 1992. BMDP soft ware Inc., release 7, 1140 Sepulveda Boulevard suit 316 Los Angeles CA 90025.

BOARGOB A. AND MUHAMMED S.I., 1989. The prevalence of brucellosis in some sheep and goat flocks in the Western mountains of Libya, Bull. Anim. Hlth. Prod. Afr. **37(1)**: 9.

BOTHWELL P.W., 1962. Brucellosis in children, Arch. Dis. Child., **37**: 628.

BOUZA E., GARCIA DE LA TOURE M., PARRAS F., GUERRERO A., RODRIGUES-CREIXEMS M. AND GOBERNANDO J., 1987. Brucella meningitis, Rev. Infect. Dis., **9**: 810.

BUNNEL D.E., BAY W.W. AND HUTCHINGS L.M., 1953. Studies on Aureomycin therapy of brucellosis in swine, Am. J. Vet. Res., **14**: 160.

BUCHANAN T.M. AND FABER L.C., 1980. 2-Mercapto-ethanol brucella agglutination test: usefulness for predicting recovery from brucellosis, J. Clin. Microbiol., **11**: 691.

BRAUDE A.I., 1951. II The formation of hepatic granuloma and its evolution, J. Infect. Dis., **89**: 87.

BRINKMANN U. AND BRINKMANN A., 1991. Malaria and Health in Africa: the present situation and epidemiological trends. Trop. Med. Parasitol. 42 **(3):** 198.

BRINLEY MORGAN W.J., 1970. In: Fertility and Infertility in domestic animals, Ed. J.A Laing, 2nd ed. London: Bailliere Tindall, pp 241-268.

CAMERON R.D.A., 1971. The incidence of Brucella ovis in some Kenya flocks and its relationship to clinical lesions and semen quality, Vet. Rec., **89**: 552.

CARMICHAEL L.E., 1967. Canine brucellosis: isolation, diagnosis, transmission, Proc. U.S. livestock sanitary assoc., **71**: 517.

CARMICHAEL L.E. AND KENNEDY R.M., 1968. Canine abortion caused by *B.canis*, J. Am. Vet. Med. Assoc. **152**: 605.

CARMICHAEL L.E. 1979. *B.canis* infection, In: CRC handbook series in zoonoses. Sect. A: Bacterial, Rickettsial and Mycotic diseases, Vol. 1, Ed. James H. Steele. pp 185-194.

CARTER G.R., CHENGAPPA M.M., 1991. Essentials of Veterinary Bacteriology and Mycology, Fourth Edition, pp 196-201.

CASTANEDA M.R., 1961. Laboratory diagnosis of brucellosis in man, Bull. World Health Org., **24**: 73.

CENTRE FOR DISEASE CONTROL (CDC), Annual summary of brucellosis 1975, CDC Publication No.(CDR) 76-8186, US Department of Health, Education and Welfare, Public Health Service, Atlanta.

CENTRAL BUREAU OF STATISTICS (CBS), 1983. Population projections for Kenya, 1983-1990.

CERVANTES F., BRUGUERA M., CARBONELL J., FORCE L. AND WEBB S., 1982. Liver disease in brucellosis: a clinical and pathological study of 40 cases, Postgrad. Med. J., **58**: 346

CERNYSEVA M.I., KNJAZEVA E.N. AND EGOROVA L.S., 1977. Study of the plate agglutination test with Rose Bengal antigen for the diagnosis of human brucellosis, Bull. W.H.O., **55**: 669.

CHUKWU C.C., 1985. Brucellosis in Africa, Part I. The prevalence. Bull. Anim. Hlth. Prod. Afr. **33:** 193.

CHUKWU C.C., 1987. Brucellosis in Africa, Part II. The Importance. Bull. Anim. Hlth. Prod. Afr. **35**: 92.

CISNEROS J.M., VICIANA P., COLMENERO J., PACHON J., MARTINEZ C. AND ALARCON A., 1990. Multicenter prospective study of treatment of *Brucella melitensis* brucellosis with Doxycycline for 6 weeks plus streptomycin for 2 weeks, Antimicrobial agents and chemotherapy, **34(5)**: 881.

CLARA M.M., MARIA P.J.B., MONTSERRAT B., AND JOSE' M.B., 1989. Efficacy of long acting oxytetracycline alone or in combination with streptomycin for treatment of *Brucella ovis* infection in rams, Am. J. Vet. Res., **50(4)**: 560.

COLLARD P., 1962. Antibodies against *Brucellae* in the sera of healthy persons in various parts of Nigeria, West Afr. Med. J., **11**: 172.

COLLINS F.M. AND CAMPBELL S.G., 1982. Immunity to intracellular bacteria, Vet. Immunol. Immunopathol., **3**: 5.

COLMENERO J.D., HERNADEZ S., REGUERA J.M., CABRERA F., RIUS F. AND ALONSO A., 1989. Comparative trial of doxycycline plus streptomycin versus doxycycline plus rifampin for the therapy of human brucellosis. Chemotherapy (Basel) **35**: 146.

COLMENERO J.D., REGUERA J.M., FERNADEZ N.A. AND CABRERA F.F., 1991. Osteo-articular complications of brucellosis, Ann. Rheum. Dis., **50(1)**: 23.

COLMENERO J.D., CISNEROS J.M., ORJUELA D.L., PACHON J., GARCIA P.R., RODRIGUES S.F. AND JUAREZ C., 1992. Clinical course and prognosis of *Brucella* spondylitis, infection, **20(1)**: 38.

COOPER C. W., 1992. The risk factors in the transmission of brucellosis from animals to humans in Saudi Arabia, Trans. Roy. Soc. Med. Hyg. **25(1)**: 206.

COOPER A.C.D. AND CARMICHAEL I.H., 1974. Incidence de la brucellose chez les animaux sauvages au Botswana, Bull. Epizoot.Dis. Afr., **22**: 125.

COOMBS R.R.A., MOURANT A.E. AND RACE R.R., 1945. A new test for the detection of weak and incomplete Rh agglutinins, Br. J. Exp. Pathol., **26**: 255.

COX P.S.V., 1966. Brucellosis: A survey in South Karamoja, E. Afr. Med. J. **43**: 43.

COX P.S.V., 1968. Quoted by Oomen, 1975.

CRISCUOLO E. AND DICARLO F.C., 1954. El aborty otras manifestaciones ginecobstetricas en el curso de la brucellosis humana, Rev. Fac-cienc. Min. Educ. Univ. Cardoba, **12**: 231.

DAVIS B.D., DULBECO R., ELSEN H.N., GINSBERG H.S. AND WOOD B.W.Jr., 1973. Brucellosis, In: Microbiology, 2nd ed. Harper and Row, New York, 765.

DBASE IV, 1990. Ashton-Tate corporation, 20101 Hamilton Avenue, Torrance, CA 90502-1319, U.S.A.

D'CRUZ S., 1976. Second International Conference of institutions of Tropical Veterinary Medicine, West Berlin, pp 387-395.

DEBONO J.E., 1964. Brucellosis resembling acute anterior poliomyelitis, Lancet **1**: 1132.

DELFINI L.F., 1973. The relationship between body temperature and malaria parasitaemia in a rural forested area of Western Nigeria, J. Trop. Med. Hyg., **76:** 111.

DELVECCHIO G., FRACCASSETTI O., LORENZI N., 1991. *Brucella* endocarditis, Int. J. Cardiol., **33(2)**: 328.

DENNY H.R., 1972. Brucellosis in the horse, Vet. Rec., **90**: 86.

DEYOE B.L, 1970. Studies on the pathogenesis of a canine abortion agent (*B.canis*) in dogs and other domestic animals, Ph.D Thesis, Iowa state University, Ames.

DEYOE B.L., 1972. Immunology and Public Health significance of Swine Brucellosis, J.Am. Vet. Med. Assoc., **160(4)**: 640.

DIAZ R., JONES L.M., LEONG D.AND WILSON J.B., 1968. surface antigens of smooth *Brucellae*, J. Bacteriol., **96**: 893.

DIAZ R., MARAVI-POMA E.AND RIVERO A., 1976. Comparison of counter immuno-electrophoresis with other serologic tests in the diagnosis of human brucellosis. Bull. World Health org., **53:** 417.

DUNEA G., KARK R. LANNIGAN R.M., D'ALLESIO D. AND MUEHRCKE R.C., 1969. Brucella nephritis, Ann. Intern. Med. **70**: 783.

EL-FOURGI M.H., 1973. Bovine brucellosis in Tunisia, Report No.122, XLIst general session of the OIE Committee, pp 136.

ELLIOT R.E. AND CHRISTIANSEN K.H., 1977. Brucellosis: A veterinarians guide to the literature. Animal health division, Ministry of Agriculture and fisheries, Wellington, New Zealand.

ENTESSAR F., ARDALAN A., EBADI A. AND JONES L.M., 1967. Effect of living Rev. 1 vaccine in producing long-term immunity against *Brucella melitensis* in sheep in Iran, J. Comp. Pathol., **77**: 367.

ESCALANTE J.A. AND HELD J.R., 1969. Brucellosis in Peru, JAVMA, **155**: 2146.

EZEH E. N., 1978. The fate of *B. abortus* and associated antibodies in traditionally soured milk. Bull. Anim. Hlth. Prod. Afr. **25(1)**: 5.

FAZIL M.A., 1975. Personal communication (Quoted by Kagunya D.K.J., 1977).

FELSENFELD C.O., YOUNG V.M., COEFFER E., ISHIHARA S.J., AND SCHROEDER W.F., 1951. A study of the Nature of Brucellosis in chickens, Am. J. Vet. Res. **12**: 48.

FERNSTERBANK R., PLOMMET M. AND PARDON P., 1975. Traitment de la brucellose bovine par L'oxytetracycline, Ann. Rech. Vet. **6**: 43.

FERNSTERBANK R., 1985. Brucella melitensis (Eds J.M. Verger and M. Plommet), Martinus Nijhoff, dordrecht, the Netherlands, pp 167 and 241.

FEITZ J.M., SABBAGHIAN. AND SOHRABI F., 1973. A comparative study of therapeutic agents used for the treatment of acute brucellosis, J. Clin. Pract., **22**: 410.

FEIZ J., SABBUGHIAN H. AND MIRALA M., 1978. Brucellosis due to *B. melitensis* in children, Clinical and epidemiological observation of 95 patients studied in central Iran, Clin. Pediatr. **12**: 904.

FOOD AND AGRICULTURAL ORGANISATION/WORLD HEALTH ORGANISATION. 1986. FAO/WHO Expert Committee on Brucellosis, 6th report, WHO Tech. Rep. Ser. 740:56.

FOOD AND AGRICULTURAL ORGANISATION/WORLD HEALTH ORGANISATION. 1971. FAO/WHO Expert Committee on Brucellosis, 5th report. WHO Tech. Rep. Ser. 464:82.

FLORES-CASTRO R. AND BAER G.M., 1979 . Brucellosis (*Brucella melitensis*)-Zoonotic implications, In: CRC hand book series in zoonosis. Section A: Bacterial, Rickettsial, and Mycotic diseases. Vol.1. Ed. James H. Steele. pp 195-216.

GIDEL R., ALBERT J.P., LEMAO G., AND RATIF M., 1976. Epidemiologique de la brucellose humaine et animale en Afrique de L'ouest, R'esultats de dix enquetes effectuees en C^cte d'Ivoire, Haunte-Volta et Niger In' International sympossium on Brucellosis II, Rabat. Dev. Biol. Stand., **31**: 187.

GILBERT G.L.AND HAWES L.A., 1981. The antibody response to *Brucella*: Immunoglobulin response measured by ELISA and conventional tests. Aust. N.Z. J. Med., **11**: 40.

GLOSSER J.W., 1972. Comments on abattoir associated Brucellosis. J. Am. Vet. Med. Assoc., **160 (4)**: 643.

GOOSENS H., MARCELIS L., DEKEYSER P. AND BUTZLER J.P., 1983. *Brucella melitensis*: Person to person transmission?, Lancet 1: 773.

GOTUZZO E., ALARCON G.S., BOCANEGRA T.S., CARILLO C., GUERRA J.C., ROLAND T. AND ESPINOZA L.R., 1982, Articular involvement in human brucellosis: a retrospective analysis of 304 cases, Sem. Arthritis Rheum., **12**: 245.

GUBINA E.A., 1982. Prevention of brucellosis in man, In: Zoonoses control, Vol. II, ed. Lysenko A., Centre of International Projects, GKNT, Moscow. pp. 116-20.

HALL W.H. AND MANIONB R.E., 1953. Comparison of the Coombs test with other methods for brucella agglutinins in human serum, J. Clin. Invest., **32**: 96.

HARRIS H.J., 1943. Brucellosis: diagnosis, differential diagnosis and treatment, Bull. N. Y. Acad. Med., **19**: 631.

HART F.D., MORGAN A. AND LACEY B., 1951. Brucella abortus endocarditis, Br. Med. J., **1**: 1048.

HARTLEY W.J., JEBSON J. L., AND MCFARLANE D., 1954. Some observations on the natural transmission of ovine brucellosis. N.Z. Vet. J., **2**: 80.

HASSAN A., EVIAN M.M., FARID Z., HATHOUT S.D. AND SORENSEN K., 1971. Trimethoprim-sulfamethoxazole in acute brucellosis, Br. Med. J., **23**: 700.

HEISCH H.B., COOKE E.R.N., HARVEY A.E.C., AND D'SOUZA J.A.M., 1963. The isolation of *B.suis* from rodents in Kenya, East African Medical Journal, **40**: 32.

HENDERSONR.J. AND HILL D.M., 1972. Subclinical brucella infection in man, Br. Med. J., **3**: 154.

HENDERSON R.A., HOERLEIN B.F., KRAMER T.T. AND MEYER M.E., 1974. Disco-spondylitis in three dogs infected with *B.canis,* J. Am. Vet. Med. Assoc., **165 (5)**: 451.

HENDRICKS S.L AND MEYER M. E., 1975. Brucellosis, In: Diseases transmitted from animals to man. 6th Ed.

HERRELL W.E., BARBER T.E., 1952. Treatment of brucellosis with aureomycin or terramycin combined with dihydrostreptomycin, Postgrad. Med., **11**: 476.

HO H., ZUCKERMAN M.J., SCHAEFFER L. AND POLY S., 1986.Brucellosis: atypical presentation with abdominal pain, Am. J. gastroenterol., **81**: 375.

HOSSAIN A., BAKIR T.F., CHOWDHURY M.N., AND KURSTAKE E., 1991. J. Hyg. Epidemiol. Microbiol. Immunol., **35(3)**: 325.

HUDDLESON I.F., 1929. The differentiation of the species of the genus *brucella*, Mich. State Univ. Agric. Exp. Stn., Technical bulletin No. 100.

HUDDLESON I.F., 1943. Brucellosis in man and animals. The commonwealth Fund, New York.

HUDDLESON I.F., 1952.The dissociation pattern in the species of the genus *Brucella* In: Studies in Brucellosis. III, Michigan State College, agricultural experimentation station.

HUMMEL P.H. AND STAAK C., 1974. *Brucella abortus* biotype 3 in Tanzania, Vet. Rec. **94**: 579.

HUSSEIN A., SINGH S.S. AND HUSSEIN H., 1978. A survey of Bovine brucellosis in the southern parts of Somalia Democratic Republic: a comparative study of prevalence of the disease in farm animals and animals from nomadic herds, Bull. Anim. Hlth. Prod. Africa, **26**: 150.

IBRAHIM A.E., 1975. Milk hygiene and bacteriology in the Sudan: Isolation of *Brucella abortus* from cow milk, Bull. Anim. Hlth. Prod. Afr., **23**: 51.

JIMENEZ de BAGUES M.P., MARIN C.M., BLASCO J.M., MORIYON I. AND GAMAZO C., 1992. An ELISA with *Brucella* lipopolysaccharide antigen for the diagnosis of *Brucella melitensis* infection in sheep and for the evaluation of serological responses following subcutaneous or conjunctival *B. melitensis* Rev 1 vaccination. Vet. Microbiol., **30(2-3)**: 233.

JONES L.M., DIAZ R. AND BERMAN D.T., 1976. Endotoxic activity of rough organisms of *Brucella* species, J.Infect. Immunol., **13**: 1638.

JONES T.C. AND HUNT R.D., 1983. In' Veterinary Pathology. 5th Ed. pp 610-615.

JONES L.M., BERMAN D.T., 1976. Studies of *Brucella* lipopolysaccharide, Dev. Biol., Stand., **31**: 62.

JUBB K.V.F., KENNEDY P.C. AND PALMER N., 1985. Brucellosis, In: Pathology of domestic animals, 3rd edition, Vol.3, Academic Press Inc., pp. 345-350.

KAGUMBA M. AND NANDOKHA E., 1978. A survey of the prevalence of Bovine brucellosis in East Africa, Bull. Anim. Hlth. Prod. Africa, **26:** 224.

KAGUNYA D.K.J., 1977. Animal brucellosis in the North-Eastern province of Kenya, Msc. thesis, University of Nairobi.

KAMBAL A.M., MAHGOUB E.S., JAMJOOM G.A. AND CHOWDHURY M.N.H., 1983. Brucellosis in Riyadh, Saudi Arabia. A microbiological and clinical study. Trans. Roy. Soc. Trop. Med. Hyg. **77(6):** 820.

KELLAR J., MARRA R., AND MARTIN W., 1976. Brucellosis in Ontario: a case control study, Can. J. Comp. Med., **40**: 119.

KELLY P.J., MARTIN W.J., SCHINGER A. AND WEED L.A., 1960. Brucellosis of the bones and joints: Experience with thirty six patients. J. Am. Vet. Med. Assoc., **174**: 347.

KELLY R.I. AND RIBBINS B., 1987. Pregnancy and brucellosis, Texas Med., **83**: 39.

KELSEY J.L., THOMPSON W.D. AND EVANS A.S., 1986. Methods in observational epidemiology, monographs in epidemiology and biostatistics vol. 10, pp 128-47.

KENYA RANGELAND ECOLOGICAL MONITORING UNIT (K.R.E.M.U), 1993. Livestock and wildlife summaries for Kenya.

KERR W.R., MCCAUGHEY W.J., COGHLAN J.D., PAYNE D.O.H., QUAIFE R.A., ROBERTSON L. AND FARREL I.D., 1968. Techniques and interpretations in the serological diagnosis of brucellosis in man, J. Med. Microbiol. **1**: 181.

KILELU E.S., KIRUI M., 1992. Retrospective prevalence study of the distribution of Rift Valley fever virus in Kenya, Indian Journal of Animal Sciences **63(7)**: 724.

KOSMIDIS J., LARAGOUNIS A., TSELENTIS J. AND DAIKOS G.K., 1982. The combination rifampin-doxycycline in brucellosis is better than the WHO regimen. Chemioterapia 1(suppl. 4): 107.

KUPPASWAMY P.B., 1954. Chemotherapy of brucellosis in rams, N. Z. Vet. J., **2**: 110.

LEIVA LEON J., De La ROSA M., PLATA J., MARTINEZ M. J. AND JIMENEZ ALFONSO J., 1991. An immuno-blotting study of serologic response in patients with acute brucellosis, Diagn. Microbiol. Infect. Dis. **14(6):** 515.

LIFESO R.M., HARDER E. AND MCCORKELL S.J., 1985. Spinal brucellosis, J. Bone Joint Surgery. **67B**: 345.

LINDBERG J. AND LARSSON P., 1991. Transmission of Brucella melitensis by coitus, Lancet **337**: 648.

LOTUS FREELANCE PLUS, 1988. Lotus development corporation, 55 Cambridge Parkway, Cambridge, MA 02142, U.S.A.

LUBAN M., SHARDA D. AND HELIN I., 1988. Probable transmission of brucellosis from breast milk to a new-born, Trop. Geogr. Med., **40**: 151.

MAGEE J.T., 1980. An enzyme-Labelled Immuno-sorbent Assay for *Brucella abortus* antibodies, J. Med. Microbiol., **13**: 167.

MAGILL G.B. AND KILLOUGH J.H., 1953. Oxytetracycline-streptomycin therapy in brucellosis due to *Brucella melitensis*. Arch. Intern. Med. 23: 204.

MANSON-BAHR P.E.C., 1956. Clinical aspects of Brucellosis in East Africa, E. Afri. Med. J. **33**: 489.

MARTIN C.M., JIMENEZ de BAGUES M.P., BARBERAN M., BLASCO J. M., 1989. Efficacy of long acting oxytetracycline alone or in combination with streptomycin for the treatment of *Brucella ovis* infection in rams, Am. J. Vet. Res., **50(4):** 560.

MARTIN S.W., MEEK A.H., and WILLEBERG P., 1987. veterinary Epidemiology: Principles and Methods.

MARTIN W.J., NICHOLS D.R., BEAHRS O.H., 1961. Chronic localized brucellosis, Arch. Intern. Med. **107**: 143.

McCULLOUGH N.B., 1970. Microbial and host factors in the pathogenesis of brucellosis. in: Infectious agents and host reactions. Mudd S. Ed. W.B Saunders, Philadelphia, 330.

McDERMOTT J.J., K.A. DENG, T.N. JAYATILEKA AND E.L. JACK, 1987. A cross-sectional cattle disease study in Kongor rural council, Southern Sudan II. Brucellosis in cows: Associated factors, impact on production, and disease control. Prev. Vet. Med. **5**: 125.

McDERMOTT J.J., DENG K.A., JAYATILEKA T.N., EL JACK M.A., 1987. A cross-sectional disease study in Kongor Rural council, Southern Sudan.I. Prevalence estimates and age, sex and bred associations for brucellosis and contagious bovine pleuropneumonia, Prev. Vet. Med., **5**: 111.

McDONALD R.H., 1939. Acute empyema with B. abortus as the primary causative agent, J. Thorac. Surg. **9**: 92.

MEYER M.E., 1964. The epizootiology of brucellosis and its relationship to the identification of *Brucella* organisms, Am. J. Vet Res., **25**: 553.

MEYER M.E., 1979. Brucellosis (non-zoonotic infection). In: CRC Handbook series in zoonoses, Section A: Bacterial, Rickettsial and Mycotic diseases. Vol.1. Ed.James H. Steele. pp 217-223.

MILWARD F.W., NICOLETTI P., HOFFMAN E., 1984. Effectiveness of various therapeutic regimens for bovine brucellosis, Am. J. Vet. Res, **45(9)**: 1825.

MORGAN W.J.B., 1970. In: Fertility and Infertility in Domestic animals, 2nd. Ed., Ed. Leung J.A., pp 241-248.

MORGAN W.J.B., 1967. The serologic diagnosis of bovine brucellosis, Vet. Rec. **80**: 612.

MORRISSET R., AND SPINK W.W., 1969. Epidemic canine brucellosis due to a new species, *B. canis*, Lancet **1000**: 8.

MOUSA A.R., KOSHY T.S., ARAY G.F., MARAFIE A.A., MUHTASEB S.A., AL-MUDALLAL D.S. AND BUSHARETULLA M.S., 1986. Brucella meningitis: Presentation, diagnosis and treatment: a prospective study of ten cases. Quart. J. Med., **60**: 873

MUGAMBI J.T.M., 1992. Personal communication, National Veterinary Research Laboratories, Kabete.

MUNFORD R.S., WEAVER R.E., PATTON C., FEELY J.C. AND FELDMAN R.A.,1975. Human diseases caused by *B. canis*, a clinical and epidemiological study of two cases, J. Am. Vet. Med. Assoc., **231**: 1267

MURRAY M.J., MURRAY A.B. AND MURRAY C.J., 1980. An ecological interdependence of diet and disease: A study of one tribe consuming different diets. Am.J. Clin. Nutr. 33: 697-701.

MUTERO C.M., MUTINGA M.J., NGINDU A.M., KENYA P.R. AND AMIMO F.A., 1992. Visceral leishmaniasis and malaria prevalence in West Pokot District, Kenya. East.Afr. Med. J. **69(1)**:3.

NAPARSSTEK E., BLOCK C.S. AND SALVIN S., 1983. Transmission of brucellosis by bone marrow transplantation, Lancet **1:** 773.

NDARATHI C.M. AND WAGHELA S., 1991. Brucellosis in Maasai livestock in Kajiado District in Kenya, Indian Journal of Animal sciences **61(2):** 156.

NICOLETTE P., MILWARD P.W. AND HOFFMAN E., 1985. Efficacy of long acting oxytetracycline alone or in combination with streptomycin in the treatment of bovine brucellosis, JAVMA, **187**: 493.

NICOLETTI P.L., 1989. Relationship between animal and human disease, In: Brucellosis: clinical and laboratory aspects, edited by Young and Corbel.

OLITZKI A., 1970. Immunological research in brucellosis II. In vivo procedures. In' Bibliotheca Medica. Vol.9 S Kanger, Basel; 22.

OLLE-GOIG J.E. AND CANELA-SOLER J., 1987. An outbreak of *Brucella melitensis* infection by airborne transmission among laboratory workers, Am. J., Public Health, **77**: 335.

OKOH A.E.J., ALEXIEVE I. AND AGBONLAHOR D.E., 1978. Brucellosis in dogs in Kano, Nigeria, Trop. Anim. Hlth. Prod., **10**: 219.

OOMEN L.J.A., 1975. Human brucellosis in Kenya, Dr of Medicine Thesis, University of Amsterdam.

OOMEN L.J.A., 1976. Human brucellosis in Kenya, Tropical and Geographical Medicine, **28**: 45.

OOMEN L.J.A. AND WEGNER J., 1982. Brucellosis, In: health and disease in Kenya, Kenya literature bureau, Eds. Vogel L.C., Muller A.S., Odingo R.S., Onyango Z., De Geus A., pp 221-224.

OOMEN L.J.A AND WAGHELA S., 1974. The Rose Bengal Plate Test in human Brucellosis, Trop. Geogr. Med. **26**: 300.

OPALEICHUK I. S., UMNOVA N.S., ZHELUDKOV M.M., PAVLOVA I.P., 1991. The use of latex agglutination reaction for the diagnosis of a *Brucella* infection, Zh Mikobiol. Epidemiol. Immunobiol. **7:** 61.

OPTIZ H.M., 1969. Brucellosis in Sierra Leone: a serological survey in cattle, sheep and goats, Bull. Epizoot. Dis. Afri. **17**: 383.

OTERO J.R., FUERTES A., PALENQUE E. AND NORIEGA A.R., 1982. Microtiter-adapted Coombs method that facilitates the Coombs test for brucellosis, J. Clin. Microbiol., **16**: 737.

PALING R.W., WAGHELA S., MACOWAN K. J., HEATH B. R., 1988. The occurence of infectious diseases in mixed farming of domesticated wild herbivores and livestock in Kenya. II. Bacterial diseases, J. Wildlife Diseases, **24(2):** 308.

PANJARATHINAM R., 1984. Anti-brucella agglutinins in aborted women. J. Gynecol. Obstet. Biol. Reprod. (Paris) **13:** 433.

PARNAS J.I., 1956. Recherches concernant l'allergie et les allergenes au course de la brucellose, Rev. Immunol. **23**: 74.

PARRAT J., 1956. Recherches concernant l'allergie et les allergens au course de la brucellose, Rev. Immunol., **23**: 74.

PARRATT D., NIELSEN K.H., WHITE R.G. AND PAYNE D.J.H. 1977. Radio-immuno-assay of IgM, IgG and IgA *Brucella* antibodies, Lancet **1**: 1075.

PATRELLA R. AND YOUNG E.J., 1988. Acute brucella ileitis, Am. J. Gastroenterol., **83**: 80

PERCY D.H., EGWU I.N., AND JONAS A.M., 1972. Experimental *B.canis* infection in the monkey (Macaca arctoides), Can. J. Comp. Med., **36**: 221.

PEERY T.M. AND BELTER L.F., 1960. Brucellosis and Heart disease. II, fatal brucellosis, Am. J. Pathol, **36 (6)**:73.

PHILPOTT M.AND AUKO O., 1972. Caprine brucellosis in Kenya, Br. Vet. J. **128**: 642.

PICKERILL P.A., 1970. Canine Brucellosis: Serological host range and Epidemiological studies, Ph.D thesis, Cornell University, Ithaca, New York.

POOLE P.N., WHITEHOUSE D.B. AND GILCHRIST M.M., 1972. A case of abortion upon infection with B. abortus biotype 2, J. Clin. Pathol., **26**: 882.

PORRECO R.P. AND HAVERKAMB A.D., 1974. Brucellosis in pregnancy, Obstet. Gynecol. **44:** 597.

RAY W.C., 1979. Brucellosis due to *B. abortus* and *B. suis*, In: CRC hand book series in zoonosis, Sect. A: Bacterial, Rickettsial and Mycotic diseases. Vol.1 Ed. James H. Steele. pp 99-127

RADWAN A.I., BEKAIRI S.I., AL-MUKAYEL A.A., ABU AGLA O.S., 1984. Control of ovine brucellosis in Najdi Sheep in Saudi Arabia, Trop. Anim. Hlth. Prod. Afri., **16**: 213.

RAMON D. AND IGNACIO M., 1989. Laboratory techniques in the diagnosis of human brucellosis. In' Brucellosis: Clinical and laboratory aspects' edited by Young E.J. and Corbel M.J.

RENOUX G. AND ALTON G.G., 1955. Susceptibility of young goats to *Brucella melitensis*, Arch. Inst. Pasteur Tunis, **32**: 225.

REPORT OF SUB-COMMITTEE ON PUBLIC HEALTH, 1972. BRUCELLOSIS IN THE U.S., 1970, Arch. Environ. Health, **25**: 66.

RIEZU-BOJ J.L., MORIYON I., BLASCO J.M., AND DIAZ R., 1978. Comparison of,lipopolysaccharride and outer membrane protein-lipopolysaccharride extracts in enzyme linked immuno-sorbent assay for the diagnosis of Brucella ovis infection, J. clin. microbiol., **23**: 938.

ROBERTSON L., FARRELL I.O., HINCHLIFE P.M., QUIFE R.A., 1980. Bench book on *Brucella*, public health laboratory service monograph series number 14.

RODRIGUEZ-TORRES A., FERMOSOJ. AND LANDINEZ R., 1983. Brucellosis, Medicine (Spanish Ed.) **48**: 3126.

ROUGEMONT A., BRESLOW N., BRENNER E., MORET A.L., DUMBO O., DOLO A., SOULA G. AND PERRIN L., 1991. Epidemiological basis for clinical diagnosis of childhood malaria in endemic zone in West Africa. Lancet, **338(8778):** 1292.

ROY P.B., MEHTA N.R. AND ASNANI K.G., 1965. Serological study of brucellosis in man and cattle in Jamnagar. Indian J. Med. Res. **53:** 822.

RUBEN B., JEFFREY B.D. AND PHITOWONG J C., 1991. Person to person transmission of *Brucella melitensis*, Lancet **337:** 14.

RUSSELL A.O., PATTON C.M. AND KAUFMANN A.F., 1978. Evaluation of the card test for diagnosis of human brucellosis, J. Clin. Microbiol. **7:** 454.

SACKS N. AND VAN RENSBURG A.J., 1976. Clinical aspects of chronic brucellosis, S. Afri. Med. J. **50**: 725.

SADDLER W.W., 1960. Present evidence on the role of meat on the epidemiology of human brucellosis, Am. J. Public Health, **50**: 504.

SAJ J.V., BELTRAN M., DIAZ A., AGULLA A., MERINO F.J., VILLASANTE P.A., VELASIO A.C., 1987. Enzyme Linked Immuno-Sorbent Assay for the diagnosis of brucellosis, Eur. J. Clin. Microbiol., **6**: 71.

SALALA R.A., RAVDIN J.I., 1985. Brucella species (brucellosis), pp 1283-1290. In 'G.L. Mandell. R.G. Doughlas and J.E. Bennett (ed.), Principles and practice of infectious diseases. John Wiley & sons, Inc., New York.

SAMRA Y., SHAKED Y., HERTZ M., ALTMAN G., 1983. Brucellosis: difficulties in diagnosis and a report of 38 cases, Infection **11**: 310.

SANDE A.M., KAPUSNIK-UNER J.E., AND MANDELL G.L., 1990. Chemotherapy of microbial diseases, In: Goodman and Gilman's, The pharmacologic basis of therapeutics, 8th edition, pp. 1018-1182, Pergamon Press.

SCHIMANN B. AND STAAK C., 1971. *Brucella melitensis* in Impala (*Aepyceros melampsis*), Vet. Rec., **88:** 344.

SCHREYER P., CASPI E., LEIBA Y., ESHCHAR Y. AND SOMPOLINSKY D., 1980. Brucella septicaemia in pregnancy, Eur. J. Obstet. Gynecol. Reprod. Biol. **10**: 99.

SCHWABE C.W., 1984. Veterinary medicine and human health, 3rd edition, edited by Stamathis G., Williams and Wilkins, Baltimore/London.

SHAKIR R.A., AI-DIN A.S.N., ARAJ G.F., LULU A.R., MOUSA A.R.AND ADDAH M.A., 1987. Clinical categories of neuro-brucellosis, Brain **110:** 213.

SHASHA B., LANG R. AND RUBINSTEIN E., 1992. Therapy of experimental murine brucellosis with streptomycin, co-trimoxazole, ciprofloxacin, ofloxacin, pefloxacin, doxycycline and rifampin, Antimicroibiol. Agents chemother. **36(5):** 973.

SIMPSON W. AND FRAZIER E., 1928. Undulant fever: report of 63 cases occurring in an about Dayton ohio, JAVMA, **93**: 1958.

SINGER R., AMITAI Y., SHIMONOVITZ, HERZOG N., REISS A. AND MAAYAN S., 1991. Neonatal brucellosis possibly transmitted during delivery, Lancet **338:** 128.

SIPPEL J.E., EL-MASRY N.A. AND FARID Z., 1982. Diagnosis of human brucellosis with ELISA, Lancet, **2**: 19.

SMITH R.A., THEDFORD T.R., ESPE B.H., WOODSON P.D. AND BURROWS G.E., 1983. Effect of oxytetracycline administration on antibody response to *Brucella abortus* vaccination in calves, J. Am. Vet. Med, Ass. **183(I):** 1983.

SPINK W.W., 1956. The nature of brucellosis, 1st ed. University of Minnesota press, Mineapolis, 90.

STABLEFORTH A.W., 1959, 53. Brucellosis, In: diseases due to bacteria, Vol. 1 by Stableforth and Galloway I.A., ed. Butterworth, London.

STANTIC PULVINIC M., CEC V. AND MEHLE J., Brucellosis in spouses and the possibility of interhuman infection, Infection **11:** 313.

STATISTICAL ANANLYSIS SYSTEM, 1988. SAS Institute Inc., P.O Box 8000 Cary, NC 27512-8000 U.S.A.

STEINBERG C.L., 1948. Brucellosis as a cause of sacroiliac arthritis, J. Am. Med. Assoc., **138**: 15.

STOENNER H.G. AND LACKMANN D.B., 1957. A new species of brucella isolated from the desert wood rat, *Neotoma lepida* (Thomas) Am. J. Vet. Res., 18: 947.

STREET L., GRANT W.W.AND ALVA J.D., 1975. Brucellosis in childhood, Pediatrics, **55**: 416.

SWENSON R.M., CARMICHAEL L.E. AND CUNDY K.R., 1972. Human infection with Brucella canis, Ann. Intern. Med., **76**: 435.

TAN D.S.K., 1964. The importance of leptospirosis in Malaya. Med. J. Malaya, **18:** 167.

TAYLOR D.J., RENTON J.P., MCGREGOR A.B., 1975. *B.abortus* biotype 1 as a cause of abortion in the bitch. Vet. Rec. **96**: 428.

THAPAR M.K. AND YOUNG E.J., 1986. Urban outbreak of goat cheese brucellosis, Pediatr. Infect. Dis. **5**: 640.

THORPE B.D., SIDEWELL R.W. AND LUNDGRESS D.C., 1967. Experimental studies with 4 species of brucella in selected wildlife laboratory and domestic animals, Am. J., Trop. Med. Hyg., **16**: 665.

VANDERCAMB, ZECH F., De MCOOMEN S., BUGHIN C., GIGI J. AND WAUTERS G., 1990. Isolate of *B. melitensis* from sperm. Euro. J. Clin. Microbiol. Infect. Dis. **9:** 303.

VAN DER HOEDEN, 1964. Brucellosis, In: Zoonoses, Elsevier publishing company, pp 95-132.

VAN RENSBURG S.W.J., VAN HEEREN K.M., LE ROUX D.J., SNYDERS A.J., 1958. J. S. Afr. Vet. Ass. **29:** 223.

VANEK E. AND THIMM B., 1976. Q-fever in Kenya: Serological investigation in man and domestic animals, East African Medical Journal, **53(12)**: 678.

VERGER J.M. AND PLOMMET M., 1985 (eds.). Brucella melitensis, Martinus Nijhoff Publishers, Dordrecht, The Netherlands.

WAGHELA S., 1976. Animal Brucellosis in Kenya; A Review. Bull. Anim. Hlth. Prod. Afri. **24 (1)**: 53.

WAGHELA S., 1977. Brucellosis in Kenya; Review Article, The Kenya Veterinarian,**1**: 3.

WAGHELA S. AND GATHUMA J.M., 1975. Serological survey of the prevalence of brucellosis in pigs in Kenya, Bull. Anim. Hlth. Prod. Afr., vol. 24: no.3, 251.

WAGHELA S., FAZIL M.A., GATHUMA J.M. AND KAGUNYA D.K., 1978. A serological survey of brucellosis in camels in North-Eastern Province of Kenya, Trop. Anim. Hlth. Prod., **10**: 28.

WEED L.A., DAHLIN D.C., PUGH D.G. AND IVINS J.C., 1952. Brucella in tissues removed at surgery, Am. J. Clin. Pathol. **22**: 10.

WILLIAMS E., 1973. Brucellosis, Br. Med. J., **1**: 791.

WOOD E.E., 1955. Brucellosis as a hazard of blood transfusion, Br. Med. J., **1**: 27.

WRIGHT F.J., COOKE E.R.N., AND D'SOUZA J.A.M., 1953. Observations in human brucellosis in Kenya, Trans. Roy. Soc. Trop. Med. Hyg., **47**: 117.

YOUNG E.J., 1983. Human brucellosis, Rev. Infect. Dis. **5:** 821.

YOUNG E.J., 1989. Clinical manifestations of human brucellosis, In: brucellosis: clinical and laboratory aspects, edited by Young and Corbel.

ZANCADA DIAZ De ENTRE SOTOS F., ROLDAN MONTAUD A., FERNADEZ BALLESTEROS A., JIMENEZ F. J., AGGULLA BUDINO A., 1991. Brucellosis: A clinico-serological study in a rural health area, Rev. Clin. Esp. **191(10):** 8.

APPENDICES

Appendix 1: Dispensaries reporting to the Narok District hospital.

DISPENSARY DISPENSARY	BRUCELLOSIS CODE	TEST CODE	MONTHS REPORTED
A.I.C. SIYIAPEI	1	0	6
A/BARIGOI DISP	2	0	68
ABBOSSI H/C	3	0	24
AITONG DISP	4	0	17
E/AJIJIK DISP	5	0	48
E/DIKIRR DISP	6	0	38
E/ENTERIT DISP	7	0	53
E/ERINGA DISP	8	0	37
E/NYIRO DISP	9	0	74
EMARTI DISP	10	0	57
ENABELIBEL H/C	11	0	65
ENOOSAEN DISP	12	0	71
ENOOSUPUKIA DISP	13	0	74
ENTASEKERA DISP	14	0	67
ENTONTOL DISP	15	0	33
GK PRISON DISP	16	0	49
ILKERIN DISP	17	0	51
ILMOTIOK DISP	18	0	1
KEEKOROK H/C	19	0	77
KICHWA TEMBO DISP	20	0	3
KILGORIS H/C	21	0	79
KIMINTET DISP	22	0	20
NKARETA DISP	39	0	4
NKORNKORI DISP	40	0	19
OLASITI DISP	41	1	80
OLCHORO DISP	42	0	76
OLEDEEM DISP	43	0	15
OLMESUTIE DISP	44	0	61
OLOKIRIKIRAI DISP	45	0	56
OLOKURTO H/C	46	0	68
OLOLPIRONITO H/C	47	0	75
KOJONGA DISP	23	0	79
LEMEK DISP	24	0	46
LOLGORIAN H/C	25	0	74
MAJIMOTO DISP	26	1	69
MARA SERENA DISP	27	0	43
OLOLULUNGA H/C	48	0	68
OLOROPIL DISP	49	0	20
OLORTE DISP	50	0	7

DISPENSARY DISPENSARY	BRUCELLOSIS CODE	TEST CODE	MONTHS REPORTED
OLPUSIMORU DISP	51	0	53
POROKO DISP	52	0	7
SAKUTIEK DISP	53	0	54
SEKENANI DISP	54	0	41
SIYIAPEI DISP	55	1	84
SOGOO H/C	56	0	54
ST. ANTHONY LEMEK	57	0	2
ST. JOSEPHS HOSP	58	0	49
SUSWA DISP	59	0	1
TALEK DISP	60	0	14
MARARIANTA DISP	28	2	6
MASURURA DISP	29	0	10
MEGWARA DISP	30	0	68
MORIJO LOITA DISP	31	0	45
MOSIRO DISP	32	0	47
MULOT DISP	33	0	70
N/ENKARE H/C	34	0	65
NAROK DIST HOSP	35	2	40
NAROOSURA H/C	36	0	58
NGITO DISP	37	0	26
NKARARO DISP	38	0	58

KEY:

0: Not testing
1: Testing regularly
2: Testing occasionally

Appendix 2: The reporting of unspecific febrile diseases, brucellosis and malaria and the brucellosis testing status in Narok, Kenya. 1986-1992.

DISPENSARY	BRUCELLOSIS TEST CODE	MONTHS REPORTED	MEAN CASES PER MONTH BR.	RH.	PUO.	MAL.
A.I.C. SIYIAPEI	0	6	12.0	28.0	1.0	43.5
A/BARIGOI DISP	0	68	0.0	17.2	0.6	346.9
ABBOSSI H/C	0	24	0.0	8.1	152.5	420.1
AITONG DISP	0	17	0.0	6.2	0.8	177.9
E/AJUIK DISP	0	48	0.2	9.6	1 1	50.1
E/DIKIRR DISP	0	38	0.0	0.9	0.0	110.0
E/ENTERIT DISP	0	53	11.7	11.5	0.7	33.4
E/ERINGA DISP	0	37	3.3	6.1	0.8	75.2
E/NYIRO DISP	0	74	0.04	20.1	1.1	114.8
EMARTI DISP	0	57	0.0	9.4	0.1	238.7
ENABELIBEL H/C	0	65	0.0	17.7	22.2	277.9
ENOOSAEN DISP	0	71	0.03	10.7	15.4	270.4
ENOOSUPUKIA DISP	0	74	0.0	10.7	0.8	78.1
ENTASEKERA DISP	0	67	0.03	2.4	0.09	50.2
ENTONTOL DISP	0	33	0.3	12.7	10.3	38.5
GK PRISON DISP	0	49	0.0	2.0	0.2	46.1
ILKERIN DISP	0	51	0.02	5.5	1.8	32.4
ILMOTIOK DISP	0	1	0.0	3.0	0.0	1.0
KEEKOROK H/C	0	77	0.08	7.0	5.0	189.6
KICHWA TEMBO DISP	0	3	0.0	14.3	0.0	58.7
KILGORIS H/C	0	79	0.0	8.6	0.8	720.5
KIMINTET DISP	0	20	0.0	4.2	0.05	301.2
KOJONGA DISP	0	79	0.0	3.0	1.9	85.7
LEMEK DISP	0	46	0.04	9.7	10.0	188.0
LOLGORIAN H/C	0	74	0.0	30.9	0.7	478.4
MAJIMOTO DISP	1	69	7.5	0.6	0.3	57.8
MARA SERENA DISP	0	43	0.0	17.1	0.1	50.6
MARARIANTA DISP	2	6	51.6	16.3	5.3	111.8
MASURURA DISP	0	10	0.0	4.1	6.6	357.4
MEGWARA DISP	0	68	0.1	4.3	0.03	62.0
MORIJO LOITA DISP	0	45	0.4	8.1	2.1	34.4
MOSIRO DISP	0	47	0.06	1.1	0.04	53.9
MULOT DISP	0	70	0.1	18.3	2.4	0.1
N/ENKARE H/C	0	65	0.0	39.4	2.7	274.0
NAROK DIST HOSP	2	40	2.5	50.8	11.9	390.0
NAROOSURA H/C	0	58	0.2	22.7	18.2	51.4
NGITO DISP	0	26	1.0	4.2	1.3	69.7
NKARARO DISP	0	58	0.0	15.4	0.8	367.0
NKARETA DISP	0	4	0.0	24.8	0.0	61.3
NKORNKORI DISP	0	19	0.0	8.7	1.2	74.1
OLASITI DISP	1	80	8.1	5.9	1.6	48.6
OLCHORO DISP	0	76	0.0	14.2	2.0	81.5
OLEDEEM DISP	0	15	0.3	1.8	1.4	6.1
OLMESUTIE DISP	0	61	0.02	11.1	0.3	52.3
OLOKIRIKIRAI DISP	0	56	0.0	48.0	14.3	92.0
OLOKURTO H/C	0	68	0.1	13.4	0.2	121.5
OLOLPIRONITO H/C	0	75	2.7	5.7	0.5	68.0

DISPENSARY	BRUCELLOSIS TEST CODE	MONTHS REPORTED	MEAN CASES PER MONTH BR.	RH.	PUO.	MAL.
OLOLULUNGA H/C	0	68	0.01	30.6	0.2	191.6
OLOROPIL DISP	0	20	5.8	35.7	20.9	43.0
OLORTE DISP	0	7	0.1	1.6	0.0	13.6
OLPUSIMORU DISP	0	58	0.4	7.9	3.2	33.7
POROKO DISP	0	7	0.0	0.0	0.0	28.6
SAKUTIEK DISP	0	54	0.1	9.0	1.7	96.1
SEKENANI DISP	0	41	0.0	8.6	1.0	122.7
SIYIAPEI DISP	1	84	15.5	27.9	0.2	54.3
SOGOO H/C	0	54	0.0	17.2	0.1	305.6
ST. ANTHONY LEMEK0	2	0.0	20.0	0.0	113.5	
ST. JOSEPHS HOSP	0	49	0.2	29.8	15.3	257.9
SUSWA DISP	0	1	4.0	5.0	4.0	55.0
TALEK DISP	0	14	1.4	3.4	0.4	81.6

KEY:

Brucellosis test code

0: Not testing
1: Testing regularly
2: Testing occasionally

Abbreviations: H/C = Health centre, Disp. = Dispensary, Hosp. = Hospital, Br. = brucellosis, Rh. = rheumatism, PUO = pyrexia of unknown origin, Mal. = Malaria

Appendix 3: Some clinical attributes of 440 positive brucellosis cases examined in the study.

Record#	AGE (yrs)	SEX	DURATION (days)	DIAGNOSIS	BS	BSRESULT	BT	BTRESULT
1	10.0	0	30	B	N	-	D	+
2	10.0	0	662	B	N	-	D	+
3	30.0	0	60	M	N	-	D	+
4	62.0	1	60	B	N	-	D	+
5	9.0	1	300	B	N	-	D	+
6	10.0	1	3	O	N	-	D	+
7	10.0	0	60	O	N	-	D	+
8	20.0	0	2	B	N	-	D	+
9	12.0	0	7	BM	N	-	D	+
10	31.0	0	1424	M	N	-	D	+
11	10.0	0	30	B	N	-	D	+
12	55.0	0	361	M	N	-	D	+
13	4.0	1	14	B	N	-	D	+
14	35.0	1	210	B	N	-	D	+
15	30.0	0	365	B	N	-	D	+
16	45.0	1	365	O	N	-	D	+
17	69.0	0	60	B	N	-	D	+
18	9.0	1	60	B	N	-	D	+
19	29.0	1	1460	B	N	-	D	+
20	10.0	1	4	B	N	-	D	+
21	50.0	0	2555	R	N	-	D	+
22	4.0	1	0	BM	D	-	D	+
23	7.0	0	0	B	N	-	D	+
24	60.0	0	7	BM	N	-	D	+
25	20.0	0	30	R	N	-	D	+
26	14.0	1	60	B	N	-	D	+
27	13.0	1	7	B	N	-	D	+
28	40.0	0	90	B	N	-	D	+
29	18.0	1	60	B	N	-	D	+
30	50.0	1	7	B	N	-	D	+
31	50.0	0	3650	B	N	-	D	+
32	14.0	1	21	B	N	-	D	+
33	38.0	0	30	M	D	-	D	+
34	65.0	0	0	B	N	-	D	+
35	13.0	0	30	BM	D	-	D	+
36	35.0	1	120	R	N	-	D	+
37	13.0	1	30	R	N	-	D	+
38	50.0	0	730	R	N	-	D	+
39	28.0	0	1095	B	N	-	D	+
40	13.0	1	3	R	N	-	D	+
41	20.0	0	0	B	N	-	D	+
42	30.0	0	7	B	N	-	D	+
43	30.0	0	365	BM	D	-	D	+
44	19.0	1	6	B	N	-	D	+
45	10.0	1	7	BM	D	-	D	+
46	18.0	0	7	B	N	-	D	+
47	0.0	0	0	O	N	-	D	+
48	48.0	0	30	R	N	-	D	+
49	30.0	0	0	B	N	-	D	+
50	38.0	1	4	B	N	-	D	+
51	13.0	0	60	B	N	-	D	+
52	11.0	0	150	B	N	-	D	+
53	6.0	0	4	B	N	-	D	+
54	13.0	0	90	B	N	-	D	+
55	12.0	0	14	R	N	-	D	+
56	52.0	0	120	B	N	-	D	+
57	48.0	0	7	B	N	-	D	+
58	10.0	0	7	B	N	-	D	+
59	32.0	0	30	B	N	-	D	+
60	24.0	0	0	B	N	-	D	+
61	7.0	0	3	BM	N	-	D	+

Record#	AGE (yrs)	SEX	DURATION (days)	DIAGNOSIS	BS	BSRESULT	BT	BTRESULT
62	25.0	0	7	BM	D	-	D	+
63	12.0	1	14	B	N	-	D	+
64	26.0	0	30	B	N	-	D	+
65	20.0	0	7	B	N	-	D	+
66	28.0	0	60	B	N	-	D	+
67	24.0	1	30	B	N	-	D	+
68	27.0	0	7	R	N	-	D	+
69	36.0	0	2920	B	N	-	D	+
70	30.0	0	0	B	N	-	D	+
71	14.0	0	365	B	N	-	D	+
72	50.0	0	30	B	N	-	D	+
73	13.0	0	21	B	N	-	D	+
74	13.0	0	0	B	N	-	D	+
75	6.0	0	5	B	N	-	D	+
76	29.0	0	90	B	N	-	D	+
77	60.0	0	0	B	N	-	D	+
78	16.0	1	90	B	N	-	D	+
79	11.0	1	30	BM	N	-	D	+
80	10.0	1	30	B	N	-	D	+
81	37.0	0	90	B	N	-	D	+
82	49.0	1	120	B	N	-	D	+
83	33.0	1	11	B	N	-	D	+
84	40.0	0	0	O	N	-	D	+
85	26.0	0	0	R	N	-	D	+
86	12.0	0	14	B	N	-	D	+
87	35.0	1	0	O	N	-	D	+
88	60.0	0	120	R	N	-	D	+
89	30.0	0	7	B	N	-	D	+
90	6.0	1	14	B	N	-	D	+
91	14.0	1	90	B	N	-	D	+
92	52.0	0	90	R	N	-	D	+
93	24.0	0	180	B	N	-	D	+
94	52.0	1	5	B	N	-	D	+
95	15.0	0	4	B	N	-	D	+
96	20.0	1	730	B	N	-	D	+
97	0.0	0	0	B	N	-	D	+
98	35.0	1	120	B	N	-	D	+
99	30.0	1	60	B	N	-	D	+
100	36.0	0	30	B	N	-	D	+
101	22.0	0	14	BM	D	-	D	+
102	80.0	1	30	R	N	-	D	+
103	19.0	0	120	B	N	-	D	+
104	20.0	1	365	B	N	-	D	+
105	20.0	1	90	B	N	-	D	+
106	15.0	1	1460	M	D	-	D	+
107	50.0	1	180	B	N	-	D	+
108	17.0	0	30	B	N	-	D	+
109	0.0	1	730	B	N	-	D	+
110	33.0	0	120	B	N	-	D	+
111	50.0	0	14	B	N	-	D	+
112	45.0	0	21	R	N	-	D	+
113	26.0	0	3	B	N	-	D	+
114	16.0	1	30	B	N	-	D	+
115	20.0	0	0	R	N	-	D	+
116	70.0	1	60	B	N	-	D	+
117	28.0	1	3	B	N	-	D	+
118	45.0	0	365	B	N	-	D	+
119	19.0	1	30	R	N	-	D	+
120	30.0	1	21	B	N	-	D	+
121	0.0	0	730	B	N	-	D	+
122	25.0	0	120	B	N	-	D	+
123	30.0	1	90	B	N	-	D	+
124	16.0	1	3	B	N	-	D	+
125	0.0	0	30	O	N	-	D	+
126	22.0	1	60	BM	N	-	D	+
127	14.0	1	120	R	N	-	D	+
128	60.0	1	1095	R	N	-	D	+

Record#	AGE (yrs)	SEX	DURATION (days)	DIAGNOSIS	BS	BSRESULT	BT	BTRESULT
129	28.0	1	365	B	N	-	D	+
130	0.0	0	90	BM	N	-	D	+
131	1.0	1	730	B	N	-	D	+
132	0.0	0	5	BM	D	-	D	+
133	20.0	0	30	B	N	-	D	+
134	9.0	1	60	B	N	-	D	+
135	30.0	0	1460	B	N	-	D	+
136	75.0	1	21	B	N	-	D	+
137	0.0	0	30	BM	D	-	D	+
138	20.0	0	21	B	N	-	D	+
139	0.0	1	21	BM	D	-	D	+
140	0.0	0	21	B	N	-	D	+
141	0.0	0	24	B	N	-	D	+
142	0.0	0	25	B	N	-	D	+
143	58.0	1	16	B	N	-	D	+
144	16.0	0	21	B	N	-	D	+
145	65.0	0	24	B	N	-	D	+
146	26.0	0	30	B	N	-	D	+
147	10.0	0	27	B	N	-	D	+
148	56.0	0	7	B	N	-	D	+
149	34.0	1	60	B	N	-	D	+
150	46.0	0	1460	BM	N	-	D	+
151	10.0	0	60	B	N	-	D	+
152	23.0	0	30	BM	N	-	D	+
153	18.0	0	60	B	N	-	D	+
154	20.0	1	90	B	N	-	D	+
155	22.0	1	150	B	N	-	D	+
156	13.0	0	150	B	N	-	D	+
157	35.0	1	5	B	N	-	D	+
158	23.0	0	2	B	N	-	D	+
159	9.0	1	2	B	N	-	D	+
160	10.0	1	7	B	N	-	D	+
161	45.0	1	60	BM	N	-	D	+
162	22.0	0	365	B	N	-	D	+
163	14.0	1	21	B	N	-	D	+
164	24.0	0	60	BM	N	-	D	+
165	12.0	0	7	BM	N	-	D	+
166	34.0	0	365	BR	N	-	D	+
167	8.0	0	30	M	N	-	D	+
168	14.0	1	120	BM	N	-	D	+
169	28.0	0	60	B	N	-	D	+
170	23.0	0	60	BM	N	-	D	+
171	13.0	0	300	B	N	-	D	+
172	28.0	0	180	B	N	-	D	+
173	8.0	0	30	BM	N	-	D	+
174	27.0	0	150	B	N	-	D	+
175	32.0	0	3	BM	N	-	D	+
176	28.0	0	7	B	N	-	D	+
177	41.0	1	35	BM	N	-	D	+
178	12.0	0	21	BM	N	-	D	+
179	10.0	1	7	B	N	-	D	+
180	13.0	1	30	B	N	-	D	+
181	54.0	0	14	BM	N	-	D	+
182	11.0	0	60	B	N	-	D	+
183	19.0	0	30	B	N	-	D	+
184	24.0	0	12	B	N	-	D	+
185	13.0	0	180	B	N	-	D	+
186	32.0	1	210	B	N	-	D	+
187	18.0	1	30	B	N	-	D	+
188	16.0	0	60	BM	N	-	D	+
189	22.0	0	30	B	N	-	D	+
190	60.0	0	120	B	N	-	D	+
191	43.0	1	1825	B	N	-	D	+
192	31.0	0	7	B	N	-	D	+
193	13.0	1	30	B	N	-	D	+
194	34.0	0	1260	B	N	-	D	+
195	34.0	0	90	B	N	-	D	+

Record#	AGE (yrs)	SEX	DURATION (days)	DIAGNOSIS	BS	BSRESULT	BT	BTRESULT
196	28.0	0	365	BM	N	-	D	+
197	42.0	0	120	BM	N	-	D	+
198	9.0	0	60	BM	N	-	D	+
199	15.0	1	21	BM	N	-	D	+
200	12.0	1	21	BM	N	-	D	+
201	18.0	1	7	BM	N	-	D	+
202	5.0	0	30	B	N	-	D	+
203	4.0	0	14	B	N	-	D	+
204	7.0	1	10	B	N	-	D	+
205	15.0	0	8	BM	N	-	D	+
206	32.0	0	365	B	N	-	D	+
207	33.0	0	365	B	N	-	D	+
208	38.0	1	150	B	N	-	D	+
209	50.0	0	300	B	N	-	D	+
210	6.0	1	5	B	N	-	D	+
211	18.0	1	120	BM	N	-	D	+
212	13.0	1	0	B	N	-	D	+
213	18.0	0	60	B	N	-	D	+
214	19.0	0	1460	B	N	-	D	+
215	50.0	1	4	BM	N	-	D	+
216	28.0	0	60	BM	N	-	D	+
217	24.0	0	30	B	N	-	D	+
218	34.0	0	90	B	N	-	D	+
219	22.0	0	90	BM	N	-	D	+
220	15.0	1	30	B	N	-	D	+
221	8.0	1	7	B	N	-	D	+
222	19.0	0	210	B	N	-	D	+
223	13.0	0	30	B	N	-	D	+
224	44.0	0	60	B	N	-	D	+
225	21.0	1	0	B	N	-	D	+
226	34.0	1	730	BM	D	-	D	+
227	11.0	1	21	B	N	-	D	+
228	40.0	1	0	B	N	-	D	+
229	41.0	1	0	B	N	-	D	+
230	0.0	1	0	B	N	-	D	+
231	12.0	1	90	B	N	-	D	+
232	16.0	1	0	BM	D	-	D	+
233	70.0	1	4	BO	N	-	D	+
234	6.0	1	30	B	N	-	D	+
235	52.0	1	365	B	N	-	D	+
236	15.0	1	30	B	N	-	D	+
237	8.0	0	0	B	N	-	D	+
238	60.0	0	0	B	N	-	D	+
239	12.0	1	7	B	N	-	D	+
240	36.0	1	0	B	N	-	D	+
241	10.0	1	0	B	N	-	D	+
242	10.0	1	0	B	N	-	D	+
243	15.0	0	1095	B	N	-	D	+
244	7.0	0	7	B	N	-	D	+
245	15.0	1	14	B	N	-	D	+
246	40.0	0	30	B	N	-	D	+
247	17.0	1	14	B	N	-	D	+
248	17.0	0	730	BR	N	-	D	+
249	40.0	0	60	BM	D	-	D	+
250	70.0	1	30	B	N	-	D	+
251	14.0	0	0	B	N	-	D	+
252	26.0	1	7	B	N	-	D	+
253	15.0	1	0	B	N	-	D	+
254	40.0	0	0	B	N	-	D	+
255	12.0	1	7	B	N	-	D	+
256	33.0	0	0	B	N	-	D	+
257	51.0	1	0	BR	N	-	D	+
258	30.0	0	0	B	N	-	D	+
259	60.0	0	7	BR	N	-	D	+
260	13.0	0	0	BM	N	-	D	+
261	20.0	1	4	B	N	-	D	+
262	18.0	1	7	B	N	-	D	+

Record#	AGE (yrs)	SEX	DURATION (days)	DIAGNOSIS	BS	BSRESULT	BT	BTRESULT
263	13.0	0	0	BR	N	-	D	+
264	80.0	1	6	B	N	-	D	+
265	16.0	0	60	B	N	-	D	+
266	10.0	1	1095	BR	N	-	D	+
267	70.0	1	30	B	N	-	D	+
268	30.0	0	120	B	N	-	D	+
269	30.0	1	90	BR	N	-	D	+
270	24.0	0	0	B	N	-	D	+
271	7.0	1	120	B	N	-	D	+
272	20.0	0	90	B	N	-	D	+
273	70.0	0	30	B	N	-	D	+
274	60.0	1	120	R	N	-	D	+
275	50.0	1	60	B	N	-	D	+
276	15.0	1	30	B	N	-	D	+
277	12.0	0	14	BR	N	-	D	+
278	60.0	0	0	BR	N	-	D	+
279	24.0	1	0	B	N	-	D	+
280	13.0	1	365	BR	D	+	D	+
281	11.0	1	30	B	N	-	D	+
282	32.0	1	90	B	N	-	D	+
283	45.0	0	30	B	N	-	D	+
284	13.0	0	0	B	N	-	D	+
285	15.0	1	7	B	N	-	D	+
286	23.0	1	30	BR	N	-	D	+
287	52.0	1	2535	B	N	-	D	+
288	30.0	1	0	B	N	-	D	+
289	15.0	1	0	B	N	-	D	+
290	25.0	0	365	R	N	-	D	+
291	60.0	0	365	B	N	-	D	+
292	34.0	1	0	B	N	-	D	+
293	11.0	1	30	B	N	-	D	+
294	10.0	0	30	B	N	-	D	+
295	27.0	1	2	B	N	-	D	+
296	25.0	0	60	B	N	-	D	+
297	0.0	1	0	B	N	-	D	+
298	13.0	1	30	BM	D	-	D	+
299	10.0	1	0	B	N	-	D	+
300	25.0	1	0	B	N	-	D	+
301	13.0	0	7	B	N	-	D	+
302	65.0	1	30	BM	D	-	D	+
303	30.0	1	730	BM	D	-	D	+
304	20.0	0	0	B	N	-	D	+
305	33.0	0	0	B	N	-	D	+
306	30.0	0	365	BR	N	-	D	+
307	6.0	1	0	B	N	-	D	+
308	17.0	1	0	BR	N	-	D	+
309	9.0	0	7	B	N	-	D	+
310	40.0	1	180	BM	N	-	D	+
311	21.0	0	0	B	N	-	D	+
312	18.0	1	0	BM	N	-	D	+
313	20.0	0	60	BM	D	+	D	+
314	10.0	0	365	BR	N	-	D	+
315	65.0	0	3	B	N	-	D	+
316	10.0	1	30	B	N	-	D	+
317	13.0	1	30	B	N	-	D	+
318	14.0	0	30	B	N	-	D	+
319	40.0	1	365	BM	N	-	D	+
320	9.0	1	7	BM	N	-	D	+
321	65.0	0	90	BR	N	-	D	+
322	15.0	1	0	B	N	-	D	+
323	30.0	0	1095	B	N	-	D	+
324	25.0	0	14	BR	N	-	D	+
325	17.0	1	180	BO	N	-	D	+
326	7.0	1	30	BR	N	-	D	+
327	40.0	1	0	B	N	-	D	+
328	35.0	0	51	BM	N	-	D	+
329	40.0	0	14	BO	N	-	D	+

Record#	AGE (yrs)	SEX	DURATION (days)	DIAGNOSIS	BS	BSRESULT	BT	BTRESULT
330	23.0	0	90	BR	N	-	D	+
331	23.0	0	0	B	N	-	D	+
332	19.0	0	1460	O	N	-	D	+
333	12.0	1	0	B	N	-	D	+
334	20.0	0	30	B	N	-	D	+
335	10.0	0	0	B	N	-	D	+
336	25.0	0	210	B	N	-	D	+
337	45.0	0	210	B	N	-	D	+
338	15.0	1	210	B	N	-	D	+
339	45.0	1	44	BM	D	+	D	+
340	23.0	0	60	B	N	-	D	+
341	13.0	1	210	B	N	-	D	+
342	11.0	0	14	B	N	-	D	+
343	38.0	1	180	BM	D	-	D	+
344	30.0	1	30	BR	N	-	D	+
345	20.0	0	1825	B	N	-	D	+
346	17.0	1	730	B	N	-	D	+
347	25.0	0	120	BR	N	-	D	+
348	7.0	1	30	B	N	-	D	+
349	24.0	0	0	B	N	-	D	+
350	30.0	0	0	BM	D	-	D	+
351	40.0	1	210	B	N	-	D	+
352	23.0	0	210	BR	N	-	D	+
353	50.0	0	150	R	N	-	D	+
354	32.0	1	0	BO	N	-	D	+
355	42.0	1	0	B	N	-	D	+
356	21.0	1	730	B	N	-	D	+
357	40.0	1	4	B	N	-	D	+
358	12.0	0	30	B	N	-	D	+
359	17.0	0	7	R	N	-	D	+
360	35.0	0	30	B	N	-	D	+
361	4.0	0	30	B	N	-	D	+
362	5.0	0	120	B	N	-	D	+
363	4.0	0	0	B	N	-	D	+
364	3.0	1	30	B	N	-	D	+
365	6.0	0	18	BM	D	+	D	+
366	2.0	1	3	B	N	-	D	+
367	6.0	0	150	B	N	-	D	+
368	6.0	1	0	B	N	-	D	+
369	6.0	0	0	B	N	-	D	+
370	4.0	1	30	B	N	-	D	+
371	5.0	0	7	RO	N	-	D	+
372	6.0	1	99	B	N	-	D	+
373	60.0	1	0	B	N	-	D	+
374	25.0	0	99	B	N	-	D	+
375	32.0	0	99	B	N	-	D	+
376	12.0	1	60	B	N	-	D	+
377	4.0	0	99	B	N	-	D	+
378	50.0	0	60	B	N	-	D	+
379	16.0	1	99	B	N	-	D	+
380	16.0	1	99	B	N	-	D	+
381	30.0	0	30	B	N	-	D	+
382	25.0	0	99	B	N	-	D	+
383	50.0	0	0	B	N	-	D	+
384	25.0	0	210	B	N	-	D	+
385	13.0	1	99	B	N	-	D	+
386	15.0	1	99	B	N	-	D	+
387	14.0	1	99	B	N	-	D	+
388	5.0	1	30	B	N	-	D	+
389	10.0	0	99	B	N	-	D	+
390	10.0	0	30	B	N	-	D	+
391	5.0	1	3	B	N	-	D	+
392	17.0	0	99	B	N	-	D	+
393	25.0	1	99	B	N	-	D	+
394	40.0	1	60	B	N	-	D	+
395	40.0	0	30	B	N	-	D	+
396	8.0	0	99	B	N	-	D	+

Record#	AGE (yrs)	SEX	DURATION (days)	DIAGNOSIS	BS	BSRESULT	BT	BTRESULT
397	30.0	0	365	B	N	-	D	+
398	12.0	0	99	B	N	-	D	+
399	17.0	0	99	B	N	-	D	+
400	10.0	0	2	B	N	-	D	+
401	20.0	0	99	B	N	-	D	+
402	5.0	0	99	B	N	-	D	+
403	45.0	0	60	B	N	-	D	+
404	26.0	1	99	B	N	-	D	+
405	40.0	0	99	B	N	-	D	+
406	39.0	0	365	B	N	-	D	+
407	25.0	0	99	B	N	-	D	+
408	40.0	0	1095	B	N	-	D	+
409	40.0	0	30	BM	N	-	D	+
410	40.0	1	99	B	N	-	D	+
411	2.0	1	99	B	N	-	D	+
412	5.0	1	99	B	N	-	D	+
413	6.0	1	99	B	N	-	D	+
414	12.0	1	7	B	N	-	D	+
415	7.0	0	7	B	N	-	D	+
416	42.0	1	7	B	N	-	D	+
417	5.0	0	99	B	N	-	D	+
418	70.0	1	730	B	N	-	D	+
419	35.0	1	99	B	N	-	D	+
420	25.0	0	99	B	N	-	D	+
421	64.0	1	99	B	N	-	D	+
422	8.0	1	99	B	N	-	D	+
423	18.0	0	99	B	N	-	D	+
424	18.0	1	7	B	N	-	D	+
425	25.0	0	99	B	N	-	D	+
426	50.0	0	99	B	N	-	D	+
427	50.0	1	14	B	N	-	D	+
428	54.0	1	99	B	N	-	D	+
429	3.0	1	99	B	N	-	D	+
430	11.0	0	5	B	N	-	D	+
431	18.0	1	7	B	N	-	D	+
432	8.0	1	99	B	N	-	D	+
433	25.0	0	99	B	N	-	D	+
434	11.0	0	99	B	N	-	D	+
435	65.0	0	99	B	N	-	D	+
436	65.0	0	730	B	N	-	D	+
437	8.0	1	99	B	N	-	D	+
438	50.0	0	99	B	N	-	D	+
439	25.0	1	99	B	N	-	D	+
440	17.0	1	60	B	N	-	D	+

KEY:

Sex: 0 = Female, 1 = Male, Age: 0.0 = unknown, B = Brucellosis, M = Malaria, R = Rheumatism, O = Other illness, N = Not done, D = Done, - = Negative, + = Positive, Duration 0 = unknown

Appendix 4: Some clinical attributes of the 310 positive malaria cases examined in the study.

Record#	AGE (yrs)	SEX	DURATION (days)	DIAGNOSIS	BS	BSRESULT
1	2.0	0	6	BM	D	+
2	26.0	0	4	M	D	+
3	35.0	0	1	M	D	+
4	42.0	0	120	M	D	+
5	5.0	0	1	M	D	+
6	30.0	1	14	M	D	+
7	29.0	0	14	M	D	+
8	1.0	1	5	M	D	+
9	6.0	1	3	O	D	+
10	17.0	0	0	M	D	+
11	14.0	0	0	M	D	+
12	28.0	0	14	M	D	+
13	23.0	1	0	M	D	+
14	20.0	0	1	M	D	+
15	16.0	0	0	M	D	+
16	60.0	1	3	M	D	+
17	27.0	1	90	M	D	+
18	34.0	0	7	M	D	+
19	27.0	0	2	M	D	+
20	28.0	0	7	M	D	+
21	25.0	1	4	M	D	+
22	50.0	1	2	M	D	+
23	16.0	1	6	M	D	+
24	32.0	0	3	BM	D	+
25	46.0	0	60	M	D	+
26	12.0	1	3	M	D	+
27	38.0	1	1	M	D	+
28	3.0	1	0	M	D	+
29	29.0	1	0	M	D	+
30	10.0	1	45	M	D	+
31	49.0	0	7	M	D	+
32	32.0	0	10	M	D	+
33	7.0	0	1	M	D	+
34	28.0	0	4	M	D	+
35	28.0	1	3	M	D	+
36	2.0	0	0	M	D	+
37	60.0	0	14	M	D	+
38	14.0	1	0	M	D	+
39	30.0	1	7	M	D	+
40	22.0	0	0	M	D	+
41	25.0	1	90	M	D	+
42	73.0	1	14	M	D	+
43	24.0	0	7	M	D	+
44	48.0	1	7	M	D	+
45	26.0	1	7	M	D	+
46	5.0	1	1	M	D	+
47	4.0	1	3	M	D	+
48	28.0	0	5	M	D	+
49	30.0	0	7	M	D	+
50	40.0	0	730	M	D	+
51	50.0	1	60	M	D	+
52	25.0	0	30	M	D	+
53	23.0	0	30	M	D	+
54	13.0	0	3	BM	D	+
55	40.0	0	0	M	D	+
56	0.0	1	3	M	D	+
57	23.0	1	5	M	D	+
58	18.0	1	4	M	D	+
59	14.0	1	2	M	D	+
60	30.0	1	4	M	D	+
61	14.0	1	3	M	D	+
62	0.0	1	4	BM	D	+
63	45.0	1	14	M	D	+
64	0.0	1	0	BM	D	+

Record#	AGE (yrs)	SEX	DURATION (days)	DIAGNOSIS	BS	ESRESULT
65	30.0	0	3	M	D	+
66	12.0	0	7	M	D	+
67	20.0	0	4	M	D	+
68	20.0	0	2	M	D	+
69	2.0	1	7	M	D	+
70	36.0	1	14	M	D	+
71	1.0	0	1	M	D	+
72	0.0	1	7	M	D	+
73	45.0	1	2	M	D	+
74	26.0	0	5	M	D	+
75	5.0	0	4	M	D	+
76	15.0	1	2	M	D	+
77	8.0	0	3	M	D	+
78	2.0	0	2	M	D	+
79	1.0	1	2	M	D	+
80	32.0	0	21	M	D	+
81	16.0	0	2	M	D	+
82	11.0	1	150	MO	D	+
83	38.0	0	21	M	D	+
84	18.0	1	3	M	D	+
85	17.0	0	2	M	D	+
86	35.0	1	14	BM	D	+
87	0.0	1	1	M	D	+
88	28.0	1	3	M	D	+
89	18.0	0	10	MO	D	+
90	25.0	0	5	M	D	+
91	21.0	1	3	M	D	+
92	48.0	0	7	M	D	+
93	2.0	0	2	M	D	+
94	35.0	1	60	M	D	+
95	1.0	1	2	M	D	+
96	5.0	0	1	M	D	+
97	49.0	1	30	MO	D	+
98	19.0	1	2	M	D	+
99	3.0	0	3	M	D	+
100	2.0	1	3	M	D	+
101	0.0	0	1	M	D	+
102	25.0	0	7	M	D	+
103	0.0	1	3	M	D	+
104	8.0	1	2	M	D	+
105	2.0	0	2	M	D	+
106	0.0	0	1	M	D	+
107	3.0	1	4	M	D	+
108	3.0	0	2	M	D	+
109	0.0	1	2	M	D	+
110	29.0	0	4	M	D	+
111	16.0	1	3	M	D	+
112	12.0	0	7	M	D	+
113	9.0	0	4	M	D	+
114	0.0	1	2	M	D	+
115	0.0	1	30	M	D	+
116	0.0	1	3	M	D	+
117	21.0	0	12	M	D	+
118	0.0	0	6	M	D	+
119	11.0	0	12	M	D	+
120	13.0	1	4	M	D	+
121	20.0	0	5	M	D	+
122	35.0	1	8	M	D	+
123	10.0	1	2	M	D	+
124	18.0	1	11	M	D	+
125	0.0	1	4	M	D	+
126	45.0	0	6	MO	D	+
127	20.0	1	3	M	D	+

Record#	AGE (yrs)	SEX	DURATION (days)	DIAGNOSIS	BS	PSRESULT
128	22.0	0	4	M	D	+
129	14.0	1	3	M	D	+
130	4.0	0	4	M	D	+
131	19.0	0	10	M	D	+
132	12.0	0	3	MO	D	+
133	30.0	1	3	M	D	+
134	0.0	1	5	M	D	+
135	0.0	0	4	M	D	+
136	12.0	0	4	M	D	+
137	23.0	0	10	M	D	+
138	24.0	0	6	M	D	+
139	23.0	0	0	M	D	+
140	0.0	1	6	M	D	+
141	26.0	0	6	M	D	+
142	22.0	0	3	M	D	+
143	34.0	3	3	M	D	+
144	27.0	0	12	M	D	+
145	1.0	1	4	M	D	+
146	36.0	0	2	M	D	+
147	25.0	0	6	M	D	+
148	13.0	0	2	M	D	+
149	26.0	0	3	M	D	+
150	18.0	0	2	M	D	+
151	24.0	0	7	M	D	+
152	21.0	0	3	M	D	+
153	2.0	1	1	M	D	+
154	1.0	1	11	M	D	+
155	4.0	1	12	M	D	+
156	1.0	0	14	M	D	+
157	1.0	1	5	M	D	+
158	4.0	1	4	M	D	+
159	13.0	1	3	BM	D	+
160	18.0	0	90	M	D	+
161	45.0	0	180	BM	D	+
162	28.0	1	120	M	D	+
163	29.0	0	3	M	D	+
164	20.0	0	365	M	D	+
165	43.0	1	730	MO	D	+
166	13.0	1	2	M	D	+
167	50.0	1	30	M	D	+
168	21.0	0	14	M	D	+
169	36.0	0	3	M	D	+
170	29.0	1	30	M	D	+
171	20.0	0	6	M	D	+
172	19.0	1	14	M	D	+
173	27.0	0	2	M	D	+
174	23.0	0	1095	M	D	+
175	28.0	1	21	M	D	+
176	75.0	0	21	M	D	+
177	10.0	0	90	M	D	+
178	39.0	1	1	M	D	+
179	30.0	0	0	M	D	+
180	60.0	1	7	M	D	+
181	30.0	1	30	M	D	+
182	38.0	1	3	M	D	+
183	30.0	1	5	M	D	+
184	5.0	1	14	M	D	+
185	0.0	0	7	M	D	+
186	38.0	1	3	M	D	+
187	30.0	1	3	M	D	+
188	0.0	1	1	M	D	+
189	35.0	0	3	M	D	+
190	20.0	0	10	M	D	+

Record#	AGE (yrs)	SEX	DURATION (days)	DIAGNOSIS	BS	BSRESULT
191	30.0	1	3	M	D	+
192	23.0	0	365	M	D	+
193	40.0	1	7	M	D	+
194	26.0	1	5	M	D	+
195	20.0	0	7	M	D	+
196	17.0	0	14	M	D	+
197	30.0	1	2	M	D	+
198	7.0	0	3	M	D	+
199	40.0	1	2	M	D	+
200	40.0	0	3	M	D	+
201	30.0	1	2	M	D	+
202	26.0	0	14	M	D	-
203	34.0	0	7	M	D	+
204	24.0	1	7	M	D	+
205	23.0	0	4	M	D	+
206	20.0	0	6	M	D	+
207	27.0	1	7	BM	D	+
208	35.0	1	120	M	D	+
209	54.0	1	2	BM	D	+
210	32.0	0	30	M	D	+
211	13.0	1	365	BM	D	+
212	47.0	1	0	M	D	+
213	25.0	1	60	M	D	+
214	22.0	1	4	M	D	+
215	7.0	1	0	MO	D	+
216	0.0	0	4	M	D	+
217	53.0	1	30	M	D	+
218	21.0	1	7	M	D	+
219	10.0	1	30	M	D	+
220	14.0	1	180	M	D	+
221	22.0	0	9	M	D	+
222	18.0	0	4	M	D	+
223	42.0	1	3	M	D	+
224	12.0	1	12	M	D	+
225	30.0	0	10	M	D	+
226	16.0	1	0	M	D	+
227	30.0	1	0	M	D	+
228	19.0	1	525	MO	D	+
229	19.0	0	44	MO	D	+
230	49.0	0	44	M	D	+
231	24.0	1	0	MO	D	+
232	20.0	0	3	M	D	+
233	52.0	1	2	M	D	+
234	21.0	1	4	M	D	+
235	20.0	0	60	BM	D	+
236	25.0	0	3	M	D	+
237	35.0	0	210	M	D	+
238	18.0	0	7	M	D	+
239	19.0	0	3	M	D	+
240	7.0	1	1	M	D	+
241	18.0	0	0	BM	D	+
242	0.0	1	0	M	D	+
243	45.0	1	44	M	D	+
244	36.0	0	30	M	D	+
245	25.0	0	0	M	D	+
246	20.0	1	30	M	D	+
247	28.0	0	7	M	D	+
248	50.0	0	90	M	D	+
249	2.0	0	7	M	D	+
250	26.0	0	7	M	D	+
251	21.0	1	2	M	D	+
252	2.5	1	2	MO	D	+
253	1.0	1	1	M	D	+

Record#	AGE (yrs)	SEX	DURATION (days)	DIAGNOSIS	BS	BSRESULT
254	2.0	1	7	MO	D	+
255	5.5	0	1	M	D	+
256	2.0	1	7	M	D	+
257	1.0	1	4	M	D	+
258	3.0	0	4	MO	D	+
259	2.5	1	365	MO	D	+
260	3.0	1	1	M	D	+
261	3.0	1	0	MO	D	+
262	5.0	0	1	BM	D	+
263	4.0	0	0	M	D	+
264	4.0	0	3	M	D	+
265	0.6	0	14	M	D	+
266	2.0	1	0	M	D	+
267	4.0	0	7	MO	D	+
268	5.0	1	1	M	D	+
269	6.0	0	18	BM	D	+
270	5.0	0	7	M	D	+
271	1.0	1	1	M	D	+
272	2.0	1	3	M	D	+
273	0.8	0	3	M	D	+
274	0.7	1	0	MO	D	+
275	2.6	0	7	M	D	+
276	5.0	1	0	M	D	+
277	1.3	1	4	MO	D	+
278	2.2	1	3	M	D	+
279	4.0	0	7	M	D	+
280	4.0	0	2	M	D	+
281	2.0	0	4	M	D	+
282	1.2	0	7	MO	D	+
283	2.0	1	4	M	D	+
284	4.0	0	21	M	D	+
285	4.0	1	3	M	D	+
286	6.0	1	4	M	D	+
287	1.0	0	2	M	D	+
288	0.6	0	3	M	D	+
289	5.0	1	14	M	D	+
290	1.0	0	2	M	D	+
291	0.6	0	7	M	D	+
292	1.0	1	2	M	D	+
293	0.8	1	30	M	D	+
294	5.5	0	3	M	D	+
295	1.3	0	3	MO	D	+
296	5.0	0	4	M	D	+
297	4.5	1	3	M	D	+
298	1.8	1	3	M	D	+
299	0.7	0	2	MO	D	+
300	0.3	0	2	M	D	+
301	1.2	0	3	M	D	+
302	3.0	1	14	MO	D	+
303	0.2	1	7	M	D	+
304	0.5	1	3	M	D	+
305	3.6	0	0	M	D	+
306	0.1	1	7	M	D	+
307	6.0	0	3	M	D	+
308	3.0	1	10	M	D	+
309	0.7	0	2	O	D	+
310	0.1	0	30	M	D	+

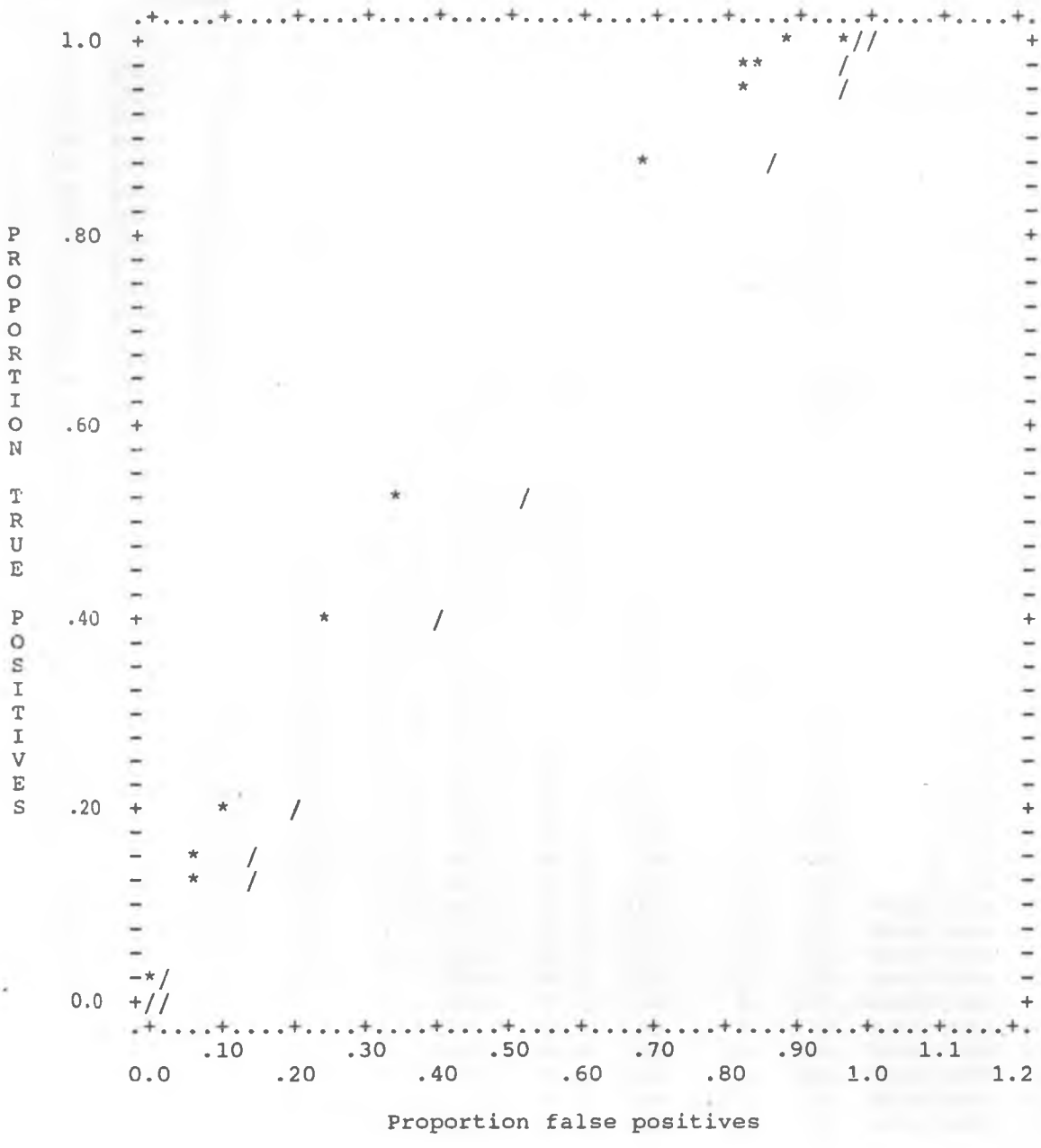
KEY: Sex: 0 = Female, 1 = Male, Age: 0.0 = unknown, B = Brucellosis, M = Malaria, R = Rheumatism, O = Other illness, N = Not done, D = Done, - = Negative, + = Positive, Duration 0 = unknown.

Appendix 5. The cost matrix of the stepwise logistic model for patients with a diagnosis of brucellosis or malaria

i). Brucellosis

CUT-POINT	CORRECT PRED *0	CORRECT PRED *1	CORRECT PRED TOTAL	% CORRECT *0	% CORRECT *1	% CORRECT TOTAL	INCORRECT PRED *0	INCORRECT PRED *1	INCORRECT PRED TOTAL	CR.PROD. RATIO	GAIN OR LOSS
0.030	184.	1.	185.	100.0	0.2	29.6	0.	439.	439.	UNDEFINED	-439.00
0.050	184.	1.	185.	100.0	0.2	29.6	0.	439.	439.	UNDEFINED	-439.00
0.070	184.	22.	206.	100.0	5.0	33.0	0.	418.	418.	UNDEFINED	-418.00
0.090	184.	22.	206.	100.0	5.0	33.0	0.	418.	418.	UNDEFINED	-418.00
0.110	182.	51.	233.	98.9	11.6	37.3	2.	389.	391.	11.93	-391.00
0.130	178.	74.	252.	96.7	16.8	40.4	6.	366.	372.	6.00	-372.00
0.150	178.	77.	255.	96.7	17.5	40.9	6.	363.	369.	6.29	-369.00
0.170	178.	77.	255.	96.7	17.5	40.9	6.	363.	369.	6.29	-369.00
0.190	176.	78.	254.	95.7	17.7	40.7	8.	362.	370.	4.74	-370.00
0.210	159.	142.	301.	86.4	32.3	48.2	25.	298.	323.	3.03	-323.00
0.230	159.	142.	301.	86.4	32.3	48.2	25.	298.	323.	3.03	-323.00
0.250	159.	142.	301.	86.4	32.3	48.2	25.	298.	323.	3.03	-323.00
0.270	159.	142.	301.	86.4	32.3	48.2	25.	298.	323.	3.03	-323.00
0.290	96.	293.	389.	52.2	66.6	62.3	88.	147.	235.	2.17	-235.00
0.310	96.	293.	389.	52.2	66.6	62.3	88.	147.	235.	2.17	-235.00
0.330	96.	293.	389.	52.2	66.6	62.3	88.	147.	235.	2.17	-235.00
0.350	96.	293.	389.	52.2	66.6	62.3	88.	147.	235.	2.17	-235.00
0.370	74.	336.	410.	40.2	76.4	65.7	110.	104.	214.	2.17	-214.00
0.390	37.	392.	429.	20.1	89.1	68.8	147.	48.	195.	2.06	-195.00
0.410	26.	412.	438.	14.1	93.6	70.2	158.	28.	186.	2.42	-186.00
0.430	26.	412.	438.	14.1	93.6	70.2	158.	28.	186.	2.42	-186.00
0.450	26.	412.	438.	14.1	93.6	70.2	158.	28.	186.	2.42	-186.00
0.470	26.	412.	438.	14.1	93.6	70.2	158.	28.	186.	2.42	-186.00
0.490	25.	413.	438.	13.6	93.9	70.2	159.	27.	186.	2.41	-186.00
0.510	5.	438.	443.	2.7	99.5	71.0	179.	2.	181.	6.12	-181.00
0.530	4.	438.	442.	2.2	99.5	70.8	180.	2.	182.	4.87	-182.00
0.550	4.	438.	442.	2.2	99.5	70.8	180.	2.	182.	4.87	-182.00
0.570	4.	438.	442.	2.2	99.5	70.8	180.	2.	182.	4.87	-182.00
0.590	4.	438.	442.	2.2	99.5	70.8	180.	2.	182.	4.87	-182.00
0.610	4.	438.	442.	2.2	99.5	70.8	180.	2.	182.	4.87	-182.00
0.630	4.	438.	442.	2.2	99.5	70.8	180.	2.	182.	4.87	-182.00
0.650	3.	440.	443.	1.6	100.0	71.0	181.	0.	181.	UNDEFINED	-181.00
0.670	3.	440.	443.	1.6	100.0	71.0	181.	0.	181.	UNDEFINED	-181.00
0.690	3.	440.	443.	1.6	100.0	71.0	181.	0.	181.	UNDEFINED	-181.00
0.710	2.	440.	442.	1.1	100.0	70.8	182.	0.	182.	UNDEFINED	-182.00
0.730	1.	440.	441.	0.5	100.0	70.7	183.	0.	183.	UNDEFINED	-183.00
0.750	1.	440.	441.	0.5	100.0	70.7	183.	0.	183.	UNDEFINED	-183.00
0.770	1.	440.	441.	0.5	100.0	70.7	183.	0.	183.	UNDEFINED	-183.00
0.790	1.	440.	441.	0.5	100.0	70.7	183.	0.	183.	UNDEFINED	-183.00
0.810	1.	440.	441.	0.5	100.0	70.7	183.	0.	183.	UNDEFINED	-183.00
0.830	0.	440.	440.	0.0	100.0	70.5	184.	0.	184.	UNDEFINED	-184.00

Receiver operating characteristic (ROC) plot of the goodness of fit of the brucellosis model.

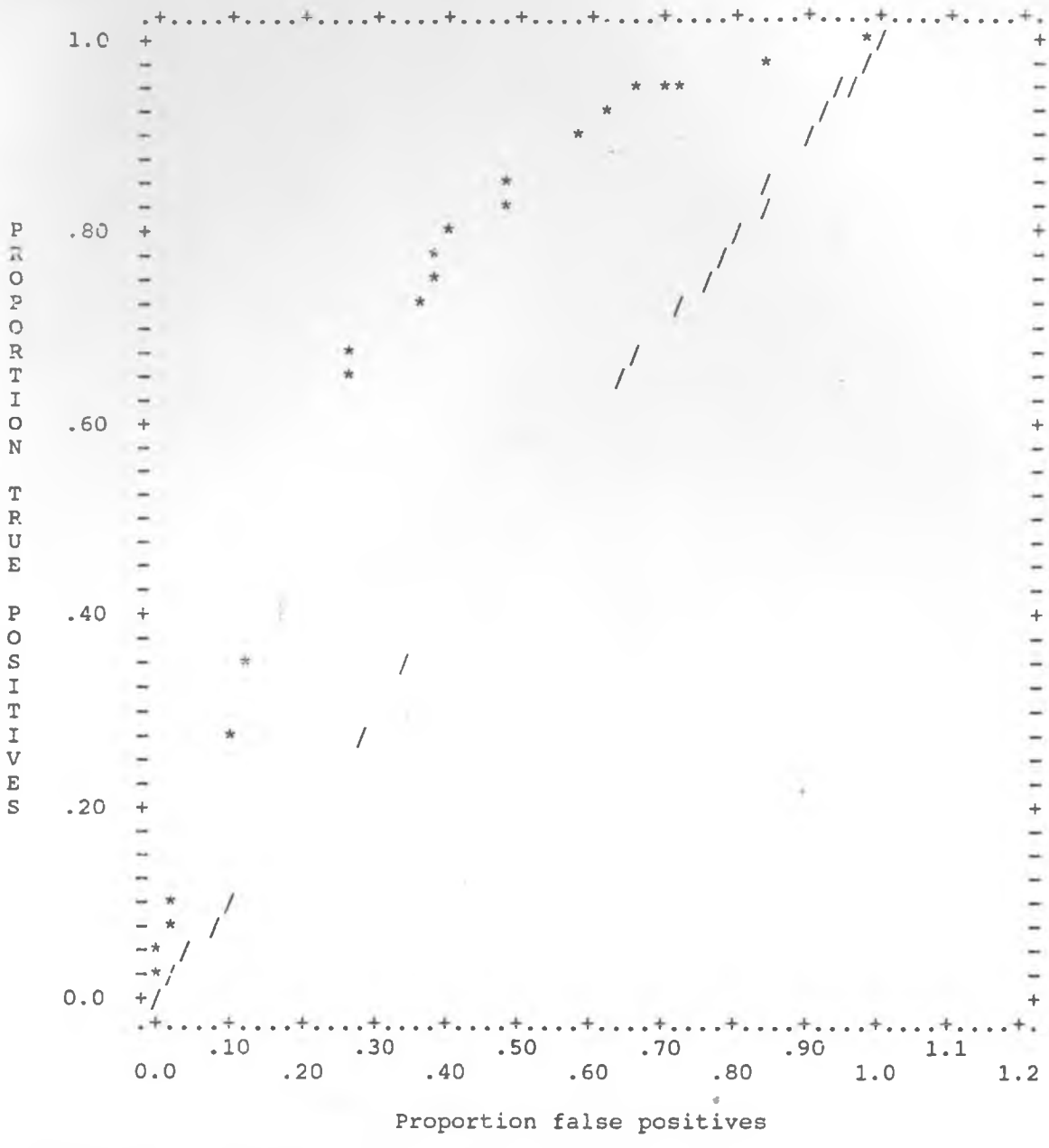


The area under the polygon, formed by connecting the points (0,0) through the asterisks to (1,1), is 0.6420 (64.2%).

ii). Malaria

CUT-POINT	CORRECT PRED *0	*1	TOTAL	% CORRECT *0	*1	TOTAL	INCORRECT PRED *0	*1	TOTAL	CR.PROD. RATIO	GAIN OR LOSS
0.030	155.	4.	159.	100.0	1.3	34.3	0.	305.	305.	UNDEFINED	-305.00
0.050	155.	9.	164.	100.0	2.9	35.3	0.	300.	300.	UNDEFINED	-300.00
0.070	153.	50.	203.	98.7	16.2	43.8	2.	259.	261.	14.77	-261.00
0.090	148.	84.	232.	95.5	27.2	50.0	7.	225.	232.	7.89	-232.00
0.110	147.	90.	237.	94.8	29.1	51.1	8.	219.	227.	7.55	-227.00
0.130	146.	102.	248.	94.2	33.0	53.4	9.	207.	216.	7.99	-216.00
0.150	143.	117.	260.	92.3	37.9	56.0	12.	192.	204.	7.26	-204.00
0.170	142.	119.	261.	91.6	38.5	56.3	13.	190.	203.	6.84	-203.00
0.190	140.	129.	269.	90.3	41.7	58.0	15.	180.	195.	6.69	-195.00
0.210	140.	130.	270.	90.3	42.1	58.2	15.	179.	194.	6.78	-194.00
0.230	130.	158.	288.	83.9	51.1	62.1	25.	151.	176.	5.44	-176.00
0.250	130.	159.	289.	83.9	51.5	62.3	25.	150.	175.	5.51	-175.00
0.270	129.	162.	291.	83.2	52.4	62.7	26.	147.	173.	5.47	-173.00
0.290	125.	185.	310.	80.6	59.9	66.8	30.	124.	154.	6.22	-154.00
0.310	125.	185.	310.	80.6	59.9	66.8	30.	124.	154.	6.22	-154.00
0.330	125.	186.	311.	80.6	60.2	67.0	30.	123.	153.	6.30	-153.00
0.350	120.	192.	312.	77.4	62.1	67.2	35.	117.	152.	5.63	-152.00
0.370	120.	192.	312.	77.4	62.1	67.2	35.	117.	152.	5.63	-152.00
0.390	118.	193.	311.	76.1	62.5	67.0	37.	116.	153.	5.31	-153.00
0.410	113.	199.	312.	72.9	64.4	67.2	42.	110.	152.	4.87	-152.00
0.430	103.	226.	329.	66.5	73.1	70.9	52.	83.	135.	5.39	-135.00
0.450	103.	226.	329.	66.5	73.1	70.9	52.	83.	135.	5.39	-135.00
0.470	99.	229.	328.	63.9	74.1	70.7	56.	80.	136.	5.06	-136.00
0.490	54.	271.	325.	34.8	87.7	70.0	101.	38.	139.	3.81	-139.00
0.510	54.	271.	325.	34.8	87.7	70.0	101.	38.	139.	3.81	-139.00
0.530	42.	279.	321.	27.1	90.3	69.2	113.	30.	143.	3.46	-143.00
0.550	42.	279.	321.	27.1	90.3	69.2	113.	30.	143.	3.46	-143.00
0.570	42.	280.	322.	27.1	90.6	69.4	113.	29.	142.	3.59	-142.00
0.590	15.	302.	317.	9.7	97.7	68.3	140.	7.	147.	4.62	-147.00
0.610	14.	303.	317.	9.0	98.1	68.3	141.	6.	147.	5.01	-147.00
0.630	14.	303.	317.	9.0	98.1	68.3	141.	6.	147.	5.01	-147.00
0.650	11.	303.	314.	7.1	98.1	67.7	144.	6.	150.	3.86	-150.00
0.670	11.	303.	314.	7.1	98.1	67.7	144.	6.	150.	3.86	-150.00
0.690	7.	308.	315.	4.5	99.7	67.9	148.	1.	149.	14.57	-149.00
0.710	7.	308.	315.	4.5	99.7	67.9	148.	1.	149.	14.57	-149.00
0.730	4.	309.	313.	2.6	100.0	67.5	151.	0.	151.	UNDEFINED	-151.00
0.750	2.	309.	311.	1.3	100.0	67.0	153.	0.	153.	UNDEFINED	-153.00
0.770	2.	309.	311.	1.3	100.0	67.0	153.	0.	153.	UNDEFINED	-153.00
0.790	2.	309.	311.	1.3	100.0	67.0	153.	0.	153.	UNDEFINED	-153.00
0.810	2.	309.	311.	1.3	100.0	67.0	153.	0.	153.	UNDEFINED	-153.00
0.830	2.	309.	311.	1.3	100.0	67.0	153.	0.	153.	UNDEFINED	-153.00
0.850	1.	309.	310.	0.6	100.0	66.8	154.	0.	154.	UNDEFINED	-154.00
0.870	1.	309.	310.	0.6	100.0	66.8	154.	0.	154.	UNDEFINED	-154.00
0.890	1.	309.	310.	0.6	100.0	66.8	154.	0.	154.	UNDEFINED	-154.00
0.910	0.	309.	309.	0.0	100.0	66.6	155.	0.	155.	UNDEFINED	-155.00

Receiver operating characteristic (ROC) plot of the goodness of fit of the final malaria model.



The area under the polygon, formed by connecting the points (0,0) through the asterisks to (1,1), is 0.7498 (74.98%).