THE EPIZOOTIOLOGY AND MEDICAL MANAGEMENT OF ASIATIC BOVINE PASTEURELLOSIS

by

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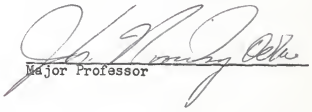

Major Professor

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INTRODUCTION

Pasteurellosis is known to affect a wide variety of animals including man, and has a world-wide distribution (Friedberger and Frohner, 1895; and Bartley and Kennedy, 1947). All these years it has been a subject of controversy in the bovine due to its differing entities. The syndrome in bovines can be distinguished by the etiologico-anatomical changes, which form this main basis of classification. However, the various manifestations of the disease due to different strains or serological types of pasteurellae have been confused with each other and in the same species.

From the Middle-East region of Asia to the Philippines as well as southern Europe and Africa, it is mainly recognized as a fulminating bacteriemia due to Pasteurella multocida Roberts' type I or Carter's type B. Since the nomenclature has been a subject of conflict in the past the disease in different countries was recognized under different names. However, in Asia the term hemorrhagic septicemia has been used to designate cases of pasteurellosis in bovine due to pasteurella multocida type I or type B. Additionally, it has been proven that the disease in bovines as it exists in Asia is quite different from that in the U.S.A. or Canada (Bain, 1954a; and Carter and Bain, 1960). In North America, it has been reported that the disease shipping fever complex originally attributed primarily to be due to Pasteurella multocida was frequently due to either myxo-virus SF-4 (para-influenza 3) or pasteurella hemolytica (Reisinger et al., 1959; and Collier et al., 1962).

Treatment of early pasteurellosis has been successful in the recent years due to the increased use of antibiotics and sulfonamides. Parallel with the increase in information regarding the various strains or serotypes, different vaccines capable of satisfactorily preventing epizootic pasteurellosis or hemorrhagic septicemia of cattle have also been developed. These vaccines have proven to be useful in the field of 'Preventive' Veterinary Medicine.

HISTORY OF PASTEURELLOSIS

In the history of epidemics, among domesticated animals in Asia, Africa and Southern Europe pasteurellosis had been one of the major devastating diseases of cattle and buffaloes. In the literature, citation of the epidemic disease of buffaloes known in Italy by the name of 'barbone' was first made by Mataxa in 1816 (Stableforth and Gallaway, 1959). Significant expansion in the knowledge of pasteurellosis was evidenced after Bollinger, cited by Friedberger and Frohner (1895), in 1878, reported a fatal outbreak of the disease among zoo animals and cattle. The etiology of which he ascribed to a bipolar bacterial rod. In the same manner the fowl cholera organism was incriminated by Rivolta in 1877, and a complete description of the organism was furnished by Pasteur in 1880 (Merchent and Packer, 1958). The authors also gave credit to Loeffler and Schutz who studied and described the organism of swine septicemia in 1882.

In 1885, Kitt, cited by Jones and Little (1921) explored the field and investigated epidemic diseases affecting cattle, swine, deer, horses, sheep and goats. He isolated similar types of organisms from all these species of animals and correlated it with the one reported by Bollinger in 1878. On the basis of a comparative study he preferred to refer them

by the name Bacterium bipolare multocidum. Huappe, 1886, cited by Rosenbusch and Merchant (1939) noted the similarity of the disease among different species of animals and suggested the name Septicemia hemorrhagica. Trevisan in 1887, gave the name of pasteurella to the bipolar organisms and attempted to differentiate the various species. The term pasteurellosis was first applied by Lignieres in 1898, (Breed et al., 1957) to the epidemic diseases of cattle, sheep, horses etc. in Argentina. According to Hutra et al. (1938), the infectious nature of the disease in cattle was reported by Frank and also by Friedberger in 1881. Later, further investigations on the etiological aspect were made by Jensen 1889, and Lignieres 1898 and 1900. In 1894, Lehman and Newman described the etiological agent under the name Pasteurella multocida. During 1936, Topley and Wilson (1946), suggested the name Pasteurella septica, but three years later Rosenbusch and Merchant (1939), once again supported the terminology used by Lehman and Newman in 1894, to designate the hemorrhagic septicemia organisms.

In the recent years, bovine pasteurellosis has ranked second among the epizootic diseases of cattle in tropical and sub-tropical countries. In the African continents it was known to invade the cattle population annually (Shirlaw, 1957). In Asia the disease had the tendency to flare up throughout the entire year, and a survey from India indicated a loss of some 33,000 cattle every year (Dhanda and Lall, 1958). Reports from Great Britain indicated that it had never been a serious disease entity in Europe (Kyaw, 1942), although the sporadic outbreaks have occurred (Turner and Holmes, 1938).

PREVALENCE OF PASTEURELLOSIS

According to Hutra et al. (1938) pasteurellosis of cattle is a disease of minor importance in regions situated in the temperate zone, but a major problem in tropical countries. In Egypt, Indochina, the Malay Peninsula, the Philippine Islands, Java, Burma, India, Pakistan, Siam, Indonesia, Kenya, etc. it occurs in a very severe form. In Manila the outbreak of hemorrhagic septicemia in Indian buffaloes was first reported by Tapacio in 1939, and its existence in Eritrea was recorded by Battelli (1946). Bain (1954), according to his own studies concluded that in most of the above mentioned countries Pasteurella multocida Roberts' type I was responsible for the fatal outbreaks.

Earlier reports from Africa indicate that a disease similar to Asian septicemic pasteurellosis was not uncommon in that continent. However, recent studies by Carter (1961) and Perreau (1961) indicated that the epizootics in Senegal, Mali, Guinea, Ivory Coast, Nigeria, The Cameroons and the Central African Republic, actually may have been due to different strains. Here, primarily the newly recognized strain Carter's type E seemed to be more prevalent; although outbreaks due to the rest of the strains of Pasteurella multocida, especially type I (Bain, 1959), were also frequently encountered.

Bain (1957a) in a survey report from Australia has shown that four of the main serotypes of Pasteurella multocida, types I, II, III and IV of Roberts' were in existence in that country. According to the author, one strain which appeared to be type I was isolated in Queensland from a bullock, but it lacked the properties which enable a strain to cause the septicemic condition. He also postulated that hemorrhagic septicemia as is known in Asia does not exist in Australia.

In Europe, and especially Great Britain, the existence of the disease has been a point of controversy. This may be partly ascribed to the lack of serological identification in the recent past (Gaiger, 1939; and Downham and Yarrow, 1939). However, reports of outbreaks of the different forms of pasteurellosis are not lacking (Dowson, 1942; Bugg, 1943; Mullaney, 1945). Later efforts made to differentiate the disease from the septicemic Asiatic pasteurellosis on clinical grounds (Pickering, 1939;and Kyaw, 1942), have led to the conclusion that the outbreaks of typical hemorrhagic septicemia were not encountered.

In the United States and Canada instead of septicemic pasteurellosis caused by Pasteurella multocida, Carter's type B pneumonic forms due to other serotypes, probably A, C or D, have been a major problem (Jones, 1921; Jones and Little, 1921; Gibbons, 1936; Gibbons and Fincher, 1937; Glenny, 1940;and Carter and Rowsell, 1958).

The condition has been reported numerous times under the septicemic form (Fincher, 1936;and Sanders, 1937), and has led to a confusion with other forms. Studies in this country within recent years have led to the conclusion that, instead of primary Pasteurella multocida type I infection, they were usually due to other etiological agents (Editorial, J. Amer. vet. med. Ass., 1958). According to Roberts (1953), the shipping fever complex of cattle, due to either a virus (Horlein et al., 1959;and Reisinger et al., 1959) or a mixed infection involving Pasteurella hemolytica (Carter, 1954;and Carter and McSherry, 1955), has been confused with and described under the name of hemorrhagic septicemia in this as well as other countries.

INCIDENCE AND PREDISPOSITION

Incidence

In most Asian countries pasteurellosis of the bovine has a marked enzootic distribution, both regionally and seasonally (Allen, 1929). In many of the endemic areas, the disease acquires a seasonal incidence with a large number of outbreaks occurring with the onset of monsoons and winter rains (Dhanda and Lall, 1958). In India, odd cases appeared very frequently after a fall of rain (Dowland, 1932). According to the author, as a rule one or two of the herds were usually affected in such outbreaks. In certain low lying, water logged areas, cases can be expected to appear during any time of the year (Masud, 1934). In such cases the onset of the disease is usually very sudden, and the course is extremely rapid.

Shirlaw (1957) in a report from Kenya stated that the outbreaks in that country were not influenced by climatic variations. The outbreaks had a tendency to spread quite rapidly and embrace all types of cattle, including high grade herds, ranch cattle and other country cattle. Such outbreaks were usually explosive and menacing.

In general, an increase in the incidence of pasteurellosis is a common finding during stress, removal from familiar quarters, transportation in unclean vehicles, homesickness etc. (Forty-seven authors, 1956). Apart from these factors, the stall fed or pasture animal has proportionately the same chance to contact the disease (Hutra et al., 1938).

Predisposition

Most of the outbreaks of 'hemorrhagic septicemia' are known to occur in conditions of heightened host susceptibility currently called "stress". The animals are considered under the stress when subjected to either physiological or nutritional variation and also when afflicted with minor infections (Bain, 1959). Reports from India indicate that approximately 3-5 per cent of the cattle and buffaloes harbor Pasteurella multocida in the tonsillar or the nasopharyngeal region. Such carrier animals when subjected to stress may develop the disease and discharge the organism in their saliva thus transmitting it to susceptible animals (Bain, 1958).

Physiological stress factors such as: exhaustion, excessive over exertion, fatigue etc. are common among working animals in the tropical countries. Along with the physical conditions, factors such as: cold, bad weather, inhalation of dust, over crowding and trauma also increase the host susceptibility (Bain, 1958;and Tweed and Edington, 1930). According to Tapacio (1939) in Manila, abrupt changes from dry to rainy weather resulted in the outbreaks of the disease. Anxiety during the journey or transit might play a part in the occurrence of disease among bovine (Hoerlein and Marsh, 1957).

Ruminants are especially sensitive to the change and irregularities in feeding and watering; consequently, any dietary change may disturb the ruminants' complex digestive system, resulting in partial or complete anorexia. This will lower the animals resistance to infection (The Merk Veterinary Manual, 1961). In a few instances, feeding of damaged feed

was responsible in reducing the animals resistance toward the disease (Tweed and Edington, 1930).

According to Tweed (1932), age could be considered a resistance factor in India, as adult animals were less commonly affected than the calves. Sex or breed differences to not seem to be predisposing factors in the bovine (Shirlaw, 1957). Although the disease was first recognized in high pedigree cattle in Kenya, there does not seem to be a hereditary predisposition.

ETIOLOGY

The organism responsible for the enzootic pasteurellosis in Asia is the Pasteurella multocida Roberts' type I or Carter's type B (Rosenbusch and Merchant, 1939; Roberts, 1947; and Carter, 1955). This organism has been recognized by several other workers e.g.: Bacterium bipolare multocidum, Kitt, 1885; Bacterium septicemia hemorrhagica, Hueppe, 1886; Bacillus boviseptícus, Flugge, 1896; Pasteurella bovine, Lignieres, 1897-1900; and later Pasteurella boviseptica on zoological basis which was changed to Pasteurella septica by Topley and Wilson in 1936 (Merchant and Packer, 1958).

Unfortunately, the controversy over the nomenclature and the difficulties encountered in the various serological types have resulted in misinterpretation of the different manifestations of the disease and its etiology. In addition, the lack of knowledge of virus diseases has also played an important part. All these resulted in a failure to recognize the primary etiological agents and the secondary invaders. Recent studies have demonstrated that no other pathogen such as a virus is incriminated with septicemic bovine pasteurellosis in Asia (Bain, 1959).

Occasional outbreaks due to other serotypes such as type IV are not uncommon and occur sporadically in Asia. However, these are not regarded as true hemorrhagic septicemia cases and are considered of little significance (Carter, 1957b). According to Bain (1959), however, the name "Asian Pasteurellosis" as suggested in the Journal A.V.M.A. editorial (1958) was not justified as the disease is neither exclusively Asian nor are all the cases of pasteurellosis septicemic as the enteric, pneumonic, edematous and nervous forms are not rare (Dhanda and Nilkantan, 1961).

Actually, the disease described as shipping fever complex in the U.S.A. is invariably an infection due to etiological agents other than Pasteurella multocida type I (Collier et al., 1962). Besides, the disease flares up when animals are subjected to "stress". In Asia there was an increase in the virulence of the pasteurella by passage. In the naturally occurring outbreaks of the disease the carrier rate was not high but the disease spread quickly. These findings also did not resemble conditions seen in countries like Australia, Britain or Canada.

GENERAL CHARACTERISTICS OF PASTEURELLA MULTOCIDA TYPE I

Classification and Distribution

Classification: According to Roberts (1947), a classification based on fermentation reactions was tried by Jones in 1921, but was not supported by others (Edington, 1930; Spray, 1923; Morch and Krogh-Lund, 1930; Newsome and Cross, 1932). Later, Khalifa (1935) tried to find the strain differences by cultural and biochemical characters although Gochenour (1924), Tanaka (1926), Frohbose (1926) and Brigham and Rettger (1935) could find no reason to appreciate the various serotypes on these grounds.

Appreciable differences were detected by agglutination and agglutinin absorption test by Cornelius (1929), Little and Lyon (1943), Batteli (1944) and later in 1952 by Ochi, cited by Carter (1958). The possibility of employing the precipitin test was explored by Yusef in 1935, while the precipitation and capsular swelling test was tried by Carter in 1953. Pribram and St. Plassaj (1921) suggested a classification based on motility.

The complement fixation test was used with some success by Matsuda (1910), Roderick (1922), Tanaka (1926), and Lal (1927). The strain differences were previously indicated by the absence of cross protection by Wasserman and Ostertag (1902), Schirop (1908), Meissner and Shern (1910), and Battelli (1944) using the cross-protection test. Evidences on the cross-protection test between strains from different hosts were given by Kelpzon, 1903-1904; Chamberland and Jonan, 1906; Citron and Putz, 1907; Gallaher, 1917; and Gochenour, 1924 (Roberts, 1947). It is rather surprising to note that no further attempts have been made on the immunological aspect as was suggested by Lignieres in 1906.

First acceptable classification of Pasteurella multocida in the literature was that suggested by Little and Lyon (1943), which was based on a slide agglutination test. He catagorised the strains into three serological groups and designated them by Types 1, 2, and 3.

Reports of different strains by cross protection experiments in mice were first submitted by Roberts (1947), who used strain specific antisera. Applying his technique to all Pasteurella multocida strains, he grouped them as type I, II, III and IV. The procedure proved to be laborious and expensive but was the only method for typing strains that were colonially smooth but antigenically rough.

In 1955, Carter employed a refined technique, using the hemagglutination test in which the specific capsular antigens were absorbed on the red blood cells. Treated red cells were then added to dilutions of the type specific immune sera. Because of the presence of a sufficient quantity of capsular antigen a hemagglutination could be observed. By means of this test he was able to separate several strains of Pasteurella multocida into four groups--type A, B, C and D. Later, on the basis of further investigations in Central Africa, he added one more serological type to his classification (Carter, 1961) designating it as type E.

By comparing the results of the studies of Roberts (1947) and Carter (1955), it could be postulated (Carter and Bain, 1960) that Roberts' type I and II corresponded to Carter's type B and A respectively, while Carter's C and D corresponded directly to Roberts' III and IV.

Distribution: According to Carter and Bain (1960) the type B strains constitute a reasonably homogenous group. The strain responsible for 'hemorrhagic septicemia' could be recovered from various parts of the hemisphere (Bain, 1954). The author confirmed its existence in six Asian countries. Bain in another report mentioned that since 1952 he recovered type B strains from Egypt, Iraq, Iran, Pakistan, India, Ceylon, Burma, Thailand, Malaya, Indonesia, and Philippines. Cultures that would appear to be variants of type B were isolated from cases of hemorrhagic septicemia from Belgian Congo and French Cameroon (Carter and Bain, 1960).

A variant of type B had also been observed in Australia (Bain, 1957a and 1959). Type B cultures have been recovered from outbreaks of pasteurellosis of buffaloes in the U.S.A. and may still be in existence.

They occur throughout Asia, Africa and Southern Europe. Although strains have been isolated in England and Australia that resemble type I or B but 'true' 'hemorrhagic septicemia' epizootics have not been reported. In North America the epizootics appear not to have occurred for at least the last three decades (Editorial, J.A.V.M.A., 1958).

Transmission

Natural: The organism is encountered in the respiratory passages (Jorgensen, 1925), chronic localised infections (Carter, 1952) and the digestive tract as a normal inhabitant in apparently healthy animals who may act as carriers. Survey reports from India indicate that the bacteria is a common inhabitant in the nasal cavity of cattle and buffaloes (Singh, 1948). Omar (1962) reported its presence in the tonsillar or the nasopharyngeal region. Such animals, according to him, may discharge the organism in their saliva and contaminate the food and water. These organisms may then be transmitted directly by the consumption of such food and water. In a few instances the transmission may be by direct contact (Marchant and Packer, 1958).

The disease is not transmitted through the contaminated soil since the organism does not survive for long in the soil (Bain, 1958). In the open it loses its pathogenicity within 40 hours.

Artificial: Feeding of large doses of Pasteurella multocida to a healthy cow may result in an infection especially if the general resistance of the animal is lowered by fatigue or cold (Jorgensen, 1925). Inoculation with virulent cultures may give rise to inflammatory edema, followed by suppuration and then after a few days the animal may recover or die

(Hutra et al., 1933). Intravenous inoculations have proven to be more lethal and will cause fatal septicemia. Experimental inhalation of a vaporised culture by cattle produced an acute congestion of the lungs and a mild carpal arthritis followed by recovery (Jorgensen, 1928).

Morphology and Staining

Pasteurella multocida type I is generally described as a coccobacillus. The small ellipsoidal rods measure 0.25 to 0.4 micron by 0.6 to 2.6 micron. Repeated cultures on agar or carbohydrate media exhibit marked pleomorphism. This will elicit elongated or longer rods which form chains and filaments. The organism is gram negative, stains distinctively at either poles by ordinary strains, thus giving rise to the term bipolar. Freshly isolated cultures usually possess a capsule. These capsules are composed of a protein-complex fraction in combination with a variable quantities of polysaccharides, the hyaluronic acid being absent in this strain (Bain, 1955 and Carter, 1958). The capsules on the organism can be demonstrated by special staining procedures e.g.: Jasmin method (Jasmin, 1945), India ink preparation (Duguid, 1951) or alcian blue method described by Bain, 1953 and Gurr, 1956 (Carter and Bain, 1960).

Growth Requirements

The organism is an aerobe and facultatively anaerobe. It grows abundantly at 37°C. It requires an optimum pH of 7.2-7.4, but will grow under a wide range. Sometimes, it may require a low oxidation reduction potential on primary isolation (Breeds et al., 1957). It can be grown in beef infusion media but better growth is obtained when blood

or blood serum are added to the media (Marchant and Packer, 1958). Jordan (1952a) noticed that the organism which required blood for its optimum aerobic growth on nutrient agar grew readily when blood was replaced by hematin, catalase or a number of other compounds which were able to catalyse the decomposition of hydrogen peroxide. In a later report (Jordan, 1952b), she concluded that in a chemically defined medium lactic acid or sucrose were adequate as sources of carbon, while glucose, maltose and galactose inhibited the aerobic growth to a variable extent, when used as the only source for carbon. In a few instances inhibition in growth was observed due to the production of toxic amounts of hydrogen peroxide during the oxidation of sugars by the organism.

Breifman and Yaw (1958), using the conventional 'Warburg' respiratory technique demonstrated that the intact cells of the type I strain of Pasteurella multocida actively oxidised ribose and galactose, but did not metabolise D-xylose or the stereoisomers of arabinose. Berkman (1942) in an attempt to grow the organism in a hydrolysed gelatin basal medium found that nicotinamide (or di or triphosphopyridine nucleotide) and pantothenic acid were required as the accessory growth factors.

Various methods were described for the production of dense cultures to be used for vaccine production. Bain and Jones (1958) have reported an aeration method using the casein hydrolysate media. Sterne and Hutchinson (1958) used an auto-digest of pancreas as a potent stimulating factor in a continuous culture vessel to increase the yield. Later a better substitute for the above, a pancreatic digest of liver was discovered (Bain, 1959), but the active substance in it could not be identified.

Biochemical Properties

According to the Bergey's manual (Breed et al., 1957) the organism does not liquify gelatin. No change or slight acidity in milk is noticed and the milk does not coagulate. The organism is indole positive and produces hydrogen sulphide. It also reduces nitrates to nitrites. The bile salts inhibit growth of the organism.

After the attempt of Newson and Cross in 1932, cited by Roberts (1947), Khalifa (1934), tried to differentiate the various pasteurellae on the basis of their capability of fermenting sugars. Some success was achieved by Rosenbusch and Merchant (1939) in differentiating the hemorrhagic septicemia group of organisms from others on the basis of xylose, arabinose, and dulcitol fermentation reactions. Roberts (1947) reported that his type I strains were all xylose positive, but failed to ferment arabinose. Subsequently, this test has been used to recognize this particular serotype from others. Bain (1957a) added that this serotype was also capable of fermenting sucrose, glucose, and levulose among other sugars.

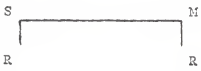
Variation

In 1921, Dekruif described diffuse and granular types of variations. Webster and Burn (1926) first reported the mucoid variation. Hughes (1930) afterwards added the intermediate and blue types. Carter (1957a) supported the terminology adopted by Braun (1953) and urged it to be recognized as the standard in order to eliminate the confusion derived from the use of different names. Braun grouped all the principal colonial variants under

three categories i.e. mucoid, smooth and rough. Carter (1955 and 1957a) has elaborated them as follows:

1. Mucoid: The colonies are comparatively large with flowing margins and have a characteristic moist appearance.
2. Smooth or fluorescent:
   a. Iridescent--small or discrete colonies which usually display a marked greenish iridescence.
   b. Non-iridescent--the organisms from these colonies possess less capsular substance and usually have a gray or greenish appearance. Most of the time these are referred to as intermediate variants.
3. Rough, non-capsulated or blue--produces small, discrete colonies.

Smith (1958) reported that the strains he had isolated from cattle generally produced non-mucoid colonies, containing little or no hyaluronic acid. While studying a 'M' variant of Pasteurella multocida type B, Carter and Annau (1953) and Carter and Bigland (1953) demonstrated the presence of hyaluronic acid within the capsules. Diagrammatically they represented the variation as:



According to Elberg and Cheng-Lee Ho (1950) little correlation exists between the morphological or cultural characteristics and virulence of a strain of Pasteurella multocida. But they suggested a relationship between the type of fluorescence and the virulence of a strain. Most studies on this aspect have been on laboratory animals only (Carter and Bain, 1960).

Resistance

Pasteurella multocida loses its pathogenecity at 60°C in ten minutes. A 0.5 per cent solution of phenol will render it nonviable within 15 minutes, while 1:5000 solution of bichloride of mercury or 3.5 per cent cresol solution are effective in a few minutes. It does not have a very long survival time on the ground. It has a longer span of life in a decomposing carcass than in manure. In vivo many antibiotics have been shown to be detrimental to it (Merchant and Packer, 1958).

This species and strain of organism differ from many other gram negative rods in that the penicillin in addition to chlor-tetracycline (Lederle Labs. -- aureomycin); oxy-tetracycline (Chas-Pfizer and Co. -- terramycin); chloramphenicol (Parke Davis and Co. -- chloromycetin); polymixin B and neomycin was highly effective against it (Gorzynski and Meter, 1953). They also noted that erythromycin and carbomycin destroyed the in vivo cultures in concentrations ranging from less than one microgram to 10 micrograms per ml. of broth. In nutrient broth growth was completely inhibited by one microgram per ml. of streptomycin (McNeil and Hinshaw, 1948; and Coles, 1948).

Muysson and Carter (1959) compared the antibiotic sensitivity of four serological types in vivo and concluded that they did not differ significantly in this respect. Shamatava (1961) on the basis of his findings with four different antibiotics--chloretetracycline, oxytetracycline, streptomycin and penicillin--reported oxytetracycline was the most effective.

The potentiality of a number of sulfonamides has been explored. An in vivo study by Shirlaw (1957) demonstrated that only sulfathiazole had a definite inhibitory effect on Pasteurella multocida. Sulfamerazine, sulfadiazine and sulfadimidine showed only a moderate degree of

inhibition and at higher concentrations. Wastrack and Lewis (1947) reported that sulfamerazine was a safe and effective treatment. In Asian countries sulfadimidine was reported to be curative (Gopalakrishnan et al., 1957).

Antigenic Structure

The organism possesses two major antigenic factors: A somatic or group antigen which is a glycolipid and a specific capsular antigen, presumably polysaccharide in nature (Carter, 1952). A protein complex fraction occurs in association with the capsular polysaccharide (Bain, 1955). This complex combination was shown to differ chemically, physically and biologically in the different colonial variants (Carter and Annau, 1953). Carter (1955) used the above observation as basis for identifying various serological types by means of the hemagglutination test.

Bain (1959) gave a detailed account of the antigenic structure of type I strain. Previously he had designated 'phase I' to a particular antigenic constitution. Later he isolated polysaccharides, lipopolysaccharides and protein fractions from the same strain. Polysaccharides he said behaved as haptens, while lipopolysaccharides were toxic in nature and could be absorbed on mammalian erythrocytes. He also demonstrated the presence of an antigen which was not a capsular polysaccharide, from the pasteurella grown in vivo in ox, using Coon's fluorescent antibody technique. He mentioned that this polysaccharide contained a ketone sugar as one of its constituents (Bain, 1960). This sugar could not be isolated from harvested cultures. In his opinion none of the antigens are exclusively somatic or exclusively capsular, although the proportions vary in different levels.

Toxins and Toxicity

Pasteurella multocida does not produce exotoxins, but cultures have been shown to contain an endotoxin. Carter and Bain (1960) have cited Pirosky (1938) and Dhanda (1960) who had isolated a toxic glycolipid. Bain and Knox (1960) reported a toxic protein. Bain (1959) in an experiment found that a toxic pyrogenic lipopolysaccharide was present in saline washings from type B strains. The author postulated that both the toxic lipopolysaccharide which is recovered from crude capsular extracts and the protein complex fraction are responsible for the inflammatory changes in mice and rabbits.

Pathogenicity

Pasteurella multocida type B is primarily pathogenic for cattle and buffaloes and is the cause of epizootic hemorrhagic septicemia (Bain, 1954; Carter, 1957; Editorial, J.A.V.M.A., 1953). Roberts (1947) also isolated type I from pigs. Agustin (1946) from Philippines reported a septicemia case in water buffalo. Smith (1955) isolated the organism from the nose and tonsillar area of dogs. Nordkvist and Karlson (1962) confirmed the epidemics in reindeer due to pasteurella. The organism was first isolated from nutria by Mlinac (1961) who recovered the organism from the spleen and kidney of a nutria dying of septicemia.

Human carrier cases are also on record (Bartly and Hunter, 1947; and Olsen and Needham, 1952). Svendsen (1947) reported a case of brain abscess in man caused by an organism which was closely related to the strain causing 'hemorrhagic septicemia'.

Pasteurellosis in cattle is encountered in three forms: exanthematous, pectoral and intestinal. Each of these may take the form of either a peracute or acute condition (Stableforth and Gallaway, 1959); however, subacute conditions are also on record (Turner, 1939). In the pectoral form, the lung and the pleural cavity are involved (Merchant and Packer, 1958), while in the exanthematous or edematous form, extensive edema of the subcutaneous tissues and the tissues and organs of peritonial cavity are most common. In Malaya, Wallace (1929) reported that with the pectoral or thoracic form edema of the maxillary space is the usual lesion. According to him and Tweed (1932) the larynx, pleura, lungs and gastrointestinal tracts are invariably involved along with the edema of dewlap and between the muscles of neck in acute or peracute cases of pasteurellosis septicemic.

Cases of the nervous form of pasteurellosis in cattle are also described (Badenashvili, 1961). Shand and Markson (1953) reported cases of meningo-encaphalitis in calves due to pasteurella. Dhanda and Nilkantan (1961) isolated Pasteurella multocida type I of low virulence from cases of paraplagia in cattle in India.

Severe outbreaks of mastitis attributed to Pasteurella multocida were reported by Barnum (1954), Thorne and Nilson (1962), etc. According to Carter (1952) the strains of Pasteurella multocida responsible for acute epizootic pasteurellosis are highly virulent and invasive for laboratory animals. The organism will kill mice, chickens or rabbits within a few days when administered orally.

SOURCES OF INFECTION

Allen (1929) suggested it might have been possible for the organism to lay dormant in the soil from one part of a rainy season to another and then be ingested by the susceptible animal drinking from the rising water level during rains or water in low lying areas. The author reported the conditions for the spread of the disease could be considered ideal in some Indian villages. Cattle were housed in dirty surroundings with the excreta allowed to collect and dry. When the rains occurred, the excreta was washed into the village tanks. The drinking of such water or water contaminated with the saliva from infected animals transmitted the disease (Bain, 1958).

According to Daubney et al. (1934) and Shirlaw (1957), the buildings are usually unsanitary and often earthen floored in tropical countries. It is not uncommon to find calves affected with enormous number of Ctenocephalus felis and surrounded by mosquitoes. It was their conclusion that 'hemorrhagic septicemia' could be transmitted by these vectors. Although many authors have reported that oral ingestion of the organism invariably precipitates a natural epizootics, most have failed to produce the disease experimentally by oral route (Dutra et al., 1938; Allen, 1929; Bain, 1958; Shirlaw, 1957). In support to the findings of Daubney et al. (1934), Masud (1934), from India reported that the disease could be routinely produced by injecting cultures of Pasteurella multocida subcutaneously.

Recent studies (Srinivasan, 1960) suggest that the hypothesis supporting the transmission of the disease from contaminated water and soil is not tenable as the organism has proven to be very fragile to external agencies, i.e. heat, sunlight etc. It is most likely that infections

occur from animal to animal directly by droplet infection through the agency of healthy carriers initially sporadically but later epizootically.

INCUBATION PERIOD

In India the incubation period of the 'hemorrhagic septicemia', during the natural epizootics, is considered to be from one to three days (Wallace, 1929;and Srinivasan, 1960).

PATHOGENESIS

The exact avenue of entrance of Pasteurella multocida has been a questionable problem. The presence of organism in the upper respiratory tract and tonsillar area of the normal cattle indicates that it could act as a pathogen under predisposing circumstances in which the animal may have lost its natural resistance, permitting the bacteria to multiply without limit (Jorgensen, 1925; and Omar et al., 1962). Mutra et al. (1938) believed that infections occurred by ingestion or in those cases characterised by edema of the buccal and nasopharyngeal mucous membrane and tongue through injury of the nasopharyngeal mucous membranes. Wallace (1929) concluded that the disease developed through the breaks in the continuity of the skin during the time of wallowing by cattle and buffaloes. Kingman (1945) identified a case of encephalitis due to pasteurella, which he considered was probably a case of hematogenous origin.

Regardless of origin of infection, the bacteria is found in the blood and bone marrow in most natural we well as experimental cases (Andrien et al., 1936; and Tweed, 1932). From the blood it spreads to the tissue fluid from where they penetrate the entire body and produce death of the animal in a short time. In such cases the bacterial endotoxins damage

the capillary endothelium resulting in hemorrhages in the tissues of the serous membranes, mucous membranes and parenchymatous organs (Lazarus and Nazawa, 1948; and Runnells et al., 1960). In less severe types of the disease where the animals do not die as rapidly, the infection gradually progresses and results in a serofibrinous inflammation of tissue surfaces and hemorrhagic inflammation of mucous surfaces (Twad, 1932).

COURSE OF THE DISEASE

After the onset of symptoms, the different manifestations of pasteurellosis are recognized as peracute, acute, subacute and chronic forms depending upon the lesions and length of time in which the disease proves fatal. The period of illness may vary from nearly six hours to six days or longer (Srinivasan, 1960; Pickering, 1939). The acute septicemic and edematous forms usually have a rapid course of eight to thirty six hours (Wallace, 1929), while the pectoral form, which is more common in many enzootics, usually continues for about three days, but in occasional cases may run a more protracted course (Hutra et al., 1938).

LESIONS

According to Gaiger (1931) 'hemorrhagic septicemia' is a true septicemia in Asian countries. The symptoms are mainly intestinal, but rare cases of pectoral and cerebral forms are also reported. In peracute cases, especially in calves, the post-mortem lesions found are exclusively those of a septicemia (Hutra et al., 1938).

1. Hemorrhages of the various parts of the body are the characteristic lesions in the acute septicemic form (Tweed, 1932). Common findings as reported by Masud, 1934; Gaiger and Davis, 1938; and Buchnan, 1939 are:
   a. Congestion of the internal organs, petechiae on the mucous and serous membranes, reddish fluid in the peritoneal, pericardial and thoracic cavities.
   b. Peritonitis, slight congestion of the parietal pleura, myocarditis, endocardial hemorrhages in the left ventricle and around the columnae carneae.
   c. Slight emphysema or patchy consolidation of the lung.
   d. Blochy hemorrhagic areas on the leaves of the omasum, acute inflammation of mucous membranes of the abomasum, severe hemorrhagic enteritis with blood stained contents, and cloudy swelling of parenchymatous organs.
2. In subacute cases, edema especially of the dewlap and between the muscles and neck is grossly evident. Frequent changes recognized by Runnells et al. (1960) are:
   a. Presence of petechial hemorrhages and gelatinous infiltration along the head, neck, jugular furrow and beneath the scapula.
   b. A state of catarrhal, fibrinous or hemorrhagic inflammation of mucous membranes of head and neck region.
   c. Acute hemorrhagic lymphadenitis of the regional lymph nodes and inflammation of vulva and lips.

3. The more chronic forms are manifested by characteristic lesions in the lungs. Commonly noted lesions by Tweed, 1932; Stone, 1937; and Mullaney, 1945 are:

   a. An acute pneumonia with red consolidation of the apices and a grayish fibrinous deposit adhered to the pleura.

   b. Focal adhesions between the lung and the chest wall or pericardium with some pleural effusion.

   Augustin (1946) observed the presence of necrotic lesions posterior to diaphragm, roughened peritoneum, petechiated omentum and a pale, dry subcutis on post-mortem in chronic septicemic pasteurellosis of a buffalo in the Philippines.

Actually the pectoral, intestinal and edematous or exanthematous types, when classified on regional pathological changes appear to be either an acute or subacute form. In the pectoral form the chief site of tissue reaction are the organs of thoracic cavity. In such cases (Mutra et al., 1938), the pleural cavity contains serous or serofibrinous and sanious exudate. The inflamed pleura is covered with petechiae and a fibrinous membrane. The lungs present a condition of Fibrino--necrotic inflammation. Certain portions of both of the lungs are hepatised, friable and on sectioning exhibit a uniform, dark, reddish brown or reddish gray, finely granular serous surface. Less acute cases contain dry caseous foci. The pericardium may contain exudate mixed with fibrin. The peribronchial lymph glands exhibit acute swelling and the usual signs of acute enteritis are a common feature.

In intestinal form the organs of abdominal cavity are primarily involved (Runnells et al., 1960). The lesions consist of several litres

of yellowish or red fluid in the abdominal cavity with signs of acute hemorrhagic inflammation in the abomasum, small intestine and less often in the colon. The intestinal contents are fluid, yellowish gray or reddish in color from an admixture of blood. Occasionally it consists of thick fluid blood of normal color. In the edematous or exanthematous form, the subcutaneous tissue of head, neck and throat or limbs are infiltrated with gelatinous material and studded with hemorrhages with serous infiltration of the deeper layers of muscles (Hall, 1937). The tongue is enlarged, dark brown in color and firm in consistency along the fraenum linguae. The floor of the mouth, the submucoa of the pharynx and ary-epiglottic folds are infiltrated with yellow gelatinous material. Hemorrhagic enteritis is not uncommon (Nutra et al., 1938; Runnells, 1960). In occasional cases the bladder contains dark colored or bloody urine (Srinivasan, 1960).

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The diagnosis of hemorrhagic septicemia is based on symptoms and may be confirmed by post-mortem examination. The presence of edematous infiltration in the tissues of the intermaxillary space extending to the sternum with inflammation of the laryngo-tracheal mucous membrane is suggestive of the disease. The trachea and bronchi are filled with a yellowish frothy or semigelatinous exudate. The pleura shows fibroblastic adhesions. The intestines show inflammation of the abomasal mucous membrane which often extends to the duodenum. Blood smears may reveal the presence of a bipolar gram negative pasteurella (Wallace, 1929; and Pickering, 1939). The inoculation of blood from these affected animals or its oral administration to mice, chickens or rabbits will results in their death in a matter of a few days.

The disease may resemble Anthrax in which there is edematous swelling and symptoms of enteritis, but the absence of vesiculation or ulceration will suggest pasteurellosis. On post-mortem examination the absence of acute swelling of spleen excludes anthrax. Finally, the bacteriological examination of blood is decisive (Mutra et al., 1938).

Other Asian diseases which are likely to be confused due to similarity with septicemic pasteurellosis are rinderpest, blackleg, piroplasmosis and contagious bovine pleuropneumonia. These may be differentiated on the basis of clinical symptoms, post-mortem examination and bacteriological examination (Wallace, 1929; and Mutra et al., 1938).

TREATMENT

A. Prophylactic

Active Immunization: Secondary to rinderpest, hemorrhagic septicemia is one of the principal decimaties of the bovine population in Southern Asia. It also causes great economic losses in other parts of the world (Bain, 1958). Consequently, the development and field application of proper control measures is a pressing problem. Following the work of Pasteur (1880), cited by Marchant and Packer (1958), many workers have tried to develop a suitable vaccine from attenuated or avirulent cultures (Priestley, 1936). Hardenbergh and Boener (1916), used a 48 hour culture of Pasteurella bovisentica, subcutaneously in one c.c. dose as a vaccine but subsequently (Hardenbergh and Boener, 1917), discarded the vaccine because of the danger of a carrier problem. Later Gochenour (1924), suggested the use of a natural aggression for preventing outbreaks of pasteurellosis.

In the year 1924, Buckley and Gochenour, on the basis of a comparative study of the effectiveness of bacterins, vaccines and aggressins as immunizing agents, concluded that bacterins afforded the best protection against septicemic pasteurellosis. Studies within recent years have shown that other vaccines are better capable of actively immunizing cattle and buffaloes for a suitable length of time (Iyer and Rao, 1959).

Until 1950 the most common Pasteurella multocida type B vaccines were simple broth bacterins, but since then, various other types of vaccines have been evolved. The most commonly used are:

1. 'Hemorrhagic septicemia' broth vaccine (Rao and Govil, 1950). In India this vaccine is prepared by mixing twenty-four hour culture in plain broth and then formalising to 0.5 per cent. This vaccine is then matched with opacity tube number 2 of the Brown's standard. The safety tests are carried out on rabbits by injecting 5 c.c. subcutaneously and observing its survival for seventy-two hours.
2. Pasteurella in agar wash vaccine. This is thought to be an improvement over hemorrhagic septicemia broth vaccine with subsequent immunity persisting up to four months.
3. Chick embryo vaccine (Carter, 1951). Chick embryo vaccine is prepared by using the most common serological types of a particular country. The organisms are freshly isolated, virulent strains harvested at the time of maximum capsulation, then bacterilising with 0.25 per cent formalin.
4. H. S. alum precipitated vaccine. Iyer and Rao, (1959), reported that the immunity developed in five days and that the protection would last for about six months.

5. Oil adjuvant vaccine (Bain, 1955 and 1956). This vaccine evolved by the author himself, proved to be very satisfactory on field trials. It was prepared either by the agar or broth method and then light mineral oil or liquid paraffin was used for emulsification. In rare cases mycobacterium are also incorporated to enhance antigenicity. The vaccine takes about seven days to develop an active immunity in the inoculated individual. The immunity will last approximately for a year. The recommended dose is three c.c. intramuscularly. Among other creditable properties, the vaccine may be stored at freezing temperature for about two years or at 40°F for about three months; however, at 80°F it deteriorates very quickly (Iyer and Rao, 1959).

Because of the sensitivity of type B strains of pasteurella, Bain suggests that it is wise to keep seed culture in a frozen state or dried infected blood to be used for the production of vaccine. Later Bain (1957b), cited by Carter and Bain (1960), suggested the use of an initial dose of oil adjuvant vaccine followed by annual injections of alum precipitated vaccine should it transpire that tissue damage follows repeated injections of oil adjuvant vaccine.

Bain (1958) recommended that vaccination of cattle and buffaloes be practiced regularly in areas where the disease frequently appears such as river deltas. In other areas the vaccine should be used when outbreaks of septicemic pasteurellosis invade the bovine population.

Passive immunization: The pasteurellosis antiserum is a fast acting prophylactic agent against the disease. It is usually administered

subcutaneously in doses of ten to 20 c.c. The passive immunity conferred by its use is of short duration, approximately 15 days (Srinivasan, 1960).

To assess the immune response provoked by use of vaccinal methods or by natural circumstances in bovine, the simple agglutination test, mouse protection test, agar agglutination test or complement fixation test are described by Bain (1954c and 1955c).

Post Vaccination Shock: According to Carter and Bain (1960), a body reaction "shock" to the inoculation of pasteurella has been a problem incidental to vaccination for many years. This reaction has been recognized in Asia and other countries for several years. It occurs with both agar grown or broth cultured bacteria. It has recently been manifested with the alum precipitated and oil adjuvant vaccines. In rare cases it may resemble an anaphylactic reaction. Age or breed of the animal does not affect the reaction.

Therapeutic

General: Where the disease appears, all the sick animals should be separated and isolated from the rest of the herd. They should be provided with good feed and adequate housing facilities. During the monsoon season, they should be placed on elevated dry land. If the disease appears in stabled animals, the feed should be discarded and animal quarters disinfected. In the low lying areas, special attention should be paid to the hygienic conditions. Efforts to maintain the resistance of the healthy animals against further infection are of prime importance (Hutra et al., 1938; Srinivasan, 1960; and the Merk Veterinary Manual, 1961).

Treatment: In Asian countries the disease is usually rapidly fatal; consequently, treatment in most cases is impractical. This is partially due to the impaired facilities under village conditions in poor countries.

When available, treatment with antibiotics, sulfonamides and antisera may be highly successful. The antiserum is given subcutaneously in doses of 50 millilitars per adult animal (Srinivasan, 1960).

The sulfonamides have proven highly effective if administered in the earlier stages of the disease (Carter, 1952a). Sulfamerazine was reported to be quite effective by Wastrack and Lewis (1947), when administered orally at the rate of 0.075 grams per kg of body weight for the first day and followed by half of the initial dose per day for two or more days. According to McAnliff (1947) 0.33 gr of sodium sulfamerazine per pound body weight given intravenously and followed by oral administration for a few days resulted in a recovery rate of 93 to 95 per cent cases.

Sulfapyridine therapy was recommended by Shirlaw (1957) working in Kenya. He recommended the usual therapeutic treatment starting with an initial dose of 60 mg per pound of body weight orally followed by half of the above dose every 12 hours for four days.

Sulfamethazine is utilized in doses of 60 mg per pound body weight every 12 hours for four days (Roberts and Kiesel, 1948). According to Manna (1952), 33 per cent solution of sulfamezathine proved to be very successful when given in 50 c.c. doses intravenously.

Sulfanilamide and sulfathiazole are recommended in the Merk Veterinary Manual (1961). The initial therapeutic dose of either drug is 60 mg per pound of body weight. The initial dose of sulfathiazole is followed every 12 hours by half of the initial dose for four days. The initial dose of sulfanilamide is followed by doses of 45 mg per pound body weight on each succeeding day until the temperature has been normal for 48 hours.

Broad spectrum antibiotics and penicillin have been shown to be quite effective when administered sufficiently early (Carter, 1952a). Shamatava (1961) reported oxytetracycline as the most effective of the antibiotics.

Oxytetracycline may be administered intravenously or intramuscularly in an initial dose of 10 mg per kg of body weight and followed by a second intramuscular injection of five to ten mg per kg body weight, 24 hours later.

Other antibiotics showing promise are:

Streptomycin or "dihydrostreptomycin" given intramuscularly at the rate of six mg per kg body weight per day in two to four divided doses.

Chlortetracycline given orally at the rate of ten to 25 mg per pound of body weight per day in divided or single doses or two to five mg per pound of body weight intravenously each day until the temperature has been normal for at least 24 hours after the last dose.

Chloramphenicol is especially recommended for calves weighing up to 800 pounds. It should be given twice daily in 200 mgm doses.

Intramuscular injections of procaine penicillin G in aqueous suspension at the rate of 3,000 to 5,000 units per pound body weight per day for four to five days is the most common treatment undertaken.

Indifferent results have been obtained in India with antiseptic solutions such as potassium permanganate one-half to one drachm in distilled water or one drachm of carbolic acid or Lugol's solution given intravenously (Srinivasan, 1960; Venkatesan, 1939).

SUMMARY

An attempt has been made to review the nomenclature, etiology, pathogenesis, lesions, prophylaxis and therapy of pasteurellosis in the bovine. The nomenclature of pasteurellosis has been in a state of confusion owing to the isolation of various strains of Pasteurella multocida and viruses associated with the disease. Recent work has proven that the condition in the bovine as it occurs today in North America is different from that found in the eastern regions of Asia and South Africa. In Asia it is a specific disease caused by Pasteurella multocida type B, while the similar condition in the U.S.A. is caused by a variety of agents including pasteurellae type A, C and D.

In Asia four strains of Pasteurella multocida viz. A, B, C and D have been recognized but the most prevalent strain is type B. This strain has been incriminated as the causal organism of hemorrhagic septicemia. Parallel to this, five strains of Pasteurella multocida have been observed in Africa while in other countries only A, C and D are the most prevalent ones.

Among the various vaccines available for the prevention of pasteurellosis, the oil-adjuvant appears to be the most potent for the production of antibodies. It has been observed that the vaccine attains good success in the control of the syndrome. Control may also be achieved by treating the infected animals with broad spectrum antibiotics and sulfa drugs.

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THE EPIZOOTIOLOGY AND MEDICAL MANAGEMENT OF ASIATIC BOVINE PASTEURELLOSIS

by

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AN ABSTRACT OF A REPORT

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A review of the nomenclature, etiology, pathogenesis, lesions, prophylaxis and therapeutics of pasteurellosis of the bovine in Asia has been attempted in the present work. Pasteurellosis ranks second among the major devastating diseases decimating the cattle population in the Asian continent. It occurs primarily in the septicemic form. The disease occurs annually in the Southeast Asian countries and in some African countries. It has a seasonal incidence in low lying marshy areas of tropical and sub-tropical regions. Enzootics may be expected to occur following a rain fall.

Four strains A, B, C and D of Pasteurella multocida are in existence in Asia. Robert's type I or Carter's type B is the strain recognized to be responsible for cases of true septicemic pasteurellosis. Five strains including the newly recognized type E have been reported from the African continent. The syndrome in North America appears to be different from the one encountered in Eastern countries. This is apparently due to the difference in the etiological agents. Nearly all cases of pasteurellosis reported from Australia, Europe and North America are due to A, C and D strains of Pasteurella multocida.

The transmission of the disease from one animal to another has been a subject of controversy. However, it is generally conceded that the Pasteurella multocida type B is transmitted through droplet infection. The apparently healthy animals act as carriers of the organism. Such animals may develop the disease when subjected to stress. In most cases, regardless of origin of infection, the bacteria are found in the blood and bone marrow. From the blood the organism spreads to the tissue fluid of the various parts of the body. Bacterial endotoxins damage the capillary

endothelium resulting in hemorrhages in the serous and mucous membranes and parenchymatous organs. In less severe forms the infection gradually progresses and results in a serofibrinous inflammation of tissue surfaces and hemorrhagic inflammation of mucous surfaces.

Different gross changes within the body are recognized and form a basis of classifying the disease viz. exanthematous, pectoral, and intestinal form. The syndrome may also be classified as peracute, acute, subacute and chronic depending on the inflammatory responses, the lapse of time following the infection, virulence of the organism, age of the susceptible host and the stress factors prevailing. In peracute cases the lesions found are exclusively those of septicemia. In acute forms petechial hemorrhages on the various parts of the body are usual. In subacute cases edema specially of the dewlap along with hemorrhages on the mucous membranes are a common finding. Chronic forms of the disease are usually identified by lung lesions on necropsy.

The diagnosis of pasteurellosis is based on the clinical examination and necropsy findings. These examinations also help to differentiate pasteurellosis from anthrax, blackleg, rinderpest, piroplesmosis and contagious bovine pleuropneumonia.

Various actively immunizing vaccines are now available for field use in the control of this disease. The newly developed oil-adjuvant vaccines have shown the most promising results when compared to pasturella broth, agar washed, chick embryo and alum precipipated vaccines. Immunity following vaccination develops in about seven days and persists for approximately one year.

Among the various therapeutic agents available, sulfonamides viz. sulfamerazine, sulfapyridine, sulfamethazine, sulfamezathine, sulfanilamide and sulfathiazole have been used with good results especially if administered during the early stages of the disease. Broad spectrum antibiotics i.e. oxytetracycline, streptomycin, chlortatracycline, chloramphenicol and penicillin are effective in combating the condition.