

PREDISPOSING FACTORS ASSOCIATED WITH DISEASES IN ANIMALS IN NIGERIA AND POSSIBLE BOTANICAL IMMUNOSTIMULANTS AND IMMUNOMODULATORS: A REVIEW

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ABSTRACT

The factors predisposing to diseases in Nigeria, Sub-Saharan was classified basically as animal, environmental, cliental among others. This review was aimed at broadening the horizon of the Veterinarian. These factors were discussed in the ~~high~~ perspective of the peculiarity of Nigeria being a developing country. The write-up also proffered some solutions using organic botanicals agents which are relatively safe in food animals with little residual effect. Some of the plants suggested are: *Allium sativum*, *Curcuma longa*, *Discorea japonica*, *Zingiber officinale*, *Jatropha gossipifolia*, *Datura spp* and *Boerhaavia diffusa*. Supplements suggested are ascorbic acid, citric acid and Vitamin E. Immunomodulating supplements suggested are interferons, L-carnitine. The immunomodulating and immunostimulating agents suggested could be used in immunocompromised animals due to contemporary predisposing factors to diseases in this geographical region.

Keywords: Predisposing, factors, diseases, botanicals and immunomodulators

INTRODUCTION

Predisposition to diseases is a latent susceptibility to diseases which may be activated under certain conditions (Studdert *et al.*, 2012). The predisposition to diseases could be classified to four basic factors which include: animal factor, environmental factor, client factor and sometimes veterinarian's factor.

Animal factors include the following; genetic and pedigree, peculiar genomic make-up, species, age, sex, allergy, status of the animal (lactation and gestation period), ability to physiologically adapt to certain external and internal stress, nutritional status and tumors (Scott, 2007; Biobaku and Shamaki, 2010; Mercks, 2010; Thiruvankandan *et al.*, 2011)

Environmental factors include; climatic and weather conditions; relative humidity, ambient temperature, sun intensity and wind speed. Geographical region, management system, disasters, insurgence, cattle rustling, vegetations and ecological factors, others environmental factors include environmental disposition to xenobiotics and desert encroachment (Garg, 2008; Okediran *et al.*, 2010; Mercks, 2010)

This write up is a review aimed at explaining some important factors (the cliental factors, educational status, socio-economical factors, philosophy, habits, and bio-security measures) that predispose animals to diseases in Nigeria, Sub-Saharan Africa and stating some readily available supplements and plants of organic source. There are some substances in plants peculiar to this region that could elicit their potentials as immunostimulants and some immunomodulators which could be used in achieving better prognosis. The predisposing factors to animal diseases in developing countries change with contemporary challenges in these Sub-regions many of which have adverse impact on the gross domestic product value and to the veterinarian. It is believed that this write-up would broaden the horizon to the modern Tropical veterinarian and might aid policy makers in the livestock industry.

METHODOLOGY

Researches, case reports, text books, reports, dissertations, thesis and other commissioned research materials that add value to the subject area were used as sources of information for this review.

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ANIMAL FACTORS

Genetic factors

Hereditary diseases are diseases that are developed mainly on hereditary basis or are inherited (Studdert *et al.*, 2012). There are diseases predisposing factors due to genetic factors. There are some peculiar breeds that suffer some disorders more than some breeds of the same species (Wiles *et al.*, 2017). Amongst the disorders most prevalent in the purebred German shepherd which is among the most bred in Nigeria could be predisposed to lipoma, skin or cutaneous cyst and hypersensitivity (O'Neill *et al.*, 2017; Wiles *et al.*, 2017). In a very recent study the short haired Weimaraner breed of dogs. This breed is predisposed to progressive retinal atrophy (Kropatsch *et al.*, 2017). This is a retinal disorder associated with gradual vision impairment due to degeneration of retinal photo receptors of the eye Kropatsch *et al.* (2017). The molecular basis for this is the first four exons of the X-linked retinitis pigmentosa GTPase regulator (RPGR) is known to be involved in the progressive retinal atrophy (Kropatsch *et al.*, 2017). Also in a previous study in dog breeds the purebred dogs are often stated to be predisposed to some diseases due to inbreeding pressure (Urfer *et al.*, 2007). Dilated cardiomyopathy is a disease common in Doberman pinscher, Boxer, Great Dane, St. Bernard, Afghan hound and Cock Spaniel (Urfer *et al.*, 2007). The clinical course of the diseases varies within breeds. Osteogenic sarcoma is common in Wolfhound after this breed of dog is the German Shepherd breed of dog. Other diseases in which the wolfhound is predisposed to is also the osteochondriosis and osteochondritis dissecans (Urfer *et al.*, 2007). In a most recent study as of the time when this write-up is compiled. The German shepherd dog which one of the most common exotic breed of dog in this region and is one of the most patronized by dog breeders (Oboebgulem and Nwakonobi, 1989). A demographic study had shown the most frequent disorders in this breed are as follows. Otitis externa, osteoarthritis, diarrhoea, obesity and aggression and its most common cause of death is musculoskeletal disorders (Kropatsch *et al.*, 2017). In poultry, there are genomic basis to the resistance of some diseases. Resistance refers to anti-disease ability or reduced susceptibility. General resistance, under the control of multigenes and influenced by environment. There is the display of defensive functions and immunity to most pathogens (Thiruvankandan *et al.*, 2011). In the case of resistance dominated gene, confers special resistance peculiar to some diseases and pathogens (Thiruvankandan *et al.*, 2011). The disease resistant genes are those encoding antibodies, microRNA and other material that help the host resist the damage caused by pathogens. *MHC* (Major histocompatibility complex) genes which confers resistance against coccidiosis by boosting the immune status of the animal, *Nramp* (Natural resistance-associated macrophage protein1) genes which encode specific proteins which restrain specific intracellular pathogens effectively (Thiruvankandan *et al.*, 2011). If mutation occurs in the *Nramp1* gene leads to marked susceptibility to *Salmonella pullorum* (Thiruvankandan *et al.*, 2011). *IFN* (Interferon) genes are said to have antiviral ability, the *IFN- α* and *IFN- β* possess this characteristics, *IFN* is also said to have antimicrobial effect. The interferon genes are resistant to infectious bronchitis virus, fowl pox and influenza virus (Thiruvankandan *et al.*, 2011). *Mx* (Myxovirus resistance) genes, which is the most studied gene family in chicken and is associated with resistance to avian influenza and infectious bursal disease virus (Thiruvankandan *et al.*, 2011). It is widely accepted that chicken *Mx* protein and *Asn/ser* at the 631st amino acid could lead resistance or susceptibility to disease. *ALV* (Avian leucosis virus) genes and *Zyxin* gene are also other genes of resistance in avian. So birds that don't have these unique genes would be more predisposed (Thiruvankandan *et al.* 2011). These resistance genes features are peculiar to some breeds that are less predisposed to disease.

SPECIES

Animal species have diseases peculiar to them due to the fact that pathogens have preference to particular hosts. For example parvovirus infection in dogs, foot and mouth disease in bovine, *Cowdria ruminantium* in goats, African horse sickness in equine, swine fever porcine, *Spring viraemia* in fish. Some unique diseases are directly species specific but have wider species host target such as rabies. Rabies could infect all warm blooded animals but in spite this; it is still one of the top ten species specific that affect canine species (Merks, 2010).

AGE

The age of an animal could be a predisposing factor to diseases. Neonates have higher tendency to be infected than their adult. This is due to the fact their cell mediated immunity and humoral immunity is still developing.

For this reason, it is advisable to the farmers and pet owners to ensure neonates take colostrums to enhance their immune status (Scott, 2007). Puppies are predisposed to parvoviral enteritis (Merks, 2010). Kids are predisposed to peste des petites ruminants, other diseases that affect the young are neonatal lamb disease, *E. coli* infection, and pneumonia due to bordetellosis because their immunity and thermoregulatory mechanism in young animals is not developed (Scott, 2007). Calves are predisposed to rotavirus, coccidiosis and cryptosporidiosis (Merks, 2010). These diseases rarely affect the adult. In the same vein, old animals are also predisposed to tumors and other diseases. So old or young age predisposes them to diseases.

Sex of the animal

Storm abortion affects pregnant females and clinically gives a manifest form of the disease. Contagious agalactia, gangrenous mastitis, toxoplasmosis, campylobacteriosis in ewe and does (Scott, 2007). Female animals are also predisposed to mycotic abortion unlike in males. In this case, pregnant animals are liable to come down with mycotic abortion if predisposed to food contaminated with aflatoxins (Biobaku *et al.*, 2016). *Chlamydia* and leptospira infections also affect female animals more than their male counterparts. Cystic ovary disease also manifest more in heifers, bitches, does, ewes and female cats (Merks, 2010). Some diseases also affect males and not the females an infection exemplified by this is *Actinobacillus seminis* infection in rams. Other diseases could affect both males and females. Examples include; genital horse pox, equine venereal balanitis in stallion caused by *Equine herpes virus type 3 (EHV-3)* (Oladosu, 1995). Ovine posthitis and vulvitis with a predisposing factor of high intake of protein coupled with Campylobacteria infection in male and female animals respectively (Scott, 2007). In males, it is manifested as the inflammation of the prepuce and glans penis (Scott, 2007). In the females it affects the vulva which is associated with swelling and bleeding. This disease is also associated with conditions of infection of *Corynebacterium renale* or other urease producing organisms such as *Mycoplasma mycoides mycoides* and *Arcanobacteria pyogenes* (Scott, 2007). In dogs, for example males Wolfhound are more predisposed to gastric dilation volvulus than the females (Urfer *et al.*, 2007).

Allergy

An individual animal might manifest anaphylactic reaction or type one hypersensitivity reaction. In cattle it can result to an atypical interstitial pneumonia. The main target organ is the lung for type hypersensitivity reaction. It had been documented that DL-tryptophan rich grasses could also predispose cattle to allergy and respiratory syndrome which is manifested as emphysema and bronchopneumonia (Bishop, 2005). Horses, cats and dogs might also have respiratory related allergies. This could predispose them to various secondary respiratory opportunistic diseases. The pathophysiological basis to this is in animals the respiratory tract is lined with pseudostratified columnar epithelial cells. Interspersed between the epithelial cells are goblet cells (Esievo, 2017). An allergen would trigger mast cells, eosinophils and other cellular components infiltration this would subsequently cause degranulation of the mast cell and the release vaso-active substance that would elicit bronchoconstriction these would stimulate the parasympathetic component of the autonomic system which is associated with increased mucous secretion coupled with bronchoconstriction (Wanamaker and Massey, 2009; Sandhu, 2014). Other immune related reactions would involve the pro-inflammatory cytokines which would result to inflammation of the respiratory tissues such as the lungs and the bronchi (Dhama *et al.*, 2008). This would result to pneumonia and bronchopneumonia. This would predispose the animal to secondary opportunistic organisms to infect the respiratory system and could manifest as sneezing, coughing, wheezing, rhinitis, sinusitis and other signs.

Animal behaviour

An animal could be aggressive agonistic, anxious or could have abnormal behaviour of dominance (Merks, 2010). This could predispose them to confrontation in competition for scarce resources. This could also predispose them to injuries and if not detected could predispose to tetanus. They could be fearful animals and defeated psychologically and not have easy access to food. This could cause starvation immunocompromise and could predispose to diseases. A rear behaviour in *Gallus domesticus* at brooding, which two hens brood mutually could result to the two hens manifesting their maternal behaviour for days even though they hatch few or none. They remain dormant and isolate themselves for more than 21 days with very little time for feeding, sun and sand bathing. They manifest this behaviour under the influence of progesterone and endorphine (Biobaku and Adeleye, 2012). This coupled with physiologic changes at laying could predispose them to stress and diseases if

not ameliorated. Animals could be adrenalized when confined as in cats and could either attack other animals, pet owners and might get themselves injured to get access to doors when enclosed in a confinement or when in a house all these could be detrimental to the health and wellbeing of the animal and could compromise the immunity due to high cortisol surge, which could predispose the animals to diseases (Ajadi *et al.*, 2012). This is because a number of neuroendocrine changes could be involved and this could have psychosomatic influence which would predispose to a distortion in the normal function and homeostasis of the animal's body.

Nutritional status of the animal

Animals that are well fed are less predisposed to diseases. This is because they have better immunity than animals that are malnourished Ameen *et al.* (2016). In Sub Saharan Africa where there are scarce resources, pets are either not well fed or are malnourished. These animals would be predisposed to arrays of diseases. Animals that are fed on balanced diets are resistant to diseases (Merks, 2010). In some experimental studies carried out in ruminants animals that are placed on good nutritional plane were able to withstand trypanosome infection than animals malnourished. In another study animals that are placed on high energy diet including maize bran were able to live longer when challenged with trypanosome infection than animals not well fed Biobaku *et al.* (2008b). The dynamics of parasitaemia would change due to the immunity and endocrine system involved to favour the animal survivability (Biobaku and Shamaki, 2010). In Sokoto red goats allowed to feed extensively fed on lush and browse which enhanced their cell mediated immunity and increased the occurrence of erythrophagocytosis which is an adaptation against foreign organisms Tambuwal *et al.* (2002). Exogenous and natural, magnesium and zinc supplements with other sources of antioxidants reduced osmotic fragility in erythrocytes and stabilized their membranes which improved the survivability of animals in trypanosome endemic areas such as Sub Sahara (Biobaku *et al.*, 2008a; Biobaku *et al.*, 2008b; Biobaku and Shamaki, 2010). The use of leguminous plants in improvement of serum protein the albumin and globulin could decrease the tendency of negative protein balance which could be improved by the immune system. *Parkia biglobosa* improved the plane of nutrition and brought about recovery in malnourished rats (Biobaku *et al.*, 2017b). All the aforementioned gave some credence to the fact that good nutrition improves immunity and prevents diseases. Malnourished animals are more predisposed to diseases, because starvation predisposes to stress. Stress compromises both the inherent and adaptive immunity and could generate oxidative radicals that are detrimental for the homeostasis this invariably at the end compromises immunity (Jibir, 2008; Biobaku *et al.*, 2016a). In the North eastern and north western zones of Nigeria at rains many farmers embark on subsistence agriculture Hassan, (2000). This leaves livestock owners no option but to keep animals in confinements. Most peasant livestock owners hardly afford maintaining their animals for long. This compromises nutrition, their immunity and predisposes them to diseases Hassan, (2000).

Tumors

Animals with tumors are predisposed to immunocompromise and are predisposed to secondary infections (Merk, 2010). This depends on the type location and the tumor. An insulinoma could cause changes in metabolism (Sandhu, 2014). This could predispose to hypoglycemia and could change blood glucose level. This would affect the health status of the animal and could cause immunocompromise. Wanamaker and Massey, (2009). The chronic nature of the tumor could also lead to a progression of disease. Tumor cells could interact with the cell mediated and humoral immunity. Hence, tumors could predispose to other forms of diseases (Merk, 2010). From the clinical perspective also, the treatment of animals using antineoplastic drugs which are cytotoxic could cause immunosuppression. These predispose the animals to super infections and secondary bacterial, protozoal and fungal infections. Malignant tumors when they undergo metastases to the neighboring tissues such as lymphoid organs such as lymph nodes, spleen, tonsils, mesenteric lymph nodes, and thymus. This could spread faster unlike benign tumors and this would further compromise the immunity of the animals which would predispose to diseases. So, in the management of tumors, clinicians should administer supportive drugs aimed at mitigating the detrimental effect of antineoplastic drugs (Temitope *et al.*, 2010; Biobaku *et al.*, 2011). Such supportive drugs are antioxidants such as Vitamin C, Vitamin A, Vitamin E, selenium and some natural nutraceutical agents such as *Parkia biglobosa*, *Vernonia amagdalina*, and *noni Juice*, Omega fatty acids, *Allium sativum* supplements among others Awoyomi *et al.*, 2013; Biobaku *et al.*, 2017c).

Physiological adaptation to internal and external stress

Animals that are subjected to internal stress such as pains due to endogenous production of cyclooxygenases, prostaglandins, thromboxane prostacyclins, substance P, serotonin, dopamine, kallikrein, bradykinin and other factors generated endogenously (Sandhu, 2014). These bring about alarm reaction if the stress factor those not persist for a long time (Biobaku *et al.*, 2016b; Biobaku *et al.*, 2017a). The neuroendocrine mechanism will triggers adjustment of the physiological distortion. The faster the body could adjust to homeostasis mechanisms to counteract the physiological upset, the less the predisposition to disease (Biobaku *et al.*, 2017b). This is because glucocorticoids from the cortex of the adrenal medulla will produce cortisol endogenously. This affects the leucocytes count which will eventually decrease the cell mediated immunity. This might cause culmination of the disease causing agent and will cause a spread of the disease from organ to organ. In some animals, cortisol could be produced as endogenously or (exogenously) xenobiotics (Garg, 2008). This might lead to secondary bacterial infection due to immunocompromise. There are also scientific basis that cortisol surge in an organism could cause joint induce corticosteroid pains (Merk, 2010). In some cases, if the stress is prolonged, this would cause the body to adjust itself by the general adaptive syndrome. This requires more time, caloric involvement and other biochemical changes. This is a syndrome and could predispose to diseases. In production animals, it could affect products like beef, chevon, hides and skin (Biobaku *et al.*, 2016a; Singh, 2007).

ENVIRONMENTAL FACTORS

Relative Humidity: High humidity at wet season and the disposition of animal housing such as in poultry farms buildings on areas that are not levels could cause accumulation of water in ditches especially when water tables to the surface. Damp litters due to high moisture and poorly constructed pens could predispose to coccidiosis (Hall, 1985; Urquhart *et al.*, 2003). Similarly, in a wet and humid environment of the tropical rain forest in Nigeria could also predispose rabbit to pneumonia and could cause snuffles due *Pasteurella spp* and other pathogenic organisms that could cause upper respiratory diseases. During the wet season, the incidence of dermatophytosis in cattle and horses tend to increase. Ectoparasites such as ticks, flees, flies, thrive better in high humid damp environment (Urquhart *et al.*, 2003). In the same vein, vector diseases that are transmitted by these parasites are on the increase in animals. The incidence of helmenthosis in high humidity also increases in ruminants, pigs and equines (Urquhart *et al.*, 2003). *Glossina spp* of river areas transmit diseases in tropical rain forest (Urquhart *et al.*, 2003). Therefore, animals are predisposed to trypanosomosis which is influenced by high humidity. *Dermatophylus congolense* occurrence increases in the wet season especially in tropical Sub-Saharan Africa (Shaibu and Adetosoye, 2008). In the dry season, the incidence of fungal skin infestation, scabies and other skin diseases decrease. Nature had made it that at high humidity, the ruminants thrive better due to good grazing because of fresh herbage that is fed upon by the animals. This tends to improve the immunity of the animals due to the flavonoids and other antioxidants present in the grasses. It had been documented in literature that animals that are extensively managed to feed on browse plants. Such animals are goats, sheep, antelope and buffalos in the wet season and at high humidity feed on selected plant that could be of medicinal value. Some of these plants include; *Khaya senegalensis*, *Annona senegalensis*, *Adansonia digitata*, *Tridax procumbens*, *Aspillia africana*, *Carica papaya*, *Acacia albida*, *Acacia nilotica*, *Balanitis aegyptica* and goat weed are among plant fed in a free range to confer immunity to the animals naturally from helminthes (Urquhart *et al.*, 2003; Sanni *et al.*, 2005; Akinyemi *et al.*, 2005; Awoyomi *et al.*, 2013). In the dry season, at low humidity grazing of animals becomes more difficult and access to fresh herbage would be difficult and this could compromise the immunity. The natural trees for browse wilt to adapt for high transpiration in the semiarid zone of the Savannah. These animals at adverse lower humidity would find it difficult to feed, this condition causes compromise in the immunity.

Ambient temperature

Temperature as it is known is the degree of hotness and coldness of a particular region. In Tropical Sub-Saharan Africa, temperature could rise high at hot dry season to a few degrees Celsius in the harmattan (Ismaila *et al.*, 2010). At high temperature and with poor nutrition predisposes animals to stress and diseases. In Northern Nigeria, *Gallus domesticus* extensively reared suffer high incidence of New castle disease and mortalities due to stress (Agaie and Uko, 1998). Other diseases transmitted are chronic respiratory disease, coryza, salmonellosis and infectious laryngotracheitis amongst others (Agaie and Uko, 1998). Prior to the wet

season, at the wet and harmattan seasons, animals could be predisposed to respiratory infections, the lambs, kids and calves due to their undeveloped thermoregulatory are predispose to some respiratory syndromes and *peste des petites ruminants* (Scott, 2007). Nasal enzootic adenocarcinoma in a West African doe was reported, initially the case manifested as a respiratory syndrome, but diagnosed to be nasal enzootic adenocarcinoma (Ajayi *et al.*, 2013). It might not be too far to correlate the climatic changes amongst factors that contribute to manifestation of oncogenic factors coupled with an incriminating pathogenic which is of class D retrovirus (Ajayi *et al.*, 2013). Pigeons are predisposed to New Castle disease and pigeon pox at harmattan (Hall, 1985; Agaie and Uko, 1998). Pigeon pox which is caused by a pox virus which could cause blindness and form lesions that could obstruct the oral cavity and oropharynx of birds which could eventually lead to death. Although, these are self limiting diseases in this species at the harmattan season in North Western Nigeria (Hall, 1985; Agaie and Uko, 1998). High ambient temperature or extreme low temperature of the harmattan could affect aquatic life and fish such as the *Clarias spp* could be dormant in early hours of the day and later feed in warmer hours. These affect the feed conversion ratio and could predispose to stress and diseases (Ezeri, 2014).

Geographical region

The geographical region where the animals are bred also could be one of the environmental factors that could contribute to predisposition of diseases (Urquhart *et al.*, 2003). Animals bred in such area could be exposed to some diseases peculiar to the region. In Nigeria, Sub Saharan Africa and South of the equator the trypanosomosis belt spreads along latitude 4° N to 13° (Onyiah, 1997). Animals that are not trypanotolerant are predisposed to trypanosomosis infection. There are various strains of trypanosomes and other haemoparasitic infections. The trypanosome breed is more resistant to this endemic parasite in Nigeria.(Onyiah, 1997).The breeds of cattle that are trypanotolerant include; the Keteku, muturu and the Ndama breeds and are more resistant than the Bororo, Gudali and white fulani breeds. The West African Dwarf goat is more resistant than the Sahel, Sokoto red and Maiduguri brown (Ameen *et al.*, 2016).These resistant breeds of animals were found to have higher magnesium concentration in their plasma than other less resistant breeds. These resistant animals thrive better in the Tropical Rain Forest better than the predisposed counterparts. The pathogenic progression of the disease might not favour survival of animals not adapted to this geographical zone. An example of this is a German shepherd dog bought from South Africa had episodes of epilepsy due to the encephalitic form of *Trypanosome congolense* (Biobaku *et al.*, 2015). This animal was predisposed to the infection due to region factor and the progression of the disease was faster which resulted to the trypanosomes sequel to meningitis to reach blood brain barrier and cause distortion in the polysynaptic mid brain and changed the dynamics of neurotransmitter (Biobaku *et al.*, 2015).Which caused the episodes convulsion. This could occur in other exotic dogs the progression of the disease takes time. Another example of the geographical factor predisposing animals to disease is a case of a Friesian breed of bull important and brought to the North western region of Nigeria. Less than three months after purchase it was predisposed to bovine babesiosis (Urquhart *et al.*, 2003). This is because this geographical zone has this diseases endemic because of the vectors of these disease (Urquhart *et al.*, 2003).The disease progression and course of the disease was very protracted, after which the animal manifested classical signs of babesiosis which was jaundice, haemoglobinuria, anaemia weight loss and anorexia (Urquhart *et al.*, 2003). This exotic bull in this geographical zone lacked pre-immunity or enzootic stability. Exotic animals when introduced into this a particular region different from where they were purchased should be offered intensive care with regular prophylaxis for some time until they develop pre-immunity and acclimatize to the new environment. Papillomatosis in cattle caused by *papilloma* viruses had been reported in Nigeria as a transboundary disease (Zwandor *et al.*, 2008). This means if animals are introduced in these regions they should be routinely vaccinated regularly and offered prophylactic therapy to enable time develop immunity over time. In North central zone of Nigeria the collaborative scheme between two business parties embarked on a diary breed cattle New Jersey for breeding and milk production (Biobaku, 2015).The management of the animals became relatively difficult and there were losses due trypanosomosis, aflatoxicosis, babesiosis, dermatophylosis and bovine contagious pleuropneumonia among others. These diseases are basically among the contending factors in the management of these exotic animals bought from outside Nigeria. The indigenous animals and the cross bred animals in this zones thrived better in this geographical zone using the same management systems than the pure bred exotic breed. So the geographical zone with its contending endemic diseases predisposes animals to diseases. Clinicians must ensure appropriate veterinary care, biosecurity and quarantine measures when animals are introduced to a new geographical zone.

Management system

Management systems also affect the immunity of animals and could predispose to diseases if compromise. Intensively managed animals are less predisposed to diseases. This is because they are routinely vaccinated and prophylactically treated overtime. They are therefore, less predisposed to dangers and stress conditions. In the South western part of Nigeria, if animals are extensively managed and while grazing they could be predisposed to injuries. Some hunters set traps in bushes. The grazing animals might be injured by the traps and animals might go unnoticed by herdsman. In literature, a case reports of *Aeromonas hydrophila* which was difficult to diagnose and treat in bovine, which affected the health of the animal (Awoyomi *et al.*, 2014) Many animals moved by transhumance and nomads might have their immunity overwhelmed and could eventually die. Poultry managed intensively are predisposed to cage stress if such birds are not properly managed could be predisposed to diseases (Hall, 1985).

In recent time animal welfare agencies frowned against keeping birds battery cages and prefer the deep litter system. In the same vein, birds kept intensively might be predisposed to disease occurrence because of the tendency that diseases could spread faster in cages. The stocking of the animals also is another factor if animals are over populated predisposes them to coccidiosis and other respiratory diseases (Hall, 1985). Management system is also another factor that affects disposition pertaining to health. Animals in captivity are predisposed to diseases, if previously managed extensively and kept to run on in a free range and suddenly changed to be managed intensively, this would predispose the locally bred animals to diseases if they are poorly nourished and exposed to stress of restraint. It had been documented in literature that animals bred in Sub-Sahara had significant changes in their haematological parameters when managed semi-intensively or intensively, even when fed on balanced rations. Animals managed extensively feeding in free range and on browse had significantly higher PCV and leukocytes count. The differential leucocytes parameters also showed better cell mediated immunity than animals managed intensively. It means that the extensive system is better for the local breed of animals (Sonibare *et al.*, 2007).

Transportation of animals during for breeding or slaughter if not done using stipulated standards could predispose the animals to diseases. In Nigeria research work carried out in transportation of food animals at long and short terms affected the animal's haemogram. The animals also had increased neutrophils-lymphocytes ratio which is evident of stress (Ayo *et al.*, 2006; Biobaku *et al.*, 2016). The cell mediated immunity was lowered and humoral this could predispose animals to diseases. There would be high cortisol surge that could be detrimental to the health of the animals (Ajadi *et al.*, 2012). Stocking rate and transportation welfare if not properly rendered would predispose the animals to infections (Biobaku *et al.*, 2017c). In the same vein, transportation stress could also affect the health which is detrimental to production (Biobaku *et al.*, 2016). Animals when transported using inappropriate or irrational stocking predispose animals to immune-compromise, injuries and death. It is not uncommon to see dead animals along the high ways this cause losses incurred by people in the livestock industry (Singh, 2007; Biobaku *et al.*, 2017a; Biobaku *et al.*, 2017b). The meat from dead animals subjected to stress is not whole some and it is not only detrimental to man but also to other animals. In a study carried out in dogs, experimental animals were fed on animals exposed much stress and a significant number of experimental animals suffered stress meat syndrome (Irwin *et al.*, 2012). This is also detrimental to reproductive health and general wellbeing of animals. The scientific basis to this is interaction of endogenously secreted cytokines and steroids from the animals subjected to stress in the consumer animal and man (Biobaku, 2015).

Natural disaster, insurgence and cattle rustling

Nigeria had environmental challenges including floods, bush fires, draught and rebellious insurgences among which predispose animal's to stress and diseases (Junaidu, 2016). Over flow of water bodies due to global warming and climatic change (Institute for Economic and Peace Development, 2015; Junaidu, 2016). Mismanagement of dams and domestic drainages cause over flow of water bodies at the wet season. Flood could affect sheep, goats and cattle and could predispose to stress, immunocompromise and diseases. Water lodged in clay and loamy soil could predispose bovine to foot rot which is cause by *fusobacterium necrophorum*, while in ovine it is caused by *Dichelobacter nodosus* and occurs only under very wet condition favours the proliferation of the bacteria in the soil (Scott, 2007). In ovine and caprine this is very infectious in the wet season and they suffer inflammation of the laminae of the hoof. Many animals are also predisposed to respiratory diseases most especially the lambs, kids and calves (Scott, 2007).

The insurgences in Nigeria had left many animal breeders in a confused state (Junaidu, 2016). Many animals might get lost in the forest and might be left to so many stress factors including envenomation, Intoxication and starvation; because are left for days without objective grazing by a herdmen who are also contending with many life threatening factors (Junaidu, 2016). In the South east the animals are predisposed to heavy metal toxicity and oil spillage. In recent study lead predispose to intoxication to many animals and man in these environmentally polluted areas. This affects the metabolism and causes neurotoxicity. Younger animals and children are more predisposed to this form of disease predisposing factor (Okediran *et al.*, 2010).

Between 2014 to 2016 about 202,017 cattle were reported rustled and over 1000 herdsmen and farmers were reported killed in Northwestern States of Nigeria; Kaduna, Kano, Katsina, Kebbi and Zamfara States (Junaidu, 2016). Livestock rearing is popular in the Northwestern States and traditionally farmers buy livestock with excess earning from annual harvest as savings also many farmers also have work oxen (De Haan,1994; Blench 2003). Cattle rustlers have on many occasion invaded these communities stealing cattle, impoverishing these rural dwellers and creating problems and controversies between farmers (Junaidu, 2016). Rustling has reduced the take-off of the nation, while insurgency had caused distortion in the cattle trade along the Northeastern corridor from the neighboring countries (Junaidu, 2016). This certainly would affect the movements of the cattle and since herdsmen embark solely on the extensive system and grazing animals on natural vegetation this change in dynamics would affect the feeding patterns of the animals and could predispose to diseases. These cattle settlements are threatened and need to wait for days to ensure safety in their routes of transhumance travel; which would affect the immune status of the animals and could predispose to disease.

Environmental disposition to xenobiotics

Nigeria is a country with diverse vegetative zones and animals interact directly or indirectly with the environment (Abatan, 2012). The vegetative and non vegetative part of the ecosystem posses various sources of xenobiotics (NRC, 2001). Some biological and non biologic sources include phytotoxins, zootoxins, mycotoxins and marine toxins (Garg, 2008; Biobaku *et al.*, 2016b). Non biologic sources include edaphic exposure to xenobiotics such as in extraction companies, refineries, drug companies, mining firms, insecticides production. Access to heavy metal toxicity also compromises the immunity of the animals (ATSDR, 2005; Al-Forkan *et al.* 2016). Animals that are exposed to xenobiotics are therefore exposed to diseases than animals that are not. Xenobiotics exposure at prenatal period exposure may result to susceptibility to infectious diseases, allergic reaction or autoimmune disease (Sandhu, 2014). Many target chemicals cause immune suppression Chemicals clearly disrupt cell proliferation and clonal expansion (ATSDR, 2005; Al-Forkan *et al.*, 2016). There could be disruption of T- cell maturation in thymus this mechanism for immunosuppression. Exogenous chemicals may also interfere with receptor ligands binding at the cell surface (Sandhu, 2014). Type I hypersensitivity reaction. (sometimes referred to as atopy) is mediated by antigen-specific cytophilic (Sandhu, 2014). Type I is also called immediate-type hypersensitivity Immediate asthmatic responses to allergen, allergic rhinitis (hay fever), atopic dermatitis (eczema), and acute urticaria (hives) (Sandhu, 2014; ATSDR, 2005). Type II hypersensitivity result of antibody-mediated cytotoxicity that occurs when antibodies respond to cell surface antigens. Autoimmune diseases can result from drug treatments with penicillin, quinidine, quinine, or acetaminophen (Sandhu, 2014). Antigen-antibody (IgG) complexes that accumulate in tissues or the circulation, activate macrophages and the complement system, and trigger the influx of granulocytes and lymphocytes (inflammation) (Eseivo, 2017). This is also referred to as the Arthurs reaction and includes post-infection squaler such as rheumatic heart diseases (Sandhu, 2014).

Vegetations and ecological factors

Nigeria is endowed with different vegetative and ecological zones (Junaidu, 2016). Animals in different zones directly interact with their environment these include ruminants, equine, birds and wildlife. The animals that are managed extensively feed on grasses and other fauna from the ecosystem (Junaidu, 1999). This source of food and drinking water might have optimal or lower or higher than adequate minerals in herbage, grasses or pasture (Junaidu, 2016). There could also be varying nutritional and anti-nutritional factors that could be detrimental or useful to the health of the animals as the case might be. In soils where trace elements are deficient this could predispose the grazing animals to mineral or trace elements deficiency (Scott, 2007). An example is hypomagnesaemia, iron deficiency anaemia, copper deficiency, iodine deficiency among others. However, care

must be taken when supplementation in feed or as salt licks in ovine because they are predisposed to copper toxicity (Scott, 2007; Mercks, 2010). For this reason serum chemistry and appropriate test should be conducted prior to supplementation. In the same vein, animals that are over exposed to some trace elements above their optimal required levels could also affect toxicities and metabolic diseases.

The edaphic factors (soil factors) such as pH, alkalinity, salinity, profile, and structure, topography of farms and vegetation steepness or scantiness could also affect the health of the animals and prevent or predispose animals to one or more diseases. In recent times for example snail and aquaculture had began to grow as a livestock enterprise in Nigeria (Ezeri, 2014). This factor affects this industry in a critical way. The soil type for example sandy soil, does not retain water, loamy possess relatively average water retention tendency. While the clay soil retains more water which would cause water lodging and eventually favors more parasites, bacterial, fungal proliferation these in warm Tropical zones could predispose to diseases (Biobaku *et al.*, 2010; Ameen *et al.*, 2015). The intensity of the sunshine and wind speed coupled with the absence or presence of moisture could predispose to diseases depending on the management system and species of the animal. High moisture and high water retention could be beneficial to good health of *Clarias spp* and other aquaculture breed species but might be challenging to Northern breed of goats such as the Sahel and other animals (Ezeri, 2014; Biobaku *et al.*, 2016a). All these factors if not controlled by appropriate management systems could predispose to diseases.

Desert Encroachment

Environmental changes and draught affects vegetation in the Tropical Sub Saharan region (GIZ, 2015). The dryness of the wind accompanied with its high speed tends to increase in the harmattan season (GIZ, 2015). This causes the sand dunes of the Sahara to move towards its Southern region and towards the equator. These movement increases the Sahara land mass which had affected adversely the Savannah zones of Nigeria. In spite all efforts of Nigerian government in planting of trees as wind breakers (FMA, 2016). The Sahara still poses a challenge to Nigerian vegetation that has the highest population of cattle, sheep, goats and camels (FMA, 2016). This results to drying of the shrubs, grasses and other browse plants. Animals are commonly managed extensively and ruminants feed on grasses in the natural environment year-in and year-out (FMA, 2016; Junaidu, 2016). Draught could affect the vegetation cover and animals depend solely on the grasses in the wild (Junaidu, 2016). In the semi arid zone of Nigeria environmental changes is accompanied by draught would result to animals roaming for a considerable distance before getting sufficient grasses to graze (Junaidu, 2016). This would affect the nutritional status of the animals and would predispose the animals to stress and malnutrition (Biobaku *et al.*, 2017c) Sequel to these conditions these would predispose the animals to various diseases condition. Apart from predisposing the animals to infectious diseases the likelihood of the grazing animals to feed on polythene bags and other materials might predispose them to rumen tympany, rumen atony, rumen stasis and bloat (Scott, 2007; Mercks, 2010). The incidence animals having high load of foreign materials could predispose them to metabolic disorders which would also predisposed to immune-compromise and disease conditions. This is because the immunity of such animals would be compromised in adversity of desert encroachment.

CLIENT FACTORS

The enlightenment of the client would aid good management of the animals (Junaidu, 2016). Good enlightenment and the level of education of the client would assist maintenance of good health. This means appropriate livestock practices in conformity with international standards would enhance good nutrition this would boost the immunity and health. In clients that are not enlightened this would not ensure good practices and this would affect immunity and hence predispose the animals to diseases. In the same vein, veterinary extension services and routine veterinary services which include health monitoring, routine; vaccination, deworming, supplementation of animals feed would be easily carried in enlightened client (Aliu, 2016). Compliance to prescription and routine vaccination schedules could be easily done in well enlightened clients unlike the unenlightened clients that misuse drugs and could predispose their animals to different conditions (Biobaku *et al.*, 2016c; Aliu, 2016).

The social strata the client belongs to could also affect the health status of their animal (Babalobi, 2016). Clients in the high strata of the society embark on high standards animal practices unlike those in the lower strata this would affect the management procedures in their farms and feeding. Those that cannot afford good animal health practices might have their animals more predisposed to diseases (Junaidu, 2016). Access to good

capital in livestock industry improves the health of the animals unlike those that are disadvantaged this would affect management and health (Aina, 2012). In Nigeria most goats keepers in the north are peasants and can only embark on the extensive systems at rain when animals are disallowed from being in the free range because of cultivation of farms this could compromise the health of the animals and predispose such animals to diseases (Aina, 2012). Farms that are well built also prevent the animals to be less predisposed to envenomation by snakes which could also compromise the animal's immunity and predispose to other diseases.

Security and biosecurity of the farms is an important factor that could predispose animals in a particular confinement to diseases (Junaidu, 2016). This because if the farms are properly secured would prevent stray animals and unrestricted humans from getting access into the vicinity where animals are bred (Junaidu, 1999). This depends on security measures such as fence, security personnel, alarms, automatic cameras and gates, guard dogs, electrical wire device and others. The more the farm is easily accessible without restriction the more the animals kept in such farm would be more predisposed to both endemic and transboundary diseases (Junaidu, 2016). This means that animal owners or clients that cannot afford such measures would have their animals more predisposed to diseases; while clients that have farms that less security and biosecurity conscious might have their animals more exposed to the risk of contracting contagious diseases.

An experience of over a decade of veterinary practice had shown that habits of the client or owners are also among the factors that predispose to diseases. Some client is fond of giving their pets such as dogs and cats alcohol and chocolates (Aliu, 2007; Garg, 2008). This predisposes the animals to liver diseases and chocolate intoxication in pets this had been previously documented in literature. Clients also that are well to do over feed their animals with vitamin rich diets this could predispose their pets to hypervitaminosis and lameness due to metabolic causes (Booth and McDonald, 2008).

THERAPEUTIC IMMUNOSTIMULATION AND IMMUNOMODULATION BY POSSIBLE BOTANICALS, SUPPLEMENTS AND INTERFERONS IN ANIMALS

The aforementioned predisposing factors to diseases in Sub-Saharan region could be minimized or mitigated using some botanicals and supplements that are consumer safe from residue and exogenous agents that are detrimental to the health and wellbeing of the public. This requires the knowledge of pharmacology and immunology (Quinn, 1990; Singh *et al.*, 2016)

Immunostimulation and modulation is prophylactic or therapeutic concept aimed at stimulation of the non specific immune system (Aliu, 2007). This means stimulation of the non antigenic dependent immunity thus causing the increased function and defense efficiency of the granulocytes, macrophages, complement and natural killer cells. It also could also involve the modulation of an increased immune reaction such as allergy or a depressed immune system as in immune compromise. (Aliu, 2007; Sandhu, 2014). Plant extracts that constitutes anethol, capiscum oleoresin, carvacrol, cinnamaldehyde, eugenol, oleoresin from *Curcuma longa* and *Allium sativum* conferred immunity in pigs (Liu, 2011). These extracts are said to increase cell viability of porcine alveolar macrophage, lipopolysaccharide and stimulation of IL-1 β secretion. Previous studies had shown the *Capiscum spp*, *Curcuma longa* and *Allium sativum* improved immunity against *E.coli* and decreased the frequency of diarrhoea in pigs (Liu, 2011). Plants that were investigated to possess immunostimulating potential in fish are *Viscum album*, *Urtica dioica*, *Zingiber officinale* (Aranha *et al.*, 2012; Singh *et al.*, 2016). Extracts from these plants were discovered to increase phagocytic capability of rainbow trout and carp. *Datura metel* extract was used to boost immunity and reduced significantly mortality of ornamental fish in microbial infection (Pandey *et al.*, 2010). In ruminants it was observed that animals that were placed on natural supplements rich in β -carotene, vitamin E, copper, zinc (such as in maize and maize bran) and selenium. Improved the cell mediated and humoral immunity (Biobaku and Shamaki, 2010; Scott, 2008). In rodents, *Ocimum sanctum* at 100mg/kg orally administered showed significant phagocytic index and boosted immunity. *Jatropha gossipifolia* considered to be safer than *J.carcus*. *L* methanolic extract at (0.25mg/kg body weight) in one-day-old specific pathogen free chicks was determined due to the plants immunostimulation tendency (Singh *et al.*, 2016). *Allium sativum* possessed effect on mitogenicity and hypersensitivity cells. There was synthesis of protein associated with the administration of *Allium sativum*. The mitogenicity towards lymphocytes of murine splenocytes and thymocytes which is evident of its immunostimulating property. *Boerhaavia diffusa* at 40mg/kg body weight elevated the levels of proinflammatory cytokines, TNF- α , IL-1 β and IL-6 in mice this result gave credence to its immunostimulating potential (Manu and Kuttan, 2009). *Dioscorea japonica* with active principles

Dj-dioscorins and TN1- dioscorins induce expression of proinflammatory cytokines and stimulates the phagocytosis of the bone, spleen and thymus. Dj-dioscorins enhances proliferation of CD4 (+) and CD8 (+), Th1 cells in spleen and CD19 (+) in both spleen and thymus (Lin *et al.*, 2009). *Acacia Catechu* produced a significant increase in phagocytic index and a significant protection against cyclophosphamide induced neutropenia (Ismail and Asad, 2009). In frugivorous birds flavonoids improved the humoral immunity and was investigated to be due to its antioxidative potentials (Caton *et al.*, 2008).

SUPPLEMENTS

Vitamin E significantly increased sephadex-elicited inflammatory exudates and the percentage of phagocytic macrophage in broiler chicks injected *in ovo* (Khan *et al.*, 2012). Percentage of macrophage and abdominal exudates cells were increased by administration of 200mg/kg (Khan *et al.*, 2012). The efficiency of phagocytosis by macrophages is increased by administration of supplemental vitamin E and phagocytosis is a membrane mediated phenomenon (Khan *et al.*, 2012). Vitamin E elevated percentage CD4:CD8 at seven week of age. CD4 (+) is the key player as a helper cells in antibody production. A level of 87 mg/kg of vitamin E increased the percentage of T helper cells CD4+CD8- in the thymus and spleen in the seventh week in broilers. Ascorbic acid is a common vitamin supplement most readily available that could be used in improvement of immune responses in most livestock (Khan *et al.*, 2012). It possesses an antioxidative property and aids the cell mediated and humoral immunity. Its immunomodulatory effect had been previously documented in avians, pigs, sheep, goats, fish and wild life. It has an advantage that it has minimal residual effect and possess wider therapeutic window (Sandhu, 2014).

Citric Acid (CA) when supplemented in broiler feed showed high density immunocompetent cells in the gastrointestinal tract which is an indicator of healthy broiler with high immune status and protection against pathogens and infectious diseases (Islam, 2012). Higher globulin levels were found in broiler fed supplemented with CA diets (Islam, 2012). This shows better ability to resist diseases in the broilers (Islam, 2012). This also reflected on the ability to resist New castle Disease since recent study had shown that serum globulin level increase due to CA supplementation which could be evidence of resistance to the disease (Islam, 2012).

USE OF HOST IMMUNE MODULATORS

L-Carnitine

Carnitine in poultry takes part in the transfer of long chain fatty acids which modifies the metabolism of fatty acid enhances secretion of hormones such as insulin, insulin-like factor-1 and triiodothyronine which may be involved with several lipids and hormones to confer its immunomodulatory effect (Aliu, 2007; Adabi *et al.*, 2011). L-Carnitine supplementation in pigeons increased Ig G and Ig A. At 100mg/kg supplementation in broiler chicken it modulated the innate immunity by enhancing the acute phase protein response (Aliu, 2007; Adabi *et al.*, 2011). In addition L- carnitine supplementation also helps as an antioxidant by regulating nitric oxide, cellular respiration, increase in the anti-oxidative enzymes such glutathione peroxidase, catalase, superoxide dismutase (Aliu, 2007; Adabi *et al.*, 2011; Sandhu, 2014). It exerts thiol and methionine sparing capacity all these decrease the predisposing to stress and improves its immunomodulatory effect (Aliu, 2007; Adabi *et al.*, 2011; Sandhu, 2014).

Interferons

Interferons are family of glycoproteins produced endogenously by mammals in response to a viral infection or viral infected cells secrete this to enhance their binding to receptor on the cell membranes of other uninfected cells, thus this confers antiviral effect to other cells and makes them inaccessible to other pathogens (Aliu, 2007; Dhama 2008; Studdert *et al.* 2012; Sandhu, 2014). Now interferon is produced by recombinant DNA technology in bacteria with aid of genes from human leukocytes (Sandhu, 2014). There are at least three types, classified previously according to their antigenic property and physical properties. Recently classified as class I which includes α , ω and β . While the class II are the interferon; IFN- α (leukocyte interferon type 1); IFN- β (fibroblast interferon type 1); IFN- γ (immune interferon, type II) which constitutes a family of hormones involved in modulation of immune reactions (Dhama, 2008; Studdert *et al.*, 2012; Sandhu, 2014). They are produced by T and natural killer cells (NK). The interferon-gamma are termed as immune interferon which

produced mainly in by T-lymphocytes as part of the immune response to both viral and non-viral antigens which include bacteria and their product, rickettsiae, protozoa, fungal polysaccharides and a range of polymeric chemicals and other cytokines (Dhama, 2008; Studdert *et al.*, 2012; Sandhu, 2014). IFN- α and IFN- β are produced by B and T lymphocytes, macrophages and fibroblasts in response to the presence of viruses and cytokines. The mechanism of action of interferons is it causes the synthesis of host cell enzymes such as protein kinase, 2', 5'-oligoadenylate synthetase, and phosphodiesterase which inhibit RNA translation and leads to the degradation of viral mRNA and tRNA. It also has antiproliferative and possibly antineoplastic activities may be due to its effect on the synthesis of RNA, DNA and cellular proteins oncogenes (Aliu, 2007). Interferon also acts by stimulation of the immune system (Dhama 2008; Studdert *et al.*, 2012; Sandhu, 2014). The therapeutic uses of interferon as IFN- α had been proven useful in the treatment of infectious bovine rhinotracheitis virus (Aliu, 2007). Given orally to treat non-neoplastic feline leucopenia virus. IFN- α is approved in the treatment of certain cancers such as hairy cell leukaemia, Kaposi sarcoma, or condylomata acuminata caused by papilloma virus, herpes simplex viral infections (Aliu, 2007). Intranasal administration of interferons could be prophylactically used to prevent rhinoviral cold but not useful in already infected subjects (Aliu, 2007). Interferons had been combined with antiviral drugs such as acyclovir or vidarabine and were proven to have promising effect in the management of chronic hepatitis B and C infections (Aliu, 2007; Dhama, 2008; Studdert *et al.*, 2012; Sandhu, 2014). An intralesional injection of interferon in genital warts was used in the speeding up of its regression (Aliu, 2007). INF-r in combination with pentavalent arsenicals was successful in the management of leishmaniasis (Aliu, 2007). Dosage and treatment regimes; IFN 30 IU rhIFN- α orally administered in cats SID for 1/52; IFN is given intravenously at a dose of 10^6 - 10^9 units daily except in cats it is not effective orally, and causes adverse effects limits its IM or SC injection (Aliu, 2007).

CONCLUSION AND RECOMMENDATION

There are many factors predisposing to diseases in different species in Nigeria, but this write-up gave a review for the basic understanding of the most pertinent causes. It is important to bear in mind that despite the fact that Nigeria and West Africa Sub-region is endowed with flora that could be exploited in complementing the modern veterinary medicine. It is important to know that good management practices, hygiene, breeding nutrition and biosecurity still remain the most economic and effective way to prevent diseases in Nigeria. There is scarcity of effective veterinary drugs and immune based agents among which is interferon, while other supplements are still in preclinical trials in veterinary practice in this region.

Enlightenment to stakeholders in the livestock industry should be increased. Veterinary extension workers and agricultural extension workers should be trained to bridge the gap between clients of different strata of social system for ensuring good animal health and profit. Good policy to ensure security in farms .This should be done using multidisciplinary approach to ensure effectiveness of a profitable livestock sector. Research should be encouraged to ensure proffering solution with peculiar reference to the region which ever changing and challenging.

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