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THE OCCURRENCE AND PATHOLOGY OF CHLAMYDIOSIS IN DOMESTIC AND LABORATORY ANIMALS: A REVIEW*

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ABSTRACT

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The literature on the various disease syndromes caused by chlamydia in domestic and laboratory animals is summarized. A review of the pathological lesions which characterize these diseases is presented and the pathogenesis of chlamydiosis is briefly discussed. Some aspects of unpublished findings on the occurrence of intestinal, kidney and genital lesions in natural and experimental cases of chlamydiosis in cattle and sheep, abortions and conjunctivitis in horses in South Africa are recorded.

INTRODUCTION

Small basophilic organisms in the tissues of birds and humans affected with psittacosis were independently described in the same year by Levinthal (1930), Coles (1930) and Lillie (1930). Since then numerous diseases in animals have been linked with the occurrence of these organisms, which are currently grouped in the genus *Chlamydia*. The aetiologic relationship between these organisms and psittacosis was conclusively established by Bedson, Western & Simpson (1930). By intra-peritoneal propagation of the organism in mice, Bedson & Bland (1932; 1934) observed various morphologic forms of the organism which bore a definite sequential relationship to one another. From this they postulated an intracellular developmental cycle involving small infectious forms (elementary bodies, 250 to 450 nm in diameter) and large forms (initial or reticulate bodies, 600 to 1 500 nm in diameter) with intermediate stages. With the advent of the electron microscope various workers later confirmed the existence of such a developmental cycle (Cutlip, 1970; Storz, 1971).

The entrance into cells by chlamydial agents is by the process of phagocytosis (Friis, 1972). The small infectious elementary bodies are initially taken up by cells, within which they are contained in cytoplasmic vesicles bounded by a membrane derived from the cellular membrane. In this milieu the elementary bodies are reorganised into large reticulate or initial bodies. Reticulate forms are not infectious: they grow and multiply by binary fission and, by a second process of reorganization involving intermediate forms, small elementary bodies which are infective, but do not divide, are formed. These elementary bodies, which are highly resistant to the extracellular environment, are then released to infect other cells.

The mode of transmission of chlamydial agents is unconfirmed in naturally occurring diseases. It is probably via the consumption or inhalation of infective particles shed in the faeces, urine or ocular discharges of infected hosts. Venereal transmission has also been postulated (McKercher, 1964; McKercher, Wada, Robinson & Howarth, 1966; Storz, Carroll, Ball & Faulkner, 1968; Eugster, Ball, Carroll & Storz, 1970). Storz (1961) found in experimental work with guineapigs that latently infected mothers pass the organisms to several subsequent litters. Chlamydia have also been isolated from various species of ticks (Storz, 1971) and in South Africa from *Musca domestica* and other dipteran flies (A. P. Schutte & C. J. Howell, unpublished data, 1974). Evidence definitely incriminating these arthropods as vectors is, however, still lacking.

The chlamydial agents form a large group of antigenically related and culturally, morphologically and tinctorially similar organisms (Storz, 1971). These microorganisms were previously known either by the vernacular term, the psittacosis—lympho—granuloma—trachoma (PLT) group or as Miyagawanella (Rake, 1947) or *Bedsonia* (Meyer, 1965) "viruses". Studies that have been made by numerous workers on the biology, morphology, cytology and chemical nature of chlamydial organisms, their independent metabolism and the therapy of the diseases they produce are summarized by Moulder (1964; 1966). These studies provide convincing evidence that warrants the recognition of these organisms as bacteria, not viruses. Chlamydiae are distinguished from rickettsiae by differences in their developmental cycle, their antigenic structure, the fact that they are cytochrome-free and that they do not produce ATP or exhibit a preferential metabolism of glutamate (Ormsbee 1969, cited by Schachter, Storz, Tarizzo & Bögel, 1973).

Page (1966) suggested that all members of this group of organisms be placed into a single genus *Chlamydia* Jones, Rake & Stearns, 1945. In 1968 Page (cited by Storz & Page, 1971) proposed a classification of these obligatory intracellular organisms into 2 well-defined species, *Chlamydia psittaci* and *C. trachomatis*. Stains of *C. trachomatis* contain an iodine-positive glycogen matrix in their colonies and are responsible for diseases such as trachoma, inclusion conjunctivitis, lympho-granuloma-venereum, etc., in man. *C. psittaci* strains do not have glycogen in their colonies and are the causative agents of psittacosis, ornithosis and various diseases in domestic and other animals. Furthermore, Storz & Page (1971) proposed that the family Chlamydiaceae, which at present contains only the genus *Chlamydia*, be placed in a new order, Chlamydiales, analogous to the order Rickettsiales Buchanan & Buchanan, 1938. The principal argument for this change is that chlamydiae multiply by a developmental cycle that is unique among the bacteria. The term psittacosis is used to indicate a generalized infection of man or psittacine birds by one of the chlamydial agents while ornithosis is used for the same infection in birds other than psittacines (Meyer, 1965). Storz (1971) included a review of chlamydiosis in birds, including domestic

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fowls. In this review only chlamydial infections of laboratory and domestic animals other than birds will be considered.

Naturally Occurring Chlamydial Infections in Animals

The pathogenic rôle of chlamydia in several diseases of domestic animals is well established (Storz, 1971). Depending on such factors as virulence of the agent, species, age and sex of the animal, environment, management practices, ecology and physiologic conditions, any one or a combination of the following syndromes may be elicited: pneumonia, meningo-encephalitis, abortions, polyarthritis, polyserositis, diarrhoea, conjunctivitis and, more recently recognised, genital infections. The following naturally occurring and experimental diseases have been reported in the literature.

Laboratory Animals

Mice

The first naturally occurring disease in mammals, other than man, caused by these organisms was described by Gönnert (1941), who discovered a pneumonia and inapparent infections in laboratory mice. Subsequently various other workers confirmed these observations (Nigg, 1942; Karr, 1943; Mooser, 1943; De Burg, Jackson & Williams, 1945; Gerloff & Watson, 1970).

Chlamydia strains of human and avian origin produce a meningo-encephalitis in mice when inoculated intracerebrally. With some exceptions intracerebral inoculation of mice with strains from mammals other than man does not cause clinical symptoms (Storz, 1971). Intraperitoneal inoculation of mice with more virulent strains produces marked splenomegaly and hepatomegaly, which frequently is associated with a serofibrinous peritonitis, focal liver necrosis, occasional patches of pneumonia and abundant organisms in the reticulo-endothelial cells. In both the natural and experimental disease in mice a focal myocarditis may also be encountered. Mice have genetic differences in their susceptibility to chlamydial infection (Schachter *et al.*, 1973).

Guinea-pigs

Storz (1964) described a natural systemic chlamydial epizootic in a guinea-pig colony resulting in heavy losses among the newborn and young animals. In 1964, Murray reported a naturally occurring conjunctivitis of young guinea-pigs which was a mild, self-limiting disease. Examination of smears from conjunctival scrapings revealed the presence of chlamydial organisms. This ocular chlamydial infection was later confirmed by Gordon, Weiss, Quan & Dressler (1966) and Kazdan, Schachter & Okumoto (1967). Mount, Bigazzi & Barron (1972) experimentally infected female guinea-pigs intravaginally with the agent of guinea-pig conjunctivitis and demonstrated ocular infections in the offspring of infected mothers as early as 3 days after birth. These workers also experimentally produced lesions in the male genital tract and showed that venereal transmission may occur in this species (Mount, Bigazzi & Barron, 1973).

Guinea-pigs are used for the experimental isolation of chlamydial organisms. Usually, the following lesions are seen after intraperitoneal inoculation: splenomegaly, focal necrosis of the liver, pneumonia and a fibrinous peritonitis. Pregnant animals may abort (Storz, 1971). Orchitis, periorchitis and epididymitis were observed after intraperitoneal inoculation of male guinea-pigs with a chlamydial agent isolated from this species (Storz, 1964).

Rabbits

Flatt & Dungworth (1971) isolated a chlamydial agent from rabbits showing pneumonia and were able to produce lung lesions experimentally by intratracheal inoculation of this organism in rabbits. Hepatic necrosis, splenomegaly and fibrinous pneumonia have been recorded in rabbits used for the experimental isolation of chlamydia (Spalatin, Iversen & Hanson, 1971). Some strains may produce a meningo-encephalitis in rabbits infected by the intracerebral route (Meyer, 1965).

Domestic Animals

Cats

Baker (1942; 1944) identified a pneumonia in cats as a chlamydia-induced disease, termed feline pneumonitis by Hamre & Rake (1944). Yerasimides (1960) isolated a chlamydial agent from conjunctival exudate of a cat showing an acute catarrhal conjunctivitis. This finding was confirmed by Cello (1967). Under natural conditions the eye condition is seen sporadically but in catteries it is often enzootic and cats may show conjunctivitis for long periods of time. Kittens born to affected or clinically recovered cats may show a severe conjunctivitis at the time when their eyelids normally open.

Dogs

In France, Giroud, Groulade, Roger & Dartois (1954) attributed an encephalitic syndrome of dogs to chlamydial infection while Groulade, Roger & Dartois (1954) described a febrile disease in young dogs in which they again incriminated a chlamydial agent as the cause. Clinically this disease resembled canine distemper in many respects. A similar report was made in Italy by Contini in 1956 (cited by Maierhofer & Storz, 1969). Acute, subacute and chronic forms were described and young dogs were most severely affected. Fever, inappetence, bronchopneumonia, peritonitis, serositis and gastrointestinal disorders with vomiting and diarrhoea were seen. In the chronic form the dogs developed a capricious appetite and became emaciated, with skin lesions appearing along the abdomen and legs.

Maierhofer & Storz (1969) experimentally produced a disease in dogs using a chlamydial agent isolated from ovine polyarthritis cases. The experimental disease was comparable symptomatically with the disease in dogs described in France. Experimental animals had fever, loss of appetite, became lethargic, showed signs of pneumonia, enteritis, inco-ordination and various degrees of muscle and joint pain.

Voigt, Dietz & Schmidt (1966) in Germany incriminated a chlamydial agent as the cause of a superficial keratitis in dogs while Scott (1968) isolated a chlamydial agent from a dog with conjunctivitis in South Africa. Frazer, Norval, Withers & Gregor (1969) detected an intestinal chlamydial infection in this species.

Pigs

Although much work will still have to be done to determine the precise relationship between chlamydial agents and polyserositis in pigs, available evidence suggests that these organisms do play a rôle in this condition. Guénov (1961) in Bulgaria isolated a chlamydia from piglets showing pericarditis, serofibrinous pleuritis, peritonitis, perihepatitis and pneumonia. Natscheff, Gabraschanski, Ognjanoff, Djuroff & Gentscheff (1965) described a similar syndrome in pigs and identified the infectious agent as a chlamydia. Antibodies against chlamydial organisms were demonstrated in a high percentage of pigs in England by Wilson & Plummer (1966). Kölbl (1969) detected intestinal chlamydia infections in apparently normal healthy pigs.

In 1961 Sorodoc, Surdan & Sarateanu (cited by Wilson & Plummer, 1966) isolated a chlamydia from swine suffering from an enzootic pneumonia in the Balkan countries. Pneumonia was produced experimentally in pigs with chlamydial agents isolated from pneumonia in goats (Storz, 1971).

Pavlov, Milanov & Tschilev (1963) presented evidence showing that infectious agents with unquestionable chlamydial properties were the cause of an infectious keratoconjunctivitis of young piglets.

Sheep

In 1950 Stamp, McEwen, Watt & Nisbet, who were the first to show that chlamydial agents can cause abortion, identified these organisms as the aetiological agent in enzootic abortion of ewes (E.A.E. or Stamp's disease) in Scotland. This disease in sheep has since been recognized in numerous countries (Storz, 1971). In South Africa it was not reported until 1972, when a massive epizootic of abortion, unparallelled in its extent and sudden appearance compared with other countries, occurred throughout the sheep raising areas within a single lambing season (A. P. Schutte, J. G. Pienaar, B. J. Erasmus, P. P. Bosman & June C. Lloyd, unpublished data, 1973).

These organisms were also established as the cause of pneumonia in lambs. They were isolated from natural cases and the disease was experimentally reproduced by McKercher (1952) and Dungworth & Cordy (1962a).

Mendlowski & Segre (1960) were the first to detect the ability of chlamydial agents to produce a polyarthritis in animals when they isolated strains of these organisms from lambs showing this condition in the U.S.A. Their observations were subsequently confirmed by other workers (Storz, Shupe, James & Smart, 1963; Livingston, Moore, Redmond & Hardy, 1965; Pierson, 1967; Page & Cutlip, 1968).

Kawakami, Kaji, Sugimara, Omori & Matumoto (1958) in Japan originally reported the detection of chlamydia in the faeces of apparently normal sheep harbouring the organisms in their intestinal tract. Sheep elsewhere in the world were found to be similarly infected (Dungworth & Cordy, 1962b; Wilson & Dungworth, 1963; Storz, 1966).

Based on cytologic findings and the effect of chemotherapeutic agents, Dickinson & Cooper (1959) suggested that chlamydia were the cause of a contagious keratoconjunctivitis of sheep in England. Storz, Pierson, Marriott & Chow (1967) confirmed this finding in sheep in the U.S.A. The ocular infection frequently occurs in association with epizootics of polyarthritis (Pierson, 1967; Hopkins, Stephenson, Storz & Pierson, 1973; Cutlip & Ramsey, 1973). In South Africa extensive outbreaks of keratoconjunctivitis in sheep have been shown to be caused by chlamydia (A. P. Schutte, J. G. Pienaar, B. J. Erasmus, P. P. Bosman & June C. Lloyd, unpublished data, 1973). In some flocks *Mycoplasma oculi* was isolated in addition to chlamydia.

Eugster *et al.* (1970) stated that McKercher and his co-workers in 1967 succeeded in isolating chlamydial agents from rams with epididymitis. In experimental work on bulls and rams, Eugster *et al.* (1970) found that chlamydial agents could be isolated from the semen after parenteral inoculation. One to 3 days after inoculation all animals developed a chlamydaemia lasting 4 to 5 days. Chlamydial agents were isolated from semen near the end of the chlamydaemic phase. Excretion of chlamydia in the semen continued until the animals were slaughtered 8 to 22 days after infection. Chlamydia were isolated from the testes, epididymides, ampullae of the *vasa deferentes*, vesicular and prostate glands.

The above findings were experimentally confirmed in sheep (A. P. Schutte, D. V. Gradwell, P. P. Bosman & J. G. Pienaar, unpublished data, 1973). These workers isolated chlamydia from the urinogenital system and semen of rams in flocks, free from *Brucella ovis*, in which cases of orchitis and epididymitis occurred. In one instance *Actinobacillus seminis* was found in conjunction with the chlamydia.

Goats

McCauley & Tieken (1968) described chlamydial abortions in goats in California. In Japan Omori, Ishii, Harada, Ischikawa, Murase, Katada & Araumi (1953, cited by Storz, 1971) and Saito (1954) reported pneumonia due to chlamydia in this species. Omori, Morimoto, Harada, Inaba, Ishii & Matumoto (1957 cited by Storz, 1971) also found that clinically normal goats harbour the organism in their intestines.

Cattle

McNutt & Waller (1940) first described sporadic bovine encephalomyelitis (S.B.E.) in calves in the U.S.A. Wenner, Harsfield, Chang & Menges (1953) identified the causative organism of S.B.E. as a chlamydial agent. Since the original recognition of S.B.E. in calves, this disease has been reported from numerous countries throughout the world (Storz, 1971) including South Africa (Tustin, Maré & Van Heerden, 1961). Calves are most susceptible, though Menges, Harsfield & Wenner (1953a; 1953b) indicated that adult cattle are also subject to the infection.

An intestinal chlamydial infection in cattle, subclinical in older animals but causing an enteritis in young calves was first reported by York & Baker (1951). This important observation was confirmed by McKercher & Wada (1959) and Storz, Collier & Altera (1968) in the U.S.A., by French (1959) in Australia, Wilson (1962) in Britain, Popovici (1964) in Rumania, Kölbl (1967) in Austria and Blanco (1968 according to Storz, 1971), in Spain. It is noteworthy that numerous faeces samples collected from

cattle within a radius of 160 km from Onderstepoort were included in the study by McKercher & Wada (1959). These workers found it rather surprising that the chlamydial agent was not recovered from the faeces of cattle in South Africa, particularly in the case of the native Afrikaner cattle, because numerous attempts were made under what were considered to be ideal circumstances.

Storz, Smart, Marriott & Davis (1966) recovered chlamydial agents from calves only 2 days old suffering from diarrhoea. York & Baker (1956) observed a transient leukocytosis in 4 to 9-month-old calves that received yolk-sac-propagated intestinal strains orally. Colostrum-deprived, 24-hour-old calves developed fever, leukocytosis and a watery, mucoid and bloody diarrhoea after oral exposure (Storz, 1971). The chlamydia-induced diarrhoea led to dehydration and frequently to the death of the affected calves.

Chlamydia were identified as the cause of epizootic bovine abortion (E.B.A.) by Schoop & Kauker (1956) in Germany and by Storz, McKercher, Howarth & Straub (1960) in the U.S.A. Reports from numerous other countries (Storz, 1971), including South Africa (A.P. Schutte, J. G. Pienaar, B. J. Erasmus, P. P. Bosman & Juen C. Lloyd, unpublished data, 1973), have since verified the aetiological significance of chlamydia in bovine abortions. Similarly, bovine chlamydial pneumonia (enzootic pneumonia of calves) has been confirmed from all over the world since its original recognition in Japan by Kiuchi & Inaba (1952, according to Storz, 1971). In the bovine, mild cases of chlamydial pneumonia may remain undetected and are usually seen as incidental findings at slaughter (Palotay & Newhall, 1958).

Following the recognition of chlamydia as a cause of polyarthritis in lambs, Littlejohns, Harris & Harding (1961) in Australia, Storz, Smart & Shupe (1964) in the U.S.A. and Kölbl & Psota (1968) in Austria reported a polyarthritis in calves due to chlamydia. Storz *et al.* (1966) concluded that some calves may have become infected *in utero* as they were weak at birth and developed first signs of disease 2 days after birth. Polyarthritis was experimentally reproduced by Storz *et al.* (1966) and Storz (1967) by parenterally inoculating young calves with chlamydial strains isolated from joints of field cases.

Dyml (1965, cited by Storz, 1971) in Czechoslovakia isolated a chlamydia from scrapings of the palpebral conjunctiva and the 3rd eyelid of cattle showing a keratoconjunctivitis. He reproduced identical lesions in the eyes of calves by intraconjunctival inoculation of the isolated organism.

Hidiroglou & Prevost (1959), according to Storz, 1971, attributed sterility of cows to chlamydia, the infections having been identified serologically and by demonstration of chlamydial elementary bodies in vaginal discharges. Endometritis was produced experimentally in cows after placing a chlamydial inoculum into the uterus (Omori, Ishii & Matumoto, 1960). According to Yilmaz (1966), Surdan, Sarateanu, Sorodoc & Fuhrer-Anagnoste (1961) isolated a chlamydial agent from an endemic granular vulvovaginitis in cattle. Storz, Carroll, Ball & Faulkner (1968) also isolated chlamydial agents from the semen of bulls showing a seminal vesiculitis syndrome, characterized by a chronic inflammation of the seminal vesicles, accessory sex glands, epididymides and testes. The agent isolated was indistinguishable in the specific neutralization test from those isolated from bovine chlamydial abortions. Mensik, Bohác & Setka (1960, according to Storz, 1971) isolated an organism which they considered to be a chlamydia from the testes of bulls with orchitis. However, they did not clearly identify this agent. According to Strauss (1967), Bohác, Věžniková, Pleva, Věžnik, Ryšanek, Rob & Toman (1963) incriminated chlamydia in bovine orchitis and vaginitis in Czechoslovakia.

Chlamydial polyarthritis, pneumonia, abortions, eye infections and inapparent intestinal infections occur similarly in both the sheep and ox. However, lesions of the extent and severity seen in the brain and spinal cord in S.B.E. have to date not been reported in natural cases of chlamydial infection in sheep.

Horses

There are very few reports in the literature on chlamydiosis in horses. Popovici & Hiastru (1968, cited by Storz, 1971) isolated chlamydia from the blood of young foals affected with bronchopneumonia on 2 different farms and Saito (1954) claimed to have induced pneumonia in horses with the chlamydial agent of goat pneumonia. In Spain, Blanco (1968, according to McChesney, Becerra & England, 1974) isolated chlamydial agents from the brains of horses and mules affected with a hepato-encephalopathic syndrome.

B. J. Erasmus (personal communication, 1973) produced abortion experimentally in pregnant mares and a polyarthritis syndrome in non-pregnant horses. He also identified a chlamydial agent as the cause of an outbreak of keratoconjunctivitis in a stable of horses. Chlamydia have also been shown to be the cause of naturally occurring cases of abortion in mares in South Africa (P. P. Bosman, R. I. Coubrough, B. J. Erasmus & A. P. Schutte, personal communication, 1973). McChesney *et al.* (1974) reported a single case of polyarthritis in a foal, due to chlamydia.

Pathology of Chlamydiosis

The chlamydial organisms primarily parasitize and multiply in cells of the host's reticulo-endothelial system and in various epithelial cells, e.g. in the intestinal tract, placenta, respiratory tract, serous membranes, central nervous system and conjunctiva. The primary effect of chlamydia is on the vascular system (Studdert & Kennedy, 1964), as evidenced by arteritis, vascular changes and occasional thrombosis in various organs (Beasley, Watkins & Bridges, 1962). Proliferation of the endothelium occurs in conjunction with perivascular infiltration of mononuclear cells and neutrophils. Similar cells also invade all layers of the vessel walls.

After entry of the agent into the body a chlamydaemia develops with infection of parenchymatous tissues. During the chlamydaemic phase, persistent infection may be established in one or more organ systems. In the pregnant animal the placenta is the predilection site for the multiplication of the chlamydial agents.

Pneumonia

The acute pulmonary lesion is a lobular interstitial pneumonitis. Affected parts of the lung are grossly consolidated and greyish-purple in colour. The consolidated parts are usually localized in the region of the hilus and the ventral portions of the apical lobes, but in severe cases may extend over entire lung lobes.

In the early stages the microscopic lesion is characterized by a marked outpouring of a fibrin-rich fluid from the capillary vessels, filling alveoli and distending interstitia. In the involved areas of the lungs prominent oedematous thickening of the interlobular septa and subpleural connective tissue is prominent. Septal capillaries are hyperaemic and contain excessive numbers of neutrophils.

Small haemorrhages may also be present in the lung in the acute stage. Polymorphonuclear leukocytes are the first cells to appear in the alveolar exudate. They mostly disappear in the later stages of the lesion when the dominant cells are mononuclear macrophages present in large numbers in the alveoli and interstitial spaces. Considerable desquamation of alveolar lining cells, and later proliferation of these cells, accompany the above changes. Lymphocytes and some plasma cells appear in the exudate later. Perivascular and peribronchiolar accumulations consisting mainly of lymphocytes, plasma cells, reticulo-endothelial cells and small numbers of neutrophils are seen.

Chlamydial organisms can be found in the epithelium of the bronchioli (Palotay & Christensen, 1959; Omori *et al.*, 1960; Phillips, Omar, Popovici, Lamont & Darbyshire, 1968), monocytes (Baker, 1944) and alveolar epithelial cells (Kitamura, 1966).

Chronic or subclinical lung lesions consist of small foci of grey-pink areas of consolidation mainly in the apical and cardiac lobes (Dungworth & Cordy, 1962a). The surface of these areas is depressed below the normal level of the pleura. Histologically, they consist of areas of collapsed alveoli containing variable numbers of macrophages. Accumulations of neutrophils and mucus are commonly seen in the terminal bronchioles. Large peribronchiolar lymphoid foci occur with variable frequency.

Ocular and conjunctival lesions

An intense conjunctivitis with an abundant watery to mucopurulent discharge, sometimes sealing the eyelids, develops after both experimental and natural infection of eyes of animals (Storz, 1971). Photophobia is commonly present in more severe cases. Superficial keratitis often follows. Due to conjunctival hyperaemia, oedema and follicle development swelling of the periorbital tissues may occur. The parotid lymph nodes may be enlarged (Hopkins *et al.*, 1973).

Localized subepithelial cell infiltrates are frequently seen in the peripheral cornea. Pannus and micropannus are also present in many cases. The degree of severity of the pannus usually parallels the severity of the keratitis. Iridal vessels are dilated and small fibrin clots are seen in the anterior chamber. Microscopic epithelial changes in the cornea consist of hydropic degeneration in the central region of the cornea.

The severity of the conjunctivitis is variable, ranging from moderate to marked hyperaemia of the entire conjunctiva and chemosis, with numerous, often confluent, enlarged lymphoid follicles on the lower and third eyelids. In the early stages the epithelium and subepithelial tissues of the conjunctiva are infiltrated with polymorphonuclear leukocytes. In the advanced stage a subepithelial collection of macrophages and mononuclear cells is found in the peripheral limbus and mononuclear cells dominate the histological picture. Some epithelial erosion is seen in the conjunctiva. Colonies of organisms are present in epithelial and monocytic cells. Hopkins *et al.* (1973) isolated chlamydia from 42% of lambs showing signs of ocular disease, using conjunctival scrapings.

Central nervous system (CNS)

In the natural disease, involvement of the CNS seems to be a regular feature only in the calf. Since the original observations on S.B.E. by McNutt & Waller (1940), various workers have described the lesions in the C.N.S. (Innes & Saunders, 1962; Csontos & Széky, 1964; Jubb & Kennedy, 1972). Meningeal and encephalitic lesions have also been described in aborted chlamydia-infected bovine foetuses (Kennedy, Olander & Howarth, 1960; Lincoln, 1968). A generalized chlamydial infection usually precedes or is concurrent with the lesions in the central nervous system (Eugster & Herrmann, 1972). Usually in acute cases of S.B.E. few gross lesions are found. The serous cavities may contain an increased amount of yellowish fluid. The commoner chronic cases have a serofibrinous exudate in the serous cavities and an associated peritonitis, pleuritis or pericarditis. Pneumonia, a serofibrinous synovitis and tendovaginitis may also occur.

Macroscopic lesions, when visible in the CNS, are primarily hyperaemia and oedema. Microscopically a vasculitis, with perivascular cuffing and foci of inflammation composed predominently of mononuclear cells with occasional polymorphonuclear leukocytes, may involve all parts of the brain and spinal cord. The endothelium proliferates secondarily to lesions in the vascular wall. Reactive microglial nodules are widespread in the brain and probably develop around obliterated terminal arterioles. Similar inflammatory reactions may be seen in the leptomeninges. The meningitis is most severe at the base of the brain. The arachnoid and ependymal tissues are favoured sites for chlamydial replication.

Pierce, Moore, Caroll & Bridges (1963) reported lesions in the brains of experimentally infected ewes. Oedema and perivascular adventitial infiltration, with lymphocytes in various parts of the brain and focal histiocytic infiltration of the leptomeninges, were found. A mild non-suppurative encephalomyelitis, characterized by widely distributed focal microgliosis and perivascular cuffing by mononuclear cells, has been noticed in conjunction with polyarthritis in feedlot lambs (Pierson, 1967).

In experimentally induced chlamydial infection in dogs an acute exudative leptomeningitis in some animals has been described (Young, Storz & Maierhofer, 1972). Neutrophils, lymphocytes and plasma cells were distributed irregularly and loosely in perivascular tissues of the pia-arachnoid of the cerebrum, the ventral aspects of the midbrain and the hypophyseal stalk. A similar exudate was seen in the spinal leptomeninges in 1 animal, associated with efferent nerve roots at several levels.

Joints and tendon sheaths

A serofibrinous polysynovitis and tendovaginitis occur in lambs and calves. The most significant lesions occur in the diarthrodial joints. Excess synovial fluid, with hyperaemia, oedema and petechiation of the synovial membrane, tendon sheaths and periarticular tissues are seen in the acute stage. The synovial exudate is greyish-yellow, more viscous than normal and contains free clumps of fibrin. Eventually large sheets of coagulated fibrinous exudate cover most of the joint surface and become firmly attached to the synovium.

Microscopically, necrosis of the cells of the synovial lining, infiltrations of neutrophils, macrophages and lymphocytes in the synovial tissue and at a later stage, proliferation of the synovial cells are seen.

When the joint lesions become chronic, affected joints are grossly enlarged as a result of extensive periarticular fibrosis (Cutlip, Smith & Page, 1972). Sequential pathological changes in the articulations of lambs after intra-articular injection of chlamydial agents have been reported (Cutlip & Ramsey, 1973).

Concomitant lesions in non-articular tissues, observed in polyarthritis in feedlot lambs, included conjunctivitis, focal non-suppurative myocarditis and hepatitis, diffuse interstitial pneumonia and mild encephalomyelitis (Pierson, 1967). In South Africa, J. G. Pienaar & A. P. Schutte (unpublished data, 1973) also infrequently observed a mild fibrinous pleuritis and peritonitis associated with polyarthritis in lambs. Because the ocular infection so frequently occurs in association with epizootics of polyarthritis, Hopkins *et al.* (1973) concluded that chlamydial conjunctivitis in lambs may be an early sign of a developing epizootic of polyarthritis. Lesions similar to those described in lambs have been encountered in dogs experimentally infected with chlamydia (Young *et al.*, 1972).

Intestinal lesions

Chlamydial agents have been shown to cause enteritis and death in young calves (York & Baker, 1956; Storz *et al.*, 1968; Doughri, Young & Storz, 1974).

Clinically a mild mucoid diarrhoea to a watery bloody diarrhoea is seen. However, studies on the lesions caused by chlamydia in the alimentary tract are limited.

Catarrhal enteritis was found in young calves infected orally. With more virulent strains, oedema, congestion and petechial haemorrhages in the ileum, particularly in the terminal part, and petechial haemorrhages and ulcers in the abomasum have been reported (Eugster, 1970; Storz, 1971; Doughri *et al.*, 1974). Microscopically mucosal pits and crypts were dilated and contained plugs of leukocytes and sloughed epithelial cells. Granulomas were found in the abomasal and intestinal mucosal, muscular and serosal layers. Eugster (1970) found that many epithelial cells as well as cells in the *lamina propria* were heavily chlamydia-infected. The organisms are recovered most consistently and in highest titres from the ileum (Eugster & Storz, 1971). The mesenteric lymph nodes also harbour organisms (Storz, Collier, Eugster & Altera, 1971).

Recently ultrastructural changes induced by chlamydial infection of mucosal cells of the ileum of newborn calves after oral inoculation were reported (Doughri, Altera, Storz & Eugster, 1973).

In lambs from chlamydia-infected flocks a marked thickening of the terminal part of the ileum was observed by J. G. Pienaar & A. P. Schutte (unpublished data, 1973). This was associated with enlargement of the mesenteric lymph nodes. Diffuse proliferation of the intestinal lymphoid tissue resulted in gross thickening of the gut. Identical changes were seen in the intestines of lambs experimentally infected by the parenteral route 1 day after birth and slaughtered 100 days later. Similar observations were made in calves.

Pathological changes associated with chlamydial abortions

(a) *Foetal pathology*

According to Storz (1971) the pathological changes in aborted foetuses and placentas depend on the stage of gestation. Bovine foetuses aborted prior to the 6th month and ovine foetuses aborted before the last third of gestation do not have specific lesions.

In calves that are aborted near term varying degrees of petechial and ecchymotic haemorrhages are commonly found in numerous organs. They are regularly seen in conjunctival and oral mucous membranes, tongue, subcutis and skin, trachea, thymus, cranial lymph nodes, salivary glands, pericardium, abomasum and mesentery (Howarth, Moulton & Frazier, 1956; Kennedy *et al.*, 1960; Storz, Call, Jones & Miner, 1967; McKercher, 1969). Linear haemorrhages frequently occur in skeletal muscles and are associated with a yellow, gelatinous infiltrate between the muscle bundles. Erythema has been observed occasionally in white-skinned foetuses (McKercher, 1969).

Hepatomegaly, with a mottled reddish-yellow colour, tough consistency and sometimes a coarsely nodular surface of the liver, is frequently seen. Ascites so extensive as to cause distension of the abdomen, oedema of the subcutis and septal oedema of the lungs also occur. The lymphoid tissues are constantly involved and show generalized enlargement and lymph stasis. Kennedy *et al.* (1960) state that the lesions which appear to be most specific are small grey foci 5 to 10 mm in diameter; these are irregularly distributed in all tissues and are seen regularly in the myocardium and in the renal cortices.

Although earlier reports of enzootic chlamydial abortion in ewes (Stamp *et al.*, 1950; Studdert & Kennedy, 1964) did not describe widespread petechial haemorrhages in the skin and subcutis in aborted lambs, Storz (1971) maintains that after skinning, such haemorrhages can be detected in a high percentage of experimental and natural cases. Haemorrhages may also be found in the thymus, salivary glands and occasionally in lymph nodes. Varying degrees of blood-tinged oedema in the subcutaneous and intramuscular tissues and blood-tinged transudates in the large serous cavities have been reported in aborted lambs (Stamp *et al.*, 1950; Studdert & Kennedy, 1964). Livers of aborted lambs may be congested and slightly swollen but do not show the striking changes seen in calves.

In a small percentage of aborted lambs, numerous whitish pinpoint foci are present in the liver. Swollen and oedematous lymph nodes are less frequently seen in aborted lambs.

Microscopically in the bovine foetus necrotic foci, composed of eosinophilic reticular cell coagulum and necrotic neutrophils, are consistently seen in the red pulp of the spleen (Kennedy *et al.*, 1960). Such necrotic foci can also be found in the adrenals, the bone marrow and lymph nodes. Mononuclear inflammatory infiltrations are present in the cortex of the kidneys, in a perivascular arrangement around arterioles of the abomasum and skeletal muscles and the heart. Inflammatory foci of proliferative glial elements, histocytes and neutrophils are found in various parts of the central nervous system. A focal choriomeningitis involving the choroid plexus and leptomeninges, accompanied by a mononuclear perivascular cellular reaction, is commonly seen.

In the portal tracts of the liver a mononuclear cell infiltration and a few neutrophils, with the portal vessels as centres of the reaction, are present (Studdert & Kennedy, 1964). Foci of degenerated and necrotic hepatocytes and accumulations of mononuclear macrophages and neutrophils are also found in the lobules away from the portal tracts. In bovine foetuses examined 30 days after inoculation, the predominant feature in the liver was focal loss of hepatic parenchyma associated with reticulo-endothelial hyperplasia (Lincoln, 1968). Marked reticulo-endothelial hyperplasia accounts for the lymphadenopathy and splenomegaly seen grossly.

Kennedy *et al.* (1960) state that in bovine foetuses the microscopic lesions in any organ may vary from frank focal eosinophilic necrosis to primary acute pleocellular inflammatory foci or to a more chronic reticulo-endothelial hyperplasia with epithelioid changes and Langhans giant cells (granulomatous inflammatory process). Studdert & Kennedy (1964) reported similar foci of necrosis associated with accumulations of reticulo-endothelial cells and moderate numbers of neutrophils in ovine foetuses. They found these lesions, which varied in size and incidence, in various organs but stated that the liver was the organ most frequently involved. In pregnant mice infected with chlamydial agents, the foetuses develop similar granulomatous lesions involving many of the same organs as in cattle abortions (Scheidegger, 1953).

(b) *Placental and uterine pathology*

Lincoln, Kwapien, Reed, Whiteman & Chow (1969) have found that after intravenous inoculation of chlamydia into pregnant cattle, a short blood infectious phase ensues, following which the organisms are rapidly eliminated from extra-genital tissues and become localized in the placenta. In both the ewe and cow a necrotic placentitis of varying degree has been reported constantly in natural and experimental cases (Stamp *et al.*, 1950; Storz, 1971). Placentas from cases of early abortions or which contain macerated foetuses show marked autolysis. In ewes that abort during advanced pregnancy a variable number of cotyledons are necrotic, with thickening and a yellowish-pink discolouration of the periplacentome. A flaky clay-coloured exudate may be present on the placenta. The uterine surface of the intercotyledonary chorion shows a turbid pinkish-yellow colour and has a tough granular consistency. Hyperaemia and haemorrhages are present at the margins of the placental lesions. Oedema of the chorio-allantois is often seen.

Stamp *et al.* (1950) first reported on the microscopic pathology in the ovine placenta. Novilla (1967) made a chronological study of these changes. Twenty days after infection changes were observed mainly in the hilar region, which was infiltrated by neutrophils, lymphocytes and macrophages. Trophoblastic cells were enlarged and contained chlamydia. Some arcades were denuded of epithelium with the result that cellular detritus and organisms collected in the haematomas. Necrosis of septal cells occurred and organisms were present in lining cells of septa. Some placentas had a periplacentomal exudate containing numerous polymorphonuclear leukocytes, erythrocytes, desquamated cells and organisms. Organisms were also found in the epithelial cells of the membranous chorion and in the periplacental endometrium.

Thirty days after infection, necrosis extended from the hilar region to the deeper parts of the placentome and in some instances involved the caruncular myometrium. Necrotic debris admixed with clusters of organisms filled the intervillous spaces of the hilar region. Denudation of the arcades and villi and the cell infiltration were prominent. Periplacentomal and interplacentomal exudates contained organisms. The chorioallantois was oedematous and denuded in some areas and infiltrated by neutrophils, macrophages and plasma cells. A dissecting neutrophilic infiltration of the chorioallantoic vessels was evident and intimal and adventitial proliferations with thrombosis were also seen. The uterine mucosa was markedly infiltrated by neutrophils. The reaction extended to the uterine glands, filling their lumens with purulent exudate. Chlamydia were present in the endometrial cells.

At 50 days the lesions were more advanced and extensive. Necrosis of the villi and septa was more severe and extended to the base of the placentomes. The caruncular myometrium was infiltrated by neutrophils, lymphocytes and plasma cells. Mainly plasma cells were present in the oedematous chorioallantois. Fibrinoid degeneration and perivascular cuffing with lymphocytes were seen in the chorionic vessels. The uterus was infiltrated with predominantly plasma cells.

The pathogenesis is explained (Novilla & Jensen, 1970) by the localization of the organisms in the chorionic epithelial cells lining the haematomas. As the haematomas are formed by intermittent bleeding from septal capillaries, extravasation of organisms into haematomas during the blood infectious phase is possible. Desquamated dead cells are probably replaced by new cells, which again become infected. The accumulation of cellular debris, exudate and organisms in the haematomas favours the dissemination of organisms into the deeper parts of the placentome and interplacentomal areas. Haematomas at the junction of the periplacentome and hilar region promote dissemination of organisms into the membranous chorion. The accumulation of exudate, containing organisms in the periplacentomal and interplacentomal spaces, facilitates entry

of organisms into the chorionic and endometrial cells.

Depending on the stage of gestation the lesion may differ in the cow. When abortion takes place prior to the 6th month of gestation the entire placenta has a yellow-brownish colour with oedema of the intercotyledonary chorion and necrosis of the cotyledons (Storz & McKercher, 1962; Storz *et al.*, 1967). Placentas from cows aborting during the later stages of gestation have lesions resembling those described for ewes. Sometimes only parts of the placenta are affected while the remaining parts appear normal. Kwapien, Lincoln, Reed, Whiteman & Chow (1970) described experimentally produced cases in heifers in which gross lesions consisting of localized to diffuse collections of fibrinopurulent exudate in the placentas occurred in 17 out of 23 cases. According to these authors the earliest gross placental lesions consisted of localized accumulations of a yellowish-brown exudate between the uterine and chorionic surfaces in the interplacentome and periplacentome with associated oedema of the chorioallantoic membrane. At later stages of the disease this exudate was more copious and widely distributed in the interplacentome and periplacentome of both uterine horns.

The earliest histopathological changes consisted of focal ulcerations of the intercaruncular endometrium and increased numbers of reticulo-endothelial and lymphocytic cells in the subepithelial and periglandular endometrial stroma. Later a severe necrotizing inflammatory reaction of the intercotyledonary chorion occurred. The infection spread radially and subsequently involved the margins of the placentomes in the arcade region.

Storz (1971) pointed out that apparently there is a noticeable difference in the placentomal reaction to the chlamydial infection in sheep and cattle. Studdert (1968) and Novilla & Jensen (1970) stressed the early involvement of the placentomes and the predilection of chlamydial agents for the chorionic epithelium of the hilar region of the ovine placentome, whereas in cattle Kwapien *et al.* (1970) found lesions first in the interplacentome followed by a later spread to the placentome.

When placental damage is sufficiently severe, abortion occurs. When damage is less extensive either a premature or a weak full-term calf may be born (Bassan & Ayalon, 1971). Premature live lambs have also been reported in E.A.E. in sheep (Stamp *et al.*, 1950).

Following experimental intravenous inoculation of chlamydia into pregnant heifers during the 2nd and 3rd trimesters of pregnancy Lincoln *et al.* (1969) found extra-genital pathologic changes at the time of abortion. These changes were only observed in the internal iliac lymph nodes, which drain the genital organs, and consisted of a mild to moderate serous lymphadenitis. Subcapsular and peritrabecular sinuses contained a large amount of proteinaceous fluid. There were many neutrophils in the sinuses and at the periphery of the hyperplastic germinal follicles.

These authors also observed a thin yellowish vaginal discharge, as a sign of impending abortion, in some of their experimental heifers. Chlamydia were frequently demonstrated in stained smears of this vaginal discharge.

Lesions in the male genital system

Genital infections with chlamydial agents in male animals have not been studied to any great extent. Consequently there is very little information on the pathology of this disease in the literature. Eugster *et al.* (1970) observed microscopic lesions of orchitis, epididymitis and ampullitis in their experimentally produced cases. The tissue changes consisted predominently of focal granuloma-like accumulations of mononuclear cells in the interstitium. The number of leukocytes in the semen increased during the course of the experiment and the semen was grossly purulent in some of the animals. The frequency of secondary morphologic abnormalities of spermatozoa increased 20 days after exposure.

Liver

Focal hepatic necrosis and reticulo-endothelial hyperplasia have been reported in various animals (Rivers & Berry, 1931; Beasley *et al.*, 1962; Storz, 1971) including experimentally infected ewes and calves (Beasley *et al.*, 1962; Pierce *et al.*, 1963).

The necrotic hepatocytes are surrounded by hyperchromatic swollen Kupffer cells, occasional lymphocytes and neutrophils. Kupffer cell hyperplasia is noted frequently throughout the liver, often with erythrophagocytosis and cytophagocytosis. Not infrequently parasitism of Kupffer cells by chlamydia has been reported (Yow, Brennan, Preston & Levy, 1959; Meyer, 1965).

The lesions in the portal tracts may vary from small foci of proteinaceous exudation associated with slight neutrophil and macrophage infiltration, to complete filling of portal areas by macrophages, slight fibroplasia and infiltration of small numbers of lymphocytes, plasma cells and neutrophils.

Myocardium

Large focal interstitial accumulations of macrophages and neutrophils, very often in a perivascular arrangement, may sometimes be scattered throughout the myocardium. This may be accompanied by cloudy swelling, fatty degeneration and focal necrosis of the myocardium, interstitial oedema and haemorrhages (Kennedy *et al.*, 1960; Meyer, 1965).

Lymphoid tissue

Gross enlargement of the spleen may be due to either acute necrotic splenitis or chronic reticulo-endothelial hyperplasia. The acute splenitis varies from minute foci of eosinophilic necrosis, with neutrophilic accumulations in the areas of the penicillary capillaries, to necrosis of large segments of the reticular elements surrounding the white pulp (Kennedy *et al.*, 1960). Accompanying these changes are a moderate congestion of the red pulp and a diffuse infiltration of the parenchyma and capsule by moderate numbers of neutrophils.

The more chronic changes consist of a diffuse hyperplasia and hypertrophy of the reticulo-endothelial cells of the red pulp and the peripheral white pulp, often resulting in blending of these elements and loss of normal architecture with desquamation of large numbers of mononuclear phagocytes into the splenic sinuses.

The pattern of lesions in the lymph nodes is very similar to that seen in the spleen. The earliest lesions are minute foci of eosinophilic necrosis of the reticular framework, usually associated with

capillaries at the peripheries of germinal centres. Moderate numbers of neutrophils and a few swollen macrophages are found in such areas and a generalized reticulo-endothelial hyperplasia and hypertrophy often involve the rest of the node. More chronic changes are similar to those described for the spleen.

Kidney

York & Baker (1956) isolated chlamydia from the kidneys of 2 fatal experimentally produced cases in calves and histopathological examination of these kidneys showed a focal interstitial nephritis. In contrast kidneys free from chlamydia found in other experimental calves showed no lesions. Chlamydia have also been isolated from the kidneys of a calf showing a focal interstitial nephritis (Kölbl & Psota, 1968).

A focal interstitial lymphocytic nephritis has frequently been found in association with epididymitis and orchitis in both natural and experimental cases in rams (J. G. Pienaar & A. P. Schutte, unpublished data, 1973). Small discrete focal lymphocytic infiltrations around blood vessels in the interstitial tissue of the kidneys were described in two experimental cases in ewes (Pierce *et al.*, 1963).

Eugster *et al.* (1970) isolated chlamydia from the kidneys and urine of rams in which orchitis and epididymitis were produced experimentally by parenteral inoculation of the organism. However, no mention was made by these authors of lesions in the kidneys.

Haematologic changes

York & Baker (1951; 1956) studied the leukocytic responses of calves to experimental infection with chlamydia. Newly-weaned, colostrum-deprived calves and cattle 4-9 months old had a transient leukocytosis lasting from 1-4 days. In 2 calves with typical lesions of E.B.A. Howarth *et al.* (1956) found an anaemia together with evidence of accelerated erythropoiesis.

Storz, Kaneko & Wada (1962) reported that cows had a leukopenia at the 3rd and 4th day after inoculation with chlamydia but a return to the original leukocyte values occurred by the 7th day. A lymphopenia on the 1st day was masked by a transient neutrophilia. The subsequent rapid decrease in the total white blood cell count appeared to be the result of a parallel decrease in neutrophils at the time when a lymphopenia was present.

One-week-old calves had a leukocytosis during the 3rd and 4th day followed by a return to normal after 7 to 9 days. One premature calf that contracted the chlamydial infection *in utero* had leukopenia and anaemia.

The difference in the leukocytic responses of the cows and the calves was attributed to age difference. It appeared that calves responded to chlamydia with a neutrophilic leukocytosis rather than a leukopenia.

Discussion

Chlamydia can cause lesions in anything from a single to many organ systems. Depending on factors such as the virulence of the agent and the species, age and condition of the animal involved the disease may be fatal. These organisms, however, are more frequently present as latent infections. In a proportion of infected individuals, after benign illness, inapparent infection persists. The chlamydial agent may then be confined indefinitely to reticulo-endothelial cells in the body (Meyer, 1965). A well-balanced host-parasite relationship in which persistence of the chlamydial agent causes no obvious harm to the host is apparently then present. This long-lasting inapparent infection, in which the organism remains in the host in a potentially virulent state, may be upset by factors disturbing the state of equilibrium to the detriment of the host. Overt infection usually follows (Storz, 1971). For example stress as a result of adjustment to the environment during transportation or weaning may cause latent chlamydial infections to flare up and produce active infections resulting in primary pneumonia (Storz, 1968).

As already stated, while the majority of cattle and sheep excreting chlamydia in their faeces are clinically normal, the frequency with which these agents are obtained from the faeces of such animals suggests that the intestinal tract is the reservoir of these agents. Schachter *et al.* (1973) state that the intestinal tract appears to be a natural habitat for chlamydia. In many instances the latent intestinal infections probably lead to generalized infection affecting other organ systems (Eugster & Storz, 1971). Ultrastructural studies by Doughri, Altera, Storz & Eugster (1973) have shown that intercellular oedema, breakdown of the basal border of the intestinal epithelial cells and festooning and ultimate loss of the basal lamina facilitate penetration of chlamydia into the *lamina propria* and its cellular components, including the endothelial cells of the lymphatic system. Infected endothelial cells liberate chlamydia into the lymphatic circulation, leading to chlamydaemia and systemic infection. Spleen, liver, lungs and kidneys were found to be other major sites, apart from the synovia, of secondary multiplication of the chlamydial agent of polyarthritis in calves, during the systemic phase (Eugster & Storz, 1971). The intestinal infection persisted after initiation of the systemic phase. Careful microbiological examination for chlamydial agents in the internal organs of clinically normal sheep shedding the agents in the faeces were consistently negative except for sporadic positive samples from intestinal and hepatic lymph nodes (Storz & Thornley, 1966). On the other hand Omori *et al.* (1960) reported the simultaneous isolation of chlamydial agents from the respiratory and intestinal tract of pneumonic cattle. Chlamydial agents isolated from the intestinal tract of cattle or sheep also caused pneumonia (Palotay & Christensen, 1959; Dungworth & Cordy, 1962b; Popovici, 1964; Smith, Cutlip & Page, 1973). Inapparent intestinal chlamydial infections have not been studied sufficiently as part of the epizootiology of chlamydial abortions. Intestinal chlamydial infection was detected in aborting ewes and all flocks investigated, which were experiencing chlamydial abortions, also had intestinal chlamydial infections (Storz, 1966; Storz & Thornley, 1966). Storz (1963) found that ewes excreting chlamydia from latent intestinal infections did not show any increased resistance to superinfection. The faecal chlamydial agent invaded the placenta and foetus and caused abortion. Lincoln *et al.* (1969) found that the presence of serum complement-fixing (CF) antibodies against chlamydia did not influence the susceptibility of pregnant experimental animals. Intravenous inoculation with massive numbers of organisms

apparently overwhelmed any protective influence of these antibodies. Storz *et al.* (1967) using other routes of inoculation, reported a similar lack of relationship between CF antibody levels and susceptibility in pregnant cows. Lincoln *et al.* (1969) expressed the opinion that inapparent intestinal infections were probably responsible for the existence of CF antibodies, as chlamydia were isolated in faeces from some of their experimental animals prior to experimental intravenous infection. It is not known whether chlamydial organisms persist in the endometrium. However, it has been postulated (Novilla & Jensen, 1970) that infection with chlamydia may result in latent infection of the uterus and that the organisms could enter the conceptus at the time of placentation, when the uterine surface is eroded by the trophoblast. Parker, Hawkins & Brenner (1966) induced abortion in ewes after oral infection with chlamydia. The intestinal chlamydial infection of ruminants seems to be comparable to the chlamydial infection of latently infected birds, which frequently excrete chlamydia in the faeces for long periods of time (Storz, 1971).

It has also been suggested that the most important role of chlamydia as a bovine respiratory pathogen may be its activity in association with other bacterial or viral pathogens (Ide, 1970; Jubb & Kennedy, 1972). Chlamydia in combination with mycoplasmas have been shown to cause pneumonitis in lambs (Boidin, Cordy & Adler, 1958). Biberstein, Nisbet & Thompson (1967) found experimental evidence that chlamydial infection increases the susceptibility of the lung to attack by the bacteria common in pneumonia. The incidence of pasteurella-like lesions was higher in sheep pre-exposed to chlamydial agents than in unexposed individuals. Infections of calves with chlamydia plus reovirus or parainfluenza-3 virus were studied experimentally (Phillips *et al.*, 1968; Frey, Ball & Morris, 1970, according to Storz, 1971). These multiple infections seemed to induce more pronounced respiratory symptoms. Feline pneumonitis is also frequently complicated by empyema of the pleural sacs, purulent otitis media and purulent meningitis. *Pasteurella multocida* is the organism chiefly responsible for these complications (Jubb & Kennedy, 1972). Calves infected orally with the virus of bovine virus diarrhoea and chlamydia show a more pronounced clinical response than calves fed either agent alone (Page, Matthews & Smith, 1973). Multiple infections with other viruses and chlamydial agents are probably not uncommon, but little work has been done on this aspect. Storz *et al.* (1971) found little change in the intestinal flora of calves fed a chlamydial strain of intestinal origin. However, calves fed a virulent polyarthritis-causing strain developed severe diarrhoea. Dramatic shifts in the bacterial ecology of different parts of the intestine in calves with primary chlamydial-induced enteritis have been reported (Storz *et al.*, 1971). High numbers of *Escherichia coli* were found in the abomasum and the small and large intestine of such calves whereas normal calves had high numbers of *E. coli* only in parts of the large intestine. During an investigation of cases of polyarthritis in calves due to chlamydia, Storz *et al.* (1966) isolated both *E. coli* and chlamydia from the joints and internal organs of 1 case. Mixed infections of pasteurella organisms and *Salmonella dublin* with chlamydia were also encountered. Chlamydial organisms occurring as latent infections in organs other than the intestinal tract and lung of apparently healthy animals may play a similar role in producing disease in such organs.

It has long been recognized that the pathogenicity and lethality of chlamydia for the animal host cannot be explained entirely by the direct damage of multiplying particles on infected cells. That a toxic factor may play a role in chlamydial diseases in man, animals and birds had been postulated (Meyer, 1965). Some chlamydial strains produce a toxic effect in mice and chicken embryos (Rake & Jones, 1944). More recently evidence has been presented that the toxic factor is closely associated with the elementary body and is not present in the large reticular bodies (Christoffersen & Manire, 1969). Specific antitoxin can be absorbed from hyperimmune serum only by the small elementary bodies. It appears that soon after entering the susceptible cell, the organism loses the toxic antigen from its cell wall. This antigen is missing during multiplication but is resynthesized at maturation. Despite the evidence for a toxic factor, attempts to isolate a toxin from chlamydia have failed and the mechanisms whereby the chlamydia produce the toxic effects are not known (Christofferson & Manire, 1969).

Similarly, nothing definite is as yet known about why a host cell is injured or dies at a specific time after infection, despite accumulating information about changes in chlamydial infected cultured cells at the subcellular and molecular levels. Multiplication of the chlamydial agents in the cytoplasm of the host cell initially appears to do little damage except in the areas occupied by the organisms (Meyer, 1965). Newer work, based on studies of chlamydial infected L cells (Kordová, Wilt & Sadiq, 1971; Friis, 1972) showed that lysosomes of L cells are not injured in the early stages of infection, but that lysosomal enzyme release occurs during the later stages of the growth cycle of the agent. Indications are that some intrinsic property of the chlamydial structure prevents the usual sequence of host lysosomal response. Instead some intimate accommodation is achieved to prevent initial lysosomal activation and successful parasitism ensues. Release of lysosomal enzymes at a later stage contributes to the cytopathic changes and finally to death and lysis of the host cell as well as to the spread of the parasite progeny. Lysosomal enzymes may also contribute in some way to the toxic effect observed in mice after intravenous administration of high doses of chlamydial particles.

Chlamydia have long been known as the cause of human diseases which vary greatly from the classic psittacosis. Trachoma, lymphogranuloma venereum, oculogenital infections, certain types of arthritis, meningoencephalitis, urethritis and perimyocarditis have been well documented in the medical literature. It is clear from the diseases in animals described above that analogous syndromes have been discovered and recorded during the past few decades in various animal species. Psittacine and other birds probably are responsible for the majority of human cases of chlamydiosis (Meyer, 1965). Human chlamydial infections traceable to mammals occurred either infrequently or remained unrecognized and unreported in the past (Storz, 1971; Schachter *et al.*, 1973). However, sources for human infection other

than birds have become more apparent during recent years (Storz, 1971). Reports of this nature suggest that under certain circumstances, domestic animals may play an important rôle as a potential source of infection for man.

Résumé

PIENAAR, J. G. & SCHUTTE, A. P., 1975. *L'apparition et l'anatomo-pathologie de la chlamydiose chez les animaux domestiques et les animaux de laboratoire: Une revue. Onderstepoort J. vet. Res.* 42 (3), 77–90 (1975)

La littérature au sujet des différentes manifestations pathologiques dues au chlamydia chez les animaux domestiques et les animaux de laboratoire est résumée. Les lésions caractéristiques en anatomo-pathologie à propos de ces maladies sont passées en revue et la pathogénie de la chlamydiose est brièvement discutée. Quelques aspects, jusqu'à présent pas encore publiés, des lésions intestinales, rénales et génitales rencontrées chez bovins et ovins infectés dans la nature et expérimentalement, ainsi que des avortements et la conjonctivite chez le cheval en Afrique du Sud, sont signalés.

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