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**Pneumonia and pleurisy in sheep:
Studies of prevalence, risk factors,
vaccine efficacy and economic impact**

A thesis presented in partial fulfilment
of the requirements for the degree of Doctor of Philosophy
at Massey University, Palmerston North
New Zealand

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Abstract

The objectives of this thesis were to investigate patterns of lamb pneumonia prevalence of a large sample of New Zealand flocks including an investigation of spatial patterns, to evaluate farm-level risk factors for lamb pneumonia, to determine the efficacy of a commercially available vaccine for the disease and to estimate the likely cost of lamb pneumonia and pleurisy for New Zealand sheep farmers.

Data were collected by ASURE NZ Ltd. meat inspectors at processing plants in Canterbury, Manawatu and Gisborne between December 2000 and September 2001. All lambs processed at these plants were scored for pneumonia (scores: 0, <10% or \geq 10% lung surface area affected) involving 1,899,556 lambs from 1,719 farms. Pneumonia prevalence was evaluated for spatial patterns at farm level and for hierarchical patterns at lamb, mob and farm levels (Chapter 3). The average pneumonia prevalence in Canterbury, Feilding and Gisborne was 34.2%, 19.1% and 21.4% respectively. Odds ratios of lambs slaughtered between March and May were vastly higher than those slaughtered in other months indicating longer growth periods due to pneumonia. Since pneumonia scores were more variable between mobs within a flock than between flocks, it was concluded that pneumonia scores were poor indicators for the flock pneumonia level due to their lack of repeatability. There was no statistically significant spatial autocorrelation in pneumonia prevalence for any region, hence lamb pneumonia appeared to be largely independent of topographical and geo-climatic factors.

A questionnaire-based case-control study was conducted investigating farm-level factors from a sample of farms with either high (case) or zero (control) pneumonia prevalence at slaughter (Chapter 4). Significant risk factors for case farms were: (1) shearing lambs on the day of weaning, (2) breeding ewe replacements on-farm (3) number of lambs sold (an indicator of flock size) and (4) increased percentage of lambs sold late in the season (March to May). Significant protective factors included: (1) set stocking lambs after weaning, (2) injecting lambs with Vitamin B12 at the time of tailing, (3) injecting lambs

with Vitamin B12 at weaning. In Canterbury, flocks with Romney ewes and other ewes had a higher risk of pneumonia than those with fine wool type ewes (Merinos, Corriedales or Halfbreds).

In a clinical trial, 8,364 lambs from seven commercial sheep farms with a history of lamb pneumonia were vaccinated with Ovipast Plus® or placebo by systematic random allocation within mob and farm. An assessment of the extent of pneumonic lesions was conducted at slaughter and lamb growth rate was monitored through the growth period (Chapter 5). The vaccination trial showed no statistically significant effect of Ovipast® vaccination on the extent of lung lesions at slaughter or ADG of lambs from the first treatment until slaughter. No significant differences were found between isolation rates of *Pasteurella* spp and patho-histological classifications from pneumonic lung samples of placebo and vaccinated lambs.

A spreadsheet-based stochastic model was constructed to estimate the cost of lamb pneumonia and pleurisy to New Zealand farmers. The estimate was based on data of the effect of pneumonia on lamb growth rate, distributions of pneumonia severity, prevalence of moderate to severe pneumonia ($\geq 10\%$ lung surface area) and pleurisy prevalence (Chapter 6). The simulated annual average cost of pneumonia was NZ \$28.1 million and that of pleurisy NZ \$25.1 million. The combined cost of pneumonia and pleurisy to New Zealand farmers had an average of NZ \$53.2 million (95% stochastic interval = \$32.4–\$78.9 million), or US \$31.9 million per annum. This would equate to NZ \$2.32 per lamb. In comparison, animal health, shearing expenses and feed expenses cost NZ \$2.37, \$2.62 and \$1.85 per lamb, respectively.

This research has demonstrated sub-clinical pneumonia to be a widespread disease in the New Zealand sheep farming population while previous research has focussed on case studies of affected farms. The estimated costs of pneumonia and pleurisy to New Zealand farmers (\$53.2 million) highlight the financial effects of these diseases and the need for further research. We also found that the commercially available vaccine could neither prevent sub-clinical effects (lamb growth rate) nor clinical manifestations (pneumonic lung lesions) of lamb pneumonia. The case-control study has revealed farm-level factors which, in the absence of effective vaccines, indicated management practices that farmers might perceive as opportunities to control lamb pneumonia. However, it is advisable to evaluate the efficiency of such management changes.

Pneumonia is aetiologically complex disease involving the interplay of many environmental, host and pathogen factors. It is also a difficult disease to study in the absence of diagnostic tests in live animals. However, further research should focus on the development of management changes until effective vaccines are available. A starting point for this research would be to evaluate the impact of such management changes in reducing the incidence of lamb pneumonia. More specifically, the roles of stress during crowding of lambs for extended periods warrants further investigation. The development of efficient vaccines requires an analysis of pathogens, especially *Pasteurella (Mannheimia) haemolytica* and *Mycoplasma* species, the sources of infection, their strain diversity and transmission dynamics.

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CHAPTER 1

Introduction

The need to further investigate lamb pneumonia arose in 1997 through a meeting of epidemiologists, pathologists, industry representatives and farmers. The focus of that meeting was to establish the current knowledge and future requirements for research. A funding application to Meat New Zealand was successful and led to a Masterate study preliminary to this Doctorate study. The objectives of the Masterate study were to quantify the impact of the disease on lamb live-weight gain. A longitudinal study was conducted involving farms known to have a history of pneumonia. It was shown that pneumonia had a significant impact on lamb growth rate. A reduction in average daily weight gain of up to 50% was evident in the most severe pneumonia cases. A panel of experts finally realised that economic loss due to lamb pneumonia was primarily at sub-clinical level through reduced growth rates and that disease related mortality was rather exceptional and low at population level.

Subsequent to the Masters study, a need arose to estimate total economic loss due to lamb pneumonia, to investigate spatial and temporal patterns of pneumonia prevalence in New Zealand, and to determine on-farm risk factors that might lead to control options and if feasible, to evaluate control. On this basis, the current PhD study was successful in attaining further funding by Meat and Wool New Zealand (MWNZ). The New Zealand sheep industry has guided our research through regular mentor meetings involving representatives from the sheep council, processing plants, MWNZ, researchers from Massey University and AgResearch and farmers. As a result of one of these meetings, the need to determine the efficacy of a commercially available vaccine against pneumonia was voiced leading to one chapter of this PhD. Pneumonia is not routinely recorded at lamb processing plants, so this project was fortunate to have the support of ASURE NZ Meat Inspectors who collected data in addition to their regular duties. Pneumonia scores were recorded for every lamb processed at three individual plants in three regions over a ten-month period. This provided the majority of the data upon which this thesis was based.

...

Review of the literature on pneumonia and pleurisy in lambs

2.1 Introduction

Pneumonia is a respiratory disease arising from an inflammatory response of the bronchioles and alveoli in the lung to infective agents and resulting in the consolidation of lung tissue. It is a common disease of sheep in all major sheep-producing countries. It is regarded as a disease complex, involving interactions between host (immunological and physiological), multiple agents (viral, bacterial, mycoplasmal) and environmental factors. When a certain threshold dose of microorganisms, host susceptibility and non-specific defence mechanisms are reached, lung defence mechanisms are compromised allowing disease to occur (Bruere et al., 2002). The disease occurs in two main forms in New Zealand sheep: an acute fibrinous pneumonia which occurs in sheep of all ages and a chronic non-progressive pneumonia (CNP) which occurs in lambs and hoggets (Bruere et al., 2002). Extension of pneumonia from the surface of the lung to the lining of the chest cavity results in inflammation of the pleura and the formation of a fibrous adhesion between lungs and the chest wall, known as pleurisy. Ovine progressive pneumonia and Jaagsiekte, (caused by an ovine retrovirus) is exotic to New Zealand (Dalefield and Alley, 1988; Alley, 2002). In lambs pneumonia causes mortality, decreased growth and a predisposition to pleurisy, at considerable cost to the industry, along with animal welfare implications. Due to its sub-clinical nature, detection of CNP is limited to examination of lungs at necropsy or after slaughter. Inability to detect the disease in the live animal and detailed knowledge of the time of onset of lesions severely limits our understanding of the epidemiology of pneumonia in sheep and its effect on productivity. The aim of this review is to give a background of sheep farming in New Zealand and provide an overview of respiratory diseases of sheep and pneumonia and pleurisy in lambs including a critique of relevant scientific trials and literature.

2.2 Sheep farming in New Zealand

Sheep farming plays an important role in New Zealand's economy especially with regard to export. In June 2004, there were 39.3 million sheep in New Zealand, comprising 26.7 million breeding ewes, 8.0 million ewe hoggets, 3.1 million wether hoggets and 1.4 million other wethers and rams (MWES, 2004). New Zealand sheep farms are, on average 506 hectares in size and are comprised of around 1,991 sheep (Table 2.1). Cattle are often farmed on the same properties. South Island farms tend to be more extensive than those of the North Island. They are generally larger in size but do not tend to differ in sheep numbers per property.

Table 2.1: Number of farms with the average and standard deviation of farm size and number of sheep per farm grouped by region (adapted from AgriBase (AgriQuality, 2004)).

Region	Number of farms (≥ 4 ha, ≥ 20 sheep)	Average (SD) of farm size (hectares)	Average (SD) number of sheep/farm
Lower South Island	5,774	678 (2,195)	2,358 (2,845)
Upper South Island	3,168	532 (1,785)	1,656 (2,040)
Lower North Island	5,236	396 (591)	2,203 (2,735)
Upper North Island	3,746	371 (667)	1,410 (2,365)
Total	17, 924	506 (1,525)	1,991 (2,616)

SD – standard deviation

2.2.1 Sheep Breeds

There are approximately 30 sheep breeds in New Zealand. The six most common are:

- Romney (originally the English Romney Marsh, brought to New Zealand in 1853).
- Coopworth (cross of Border Leicester and Romney).
- Perendale (cross of Cheviot and Romney).
- Merino (originated from North Africa or Spain).

- Corriedale (British long wool rams - Lincoln and English Leicester mainly - crossed with Merino ewes).
- Halfbred (Merino crossed with Leicester, Lincoln or Romney) (Statistics New Zealand, 1996).

The geographical distribution of breeds tends to reflect regional differences in climate and topography. Merinos predominate in the alpine grasslands of the Southern Alps. Halfbreds and Corriedales tend to be farmed on the foothills and plains east of the Southern Alps and some drier parts of the North Island. Romneys, Coopworths and Perendales typically are used for meat and wool production on hill country sheep farms elsewhere in New Zealand. Often Texel, Southdown or Suffolk rams are used for market lamb production as they are earlier maturing compared with traditional breeds. In more recent times composite breeds have played a role in breeding programmes. Breeds of higher fecundity and milk production are used in composites, such as Finish Landrace and East Friesian.

2.2.2 Sheep products and markets

Throughout the twentieth century New Zealand has enjoyed a reputation for being largest producer of crossbred wool (wool fibre >31 microns in diameter) throughout the world (MAF, 2004d). Crossbred wool is used for interior textiles such as carpets, upholstery, furnishings, rugs, hand knitting yarn, knitwear and in blankets. Fine wool (<24.5 micron) comprised five percent of export wool volume in 2003/2004 (MAF, 2005) and is used in the clothing industry.

The annual production of lamb meat in New Zealand was approximately 410,000 tonnes in 2004 (MAF, 2005), of which 91% was exported, with the remainder being consumed locally (MIA, 2004). New Zealand sheep meat accounted for 47% of the world export trade of lamb and mutton in 2002 (MAF, 2004c). The major markets of sheep meat in are the European Union, United States and Asia. In the year ended September 2004, approximately 19% of New Zealand exported lamb was chilled (contributing 29% of total lamb export revenue) and the remainder frozen (MAF, 2005). Annual mutton production was approximately 107 tonnes in 2004 (MAF, 2005), of which 83% was exported (MIA, 2004).

2.2.3 Structure of the Industry

Meat and Wool New Zealand is a body funded by livestock producer levies on all sheep slaughtered in New Zealand (MWNZ, 2004a).

Its purpose is to:

- Market New Zealand sheep meat internationally and domestically.
- Maintain and extend trade access for New Zealand red meat.
- Fund research and development to help improve the profitability of New Zealand farmers (MWNZ, 2004a).

Within the wool industry there are other groups involved in marketing, research and development. These are:

- **The National Council of New Zealand Wool Interests** (provides the forum in which all sectors involved in the New Zealand wool industry work together for the benefit of the industry) (NZTE, 2004).
- **The New Zealand Merino Company Ltd** (A joint venture between New Zealand Merino woolgrowers and Wrightson Ltd which handles the majority of the merino wool clip. It has developed a number of direct supply linkages where growers are contracted to supply agreed amounts of fibre meeting agreed specifications to particular manufacturers) (MAF, 2004a);
- **Wool Interiors Ltd** (International marketing of New Zealand wool and products through management of the Wools of New Zealand branding programme) (NZTE, 2004).
- **Canesis Network Ltd** (Jointly owned by the Wool Research Organisation of New Zealand and Wool Equities Ltd. A grower-owned investment company specialising in wool, sheep research and development on ways of using New Zealand wool, developing innovative wool and wool-blend products) (NZTE, 2004).

In the meat industry, more than 150 New Zealand meat processing companies are licensed to operate slaughter houses, the majority of which produce meat for export. The four largest exporting companies are PPCS Limited, AFFCO New Zealand, ANZCO Foods Limited and the Alliance Group (NZTE, 2004).

The Meat Industry Association of New Zealand (MIA) represents processing companies that supply sheep meat for export. The MIA provides a forum for consideration of industry-wide commercial, human resource, marketing and sanitary and phytosanitary issues. They convey a collective industry position to government, trade bodies and other agencies and organisations (MIA, 2005).

Sheep meat and wool production in New Zealand is undertaken without the assistance of government subsidies. Agricultural subsidies were removed in the mid-1980s leaving producers and exporters entirely reliant on export market returns (MAF, 2004b). Since then, sheep numbers have decreased from 70 million to 39 million and farmers have diversified, especially into dairying and deer farming. Farm productivity since this time has improved. The average slaughter weight of lambs has increased along with an increase in lambing percentage from 100% to 115%. The processing and marketing companies have moved from exports of whole frozen carcasses to chilled meat which made up 25% of lamb export value in 2004 (MAF, 2005). The current projection for the New Zealand sheep industry to 2008 is promising, with expected increases in sheep meat production, lamb carcass weights and lamb price (MAF, 2005).

2.2.4 Timing of Farm Management Events

Ewes are mated in autumn and lamb in spring (Fleming, 2003a). Table 2.2 shows average dates and ages for mating, lambing, tailing, weaning and slaughter based on a survey of 313 sheep flocks from Gisborne, Manawatu and Canterbury. On average rams are put with ewes in late March for 57 days leading to a lambing start date in late August (Table 2.2). The average lambing date is 3 September. Lambs are tailed on average at 45 days of age, weaned mid December at 101 days of age and slaughtered 72 days post-weaning. Shearing may be carried out once a year, twice a year (second-shearing) or three times every two years.

Table 2.2: Average dates of mating, lambing, weaning, ages of lambs at tailing, weaning and slaughter with each standard deviation (SD, days) and number of flocks in the calculation based on a survey of 313 sheep flocks in Gisborne, Manawatu and Canterbury (refer Chapter 4, this thesis).

Variable	Number of flocks	Average (SD (days))
Date ram out	296	29 March (23.4)
Number of days ram out	298	57 (24.2)
Start date of lambing	300	22 August (24.6)
Average lambing date	298	3 September (24.4)
Age of lambs at tailing (days)	288	45 (24.2)
Date of weaning	298	13 December (23.1)
Age of lambs at weaning (days)	297	101 (21.1)
Average slaughter age (days)	296	173 (30.6)

SD – standard deviation

2.2.5 Farming systems

There are two main types of sheep farming systems. These are;

1. Sheep breeding
 - a. Flocks of breeding ewes with ewe replacements bred ‘on-farm’ and lambs finished to slaughter weight or,
 - b. Flocks of breeding ewes with ewe replacements bred ‘on-farm’ selling a proportion of lambs as ‘forward stores’ (sale of live lambs not yet at slaughter weight) with the remaining proportion finished to slaughter weight.
2. Sheep finishing
 - a. Flocks of breeding ewes where no ewe replacements are bred ‘on-farm’. Ewe replacements are purchased from other properties (often older ewes which are then sold post weaning) and lambs are finished to slaughter weight.
 - b. No breeding ewes ‘on-farm’. Lambs purchased as ‘forward stores’ and finished to slaughter weight.

2.2.6 Disease Status

New Zealand is free of foot-and-mouth disease and scrapie, aided by its geographical isolation from affected countries (MWNZ, 2004b). Some of the most relevant health problems in New Zealand sheep are internal and external parasites, facial eczema, footrot, pneumonia, pleurisy, caseous lymphadenitis, scabby mouth, Johnes disease, toxoplasmosis, campylobacteriosis, listeriosis, leptospirosis, brucellosis and salmonella.

2.2.7 Pasture growth and climate

The generally mild temperatures and reliable annual rainfall in New Zealand favours a pasture based livestock production system. Sheep are traditionally grazed on pasture year round, often with supplements of hay or silage in the winter (MAF, 2004c). In the South Island, crops such as Swedes and Brassicas are often grown for winter feeding. Fertiliser is commonly applied and irrigation is used in areas where rainfall is low for pasture production. Pasture growth occurs for 8 to 12 months of the year depending on soil type and location. Based on values from 1971-2000 (for locations having at least 5 complete years of data), the average annual temperature and rainfall for the South Island was 11°C and 1656 mm and that for the North Island was 13.9°C and 1166 mm (NIWA, 2001). Average daily pasture growth rates in the South Island ($n = 24$ farms) and North Island ($n = 50$ farms) are shown in Figure 2.1 by calendar month.

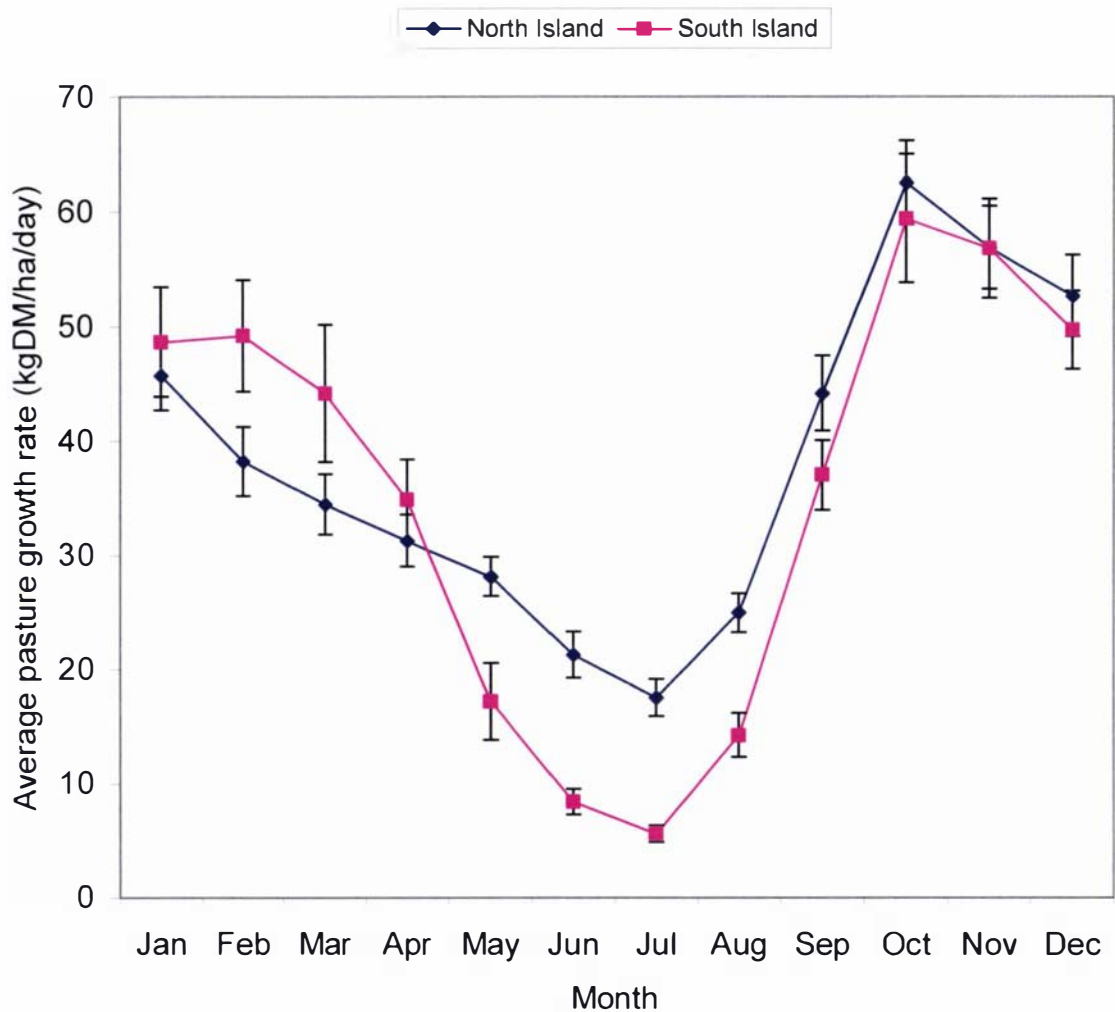


Figure 2.1: Average daily pasture growth rates for 50 North Island (◆) and 24 South Island (■) farms per month with 95% confidence intervals (adapted from Dexcel Limited (2005)).

2.3 Respiratory disease in sheep

Respiratory disease is common in most livestock around the world. There are several different types recognised in sheep:

1. Acute pneumonia (AP).
2. Chronic non-progressive pneumonia (CNP).
3. Ovine progressive pneumonia (OPP) or maedi-visna (MV).
4. Pleurisy.
5. Jaagsiekte sheep retrovirus (JSRV).

In New Zealand AP, CNP and pleurisy are the only forms of ovine respiratory disease currently recognised.

2.3.1 Clinical and patho-physiological classification

Acute pneumonia (AP)

This type of pneumonia has also been referred to as acute fibrinous pneumonia, acute necrotising pneumonia, acute exudative pneumonia or pneumonic pasteurellosis. Clinical signs of AP include fever, depression, weight loss, isolation from flock, mucopurulent nasal discharge, increased respiratory rate and rales in the anterior thorax (Gilmour and Angus, 1983). AP often results in death within 12 hours of the onset of any clinical signs in sheep of any age (Alley, 1991). Mortality rates associated with acute pneumonia vary between 2 and 8% (Bruere et al., 2002).

On post mortem examination fibrinous exudates are present in the thoracic cavity with variable amounts of swollen, dark red consolidation occurring mainly in the cranioventral lobes. The remainder of the lung becomes congested and may contain haemorrhages (Alley, 2002). Animals surviving this acute stage may recover, or become chronically affected with reduced lung capacity and reduced weight gain (Brogden et al., 1998).

Chronic non-progressive pneumonia (CNP)

CNP is a subclinical form of pneumonia occurring more commonly in lambs or hoggets between 3 and 10 months of age (Bruere et al., 2002). CNP has also been referred to as atypical pneumonia, summer pneumonia, proliferative exudative pneumonia, proliferative interstitial pneumonia or enzootic pneumonia.

CNP has few, if any, clinical signs (Alley, 1987b). Chronic coughing, difficulty in breathing, abnormally fast breathing (best demonstrated by exercise) or a mucopurulent nasal discharge may be present (Jones and Gilmour, 1983).

In experimentally induced CNP, Jones et al. (1982) observed laboured breathing or abnormal breathing during the first 14 days post inoculation. During the first 6 weeks post inoculation the majority of the lambs appeared depressed and fever was recorded in 67% of

them. Generally, CNP is associated with high morbidity and low mortality (Bouljihad and Leipold, 1995).

Lesions are usually confined to the apical lobes and vary in colour from grey to red-brown. They may be accompanied by dull red bands of collapsed tissue (Jones and Gilmour, 1983). CNP may last several months but lesions may resolve. Gilmour et al.(1982a) suggest that complete regression of lesions is unlikely in less than 7 months. Lungs may be permanently shortened but consolidated tissue can be re-aerated (Alley, 1991).

CNP and AP are considered to be pathologically different due to the severity and extent of damage to the alveolar epithelium. In both forms of pneumonia, *Pasteurella (Mannheimia) haemolytica* is considered to be the main bacterial agent responsible for lung damage where multiple serotypes may be involved (*P. haemolytica* serotype A1, A2, A6, A7 and A9). However, little is known of the frequency of recovery of *P. haemolytica* serotypes between the two disease forms (Alley, 2002).

Ovine-progressive pneumonia (OPP)

OPP is a lentivirus disease of sheep in North America, which may progress for several months to a year before death occurs. Characteristic signs of disease include severe and progressive weight loss and laboured breathing or pneumonia. In most cases infected animals show no clinical signs. Maedi visna is a disease exotic to New Zealand, caused by a lentivirus closely related physically and biochemically to that causing OPP (Cutlip et al., 1986). 'Maedi' translates as difficult breathing and 'visna' as wasting.

Clinical signs of OPP seen in animals 2 to 3 years old include laboured respiration, loss of condition, decreased milk production and abortion. Lungs become mottled greyish-blue to greyish-brown, firm and large (2 to 3 times the normal weight). Transmission of the disease is pseudo-vertical through the ingestion of infected colostrum and milk. There is no effective treatment or vaccine available (Bruere et al., 2002).

Sheep pulmonary adenomatosis

Jaagsiekte sheep retrovirus (JSRV) causes sheep pulmonary adenomatosis (SPA) which is a contagious disease characterised by a tumour in the lungs of adult sheep (Holland et al., 1999). A herpes virus and a retrovirus are often aetiologically associated with the disease. SPA has been reported in Europe, South Africa, Asia, Britain, Iceland and Israel. The disease is spread mainly by aerosol transmission. The incubation period in naturally infected sheep appears to be long, which means that the disease is generally only seen in adult animals. However, on rare occasions tumours have been seen in lambs as young as two months old.

Traditionally, classical SPA is diagnosed on the basis of chronic wasting with marked respiratory signs in adult sheep (Sharp, 2000). At necropsy, grey lesions are found in the apical and cardiac lobes of lungs and the lung is 3 to 4 times its normal size. The only method of control is by slaughter of affected animals (Bruere et al., 2002).

Pleurisy

Pleurisy is an inflammation of the pleura resulting in fibrous adhesions between lung and chest wall. It has been commonly accepted that pleurisy is not a separate entity but part of a pleurisy-pneumonia complex of poorly defined aetiology (McGowan et al., 1978; Davies, 1985a; Pfeffer, 1986). Acute pleural adhesions are likely to contain large numbers of the bacteria that caused the pneumonia from which they arose. Chronic fibrous pleurisy of any size may only contain a few of these organisms or be sterile depending on the stage of the disease process (Davies et al., 1986a).

In the early acute stage of pleurisy, contact and movement between the parietal and visceral pleurae causes pain due to inflammation of the pleura. In the second stage, serofibrinous inflammatory exudate collects in the pleural cavity and can cause collapse of the ventral parts of the lungs. This reduces lung capacity and interferes with gas exchange. In the third stage, fluid is resorbed and adhesions develop, restricting movement of the lungs and chest wall. Interference with breathing is minor and disappears with time as the adhesions stretch with respiration (Blood and Radostits, 1989). Pleurisy lesions never resolve completely and permanent fibrous scars remain on the lungs and the parietal pleura.

Animals with subclinical pneumonia and those surviving clinical pneumonia may develop pleurisy. Extension of pneumonia from the surface of the lung to the lining of the chest cavity results in the formation of a fibrous adhesion between lungs and the chest wall. These lesions persist after the pneumonia resolves and appear to accumulate with successive episodes of pneumonia (Davies, 1985b; Pfeffer, 1986).

2.3.2 Diagnosis

Diagnosis in live animals

In the case of AP, clinical signs may be present (refer 2.3.1, Acute pneumonia). However, mortality often occurs within 12 hours of the onset of any symptoms.

There are usually no clinical signs with CNP or pleurisy until the disease has reached an advanced state (refer 2.3.1, Chronic non-progressive pneumonia, Pleurisy). Serology of antibodies may indicate exposure to the main pathological agents of pneumonia in the live animal but gives no indication of whether lung damage has occurred or its extent.

Two studies have investigated the use of ultrasonographic examination to detect lung lesions (Maxson et al., 1996; Scott and Gessert, 1998). Both of these studies, however, highlighted the limitation of this diagnostic technique for use in lungs. This is because air reflects the ultrasonographic beam and prevents the visualisation of structures beneath the aerated lung surface. The study conducted by Scott and Gessert (1998) examined ten ewes with pulmonary disorders and found that abscesses involving the pleura were clearly visible. The extent of SPA (sheep pulmonary adenomatosis) lesions were able to be outlined and they identified secondary abscess formation within the tumour mass, however, no lung abscesses far away from the pleura surrounded by normal aerated lung tissue were identified during the ultrasonographic examinations. The study by Maxson et al. (1996) also found that ultrasound was limited in the detection of hydatid cysts in the lung because air in the peripheral pulmonary parenchyma reflects sound waves and prevents the imaging of deeper structures. Only hydatid cysts, which were adjacent to the chest wall, could be visualised. They reported a sensitivity and specificity of ultrasound examination for detecting hydatid cysts in sheep and goat lungs to be 54.4% and 97.6%.

Diagnosis at slaughter

The most accurate method of detecting chronic pneumonia and pleurisy in sheep is to carefully examine the lungs at necropsy (Alley, 2002). This restricts the establishment of pneumonia status to a single point in the life of a lamb, resulting in limited knowledge of disease development and progress.

2.3.3 Treatment

Antibiotics have been shown to have an effect in the treatment of pneumonia. When there have been substantial deaths attributed to AP in the field, antibiotics are used to treat the remainder of the flock to prevent further deaths. They can also be used to reduce the effects of CNP. There has been some degree of resistance of pneumonic pathogens to some types of antibiotic. A number of *in vitro*, experimental infection and field studies have tested a variety of antibiotics against strains of bacteria and mycoplasmas isolated from sheep pneumonia cases.

***In vitro* antibiotic studies**

Six *in vitro* studies have measured the susceptibility or resistance of several sheep pneumonia pathogens to different types of antibiotics (Table 2.3). Three of the studies are Turkish (Otlu, 1997; Kaya and Kirkan, 1999; Gurbuz and Sahin, 2003), two are Indian (Umesh et al., 1994; Mondal and Srivastava, 2004) and the remaining study is French (Sanchis and Abadie, 1992). These studies have shown varying results where Gurbuz and Sahin (2003) have suggested that *P. haemolytica* isolates are 97% sensitive to penicillin and 93% sensitive to streptomycin, but other studies have shown *P. haemolytica* Biotype A to be resistant to streptomycin and Biotype T to be resistant to penicillin and streptomycin (Sanchis and Abadie, 1992; Kaya and Kirkan, 1999). There are also some conflicting results between Kaya and Kirkan (1999) and Sanchis and Abadie (1992), in the sensitivity of *P. haemolytica* Biotype A to erythromycin, kanamycin and gentamycin and that of Biotype T to erythromycin and ampicillin. In some of these studies (Umesh et al., 1994; Gurbuz and Sahin, 2003; Mondal and Srivastava, 2004), there was a limitation of the number of isolates tested, particularly that of Mondal and Srivastava (2004), where only six isolates were tested. In terms of the number of isolates tested in the study of Sanchis and Abadie (1992, n=166) was superior to that of Kaya and Kirkan (1999, n=48) and Gurbuz and Sahin (2003, n=29).

Some *Mycoplasma* species are susceptible to antibiotics that *P. haemolytica* isolates are not and *vice versa*. It would appear based on these *in vitro* studies, that enrofloxacin and danofloxacin are the only two antibiotics that *P. haemolytica* and *Mycoplasma* spp. are susceptible to. In the absence of knowing which pathogen is the cause of pneumonia cases in the field, the most successful antibiotic treatment would be that to which no resistance is evident.

Table 2.3: Pathogens of sheep pneumonia and their sensitivity to antibiotics, with study references.

Pathogen	Antibiotic	Sensitivity (Reference)	Sensitive strains (Reference)
<i>Pasteurella haemolytica</i>	Danofloxacin		29/29
	Enrofloxacin		29/29
	Erythromycin		24/29
	Gentamycin		28/29
	Penicillin		28/29
	Streptomycin		27/29
	Tetracycline		27/29
	Kanamycin		26/29
	Clavulanic acid-amoxicillin		0/29
<i>P. haemolytica biotype A</i>	Penicillin	Sensitive (2)	101/219
	Ampicillin	Sensitive (2)	215/219
	Oxytetracycline	Sensitive (2)	
	Erythromycin	Sensitive (2)	103/219
	Streptomycin	Not sensitive (2)	93/217
	Kanamycin	Not sensitive (2)	199/219
	Gentamycin	Not sensitive (2)	211/220
<i>P. haemolytica biotype T</i>	Erythromycin	Sensitive (2)	22/42
	Kanamycin	Sensitive (2)	38/42
	Gentamycin	Sensitive (2)	42/42
	Penicillin	Not sensitive (2)	11/42
	Ampicillin	Not sensitive (2)	40/42
	Oxytetracycline	Not sensitive (2)	10/40
	Streptomycin	Not sensitive (2)	
<i>P. multocida</i>	Tetracycline	Not sensitive (6)	
	Ampicillin	Not sensitive (6)	
	Gentamycin	Sensitive (6)	
	Kanamycin	Sensitive (6)	
	Streptomycin	Sensitive (6)	
<i>Mycoplasma agalactiae</i>	Enrofloxacin	highly sensitive (3)	
	Oxytetracycline	highly sensitive (3)	
	Gentamycin	highly sensitive (3)	
<i>M. arginini</i>	Enrofloxacin		42/43
	Danofloxacin		40/43
	Ampicillin		39/43
	Erythromycin		7/43
	Streptomycin		0/18
<i>M. ovipneumoniae</i>	Enrofloxacin		18/18
	Oxytetracycline		17/18
	Danofloxacin		16/18
	Ampicillin		16/18
	Erythromycin		2/18
	Streptomycin		0/18

References:

- 1 – Gurbuz and Sahin (2003).
- 2 – Kaya and Kirkan (1999).
- 3 – Mondal and Srivastava (2004).
- 4 – Otlu (1997).
- 5 – Sanchis and Abadie (1992).
- 6 – Umesh et al. (1994).

Experimental antibiotic studies

In the UK, long-acting oxytetracycline was administered to specific pathogen free lambs at a dose rate of 20 mg/kg either 24 hours before or 24 hours after exposure to an aerosol of *P. haemolytica* (Gilmour et al., 1982c). Three groups of 10 lambs with antibiotic treatment 24 hours before exposure, antibiotic treatment 24 hours after exposure and non-treated, exposed lambs were compared. The pre-infection treatment delayed the appearance of clinical signs of pneumonia by 4 days and deaths of 5 lambs for 5 to 6 days. Seven untreated lambs had died by this time. The post-infection treatment resulted in rapid clinical recovery persisting until 6 days post-infection, but 2 treated lambs died 7 days post-infection. The extent of lung lesions in the post-infection treatment lambs was reduced in comparison to untreated lambs. This indicated that oxytetracycline had some effect against *P. haemolytica* but was more effective when administered post-infection.

Three-week old lambs were experimentally challenged with an aerosol of *P. haemolytica* biotype A serotype 2 (Gilmour et al., 1990). Ten lambs were treated with a clavulanic acid and amoxicillin combination (repeated twice at 24 hour intervals). There was a significant difference in death rate, 1 out of 10 treated lambs died and 7 out of 10 untreated lambs died between 3 and 6 days after treatment. Post mortem examination showed bacteriological evidence of pasteurellosis and the presence of either pleurisy or subacute pneumonia.

These experimental field studies show that antibiotics (long-acting oxytetracycline and clavulanic acid/amoxicillin) have had an effect on experimentally induced pneumonia. Recent *in vitro* studies (as described above) have indicated some level of resistance of *P. haemolytica* isolates to oxytetracycline and clavulanic acid-amoxicillin (Kaya and Kirkan, 1999; Gurbuz and Sahin, 2003).

Field studies of antibiotic use

Field studies investigating the effect of antibiotics have predominantly involved clinical or acute pneumonia. The challenge for the treatment of subclinical CNP is the ability to detect the disease in live animals and to correctly identify which animals to treat. In addition, issues involving antibiotic residues in lamb meat, antibiotic resistance and cost effectiveness of such treatments require consideration. In field studies involving acute pneumonia, antibiotic treatment has largely been effective.

On seven Scottish farms there was a laboratory confirmation of *Pasteurella*-related deaths in young lambs (Appleyard and Gilmour, 1990). Half of each flock was treated with long-acting oxytetracycline (20 mg/kg intramuscularly). On four of the farms two treatments were given and on the remaining three only one treatment was given. Fewer deaths resulted in the treatment groups where 1 out of 345 (1 treatment) and 0 out of 533 (2 treatments) lambs died compared with the untreated control group where 10 out of 345 and 8 out of 533 lambs died. The comparison of lamb deaths, between lambs treated both once and twice, with the control group was statistically significant ($p < 0.001$). Treatment (both 1 and 2 treatments) was associated with a 94.0% reduction (95%CI 58.5, 99.3%) in the risk of death compared with placebo. Nine control lambs were diagnosed with AP (which responded to long-acting oxytetracycline) and no treated lambs showed any clinical signs of disease.

In the UK, an outbreak of AP caused the death of 8 out of 188 (4%) 5 week old lambs over a period of 1 week (Sargison and Scott, 1995). Half of the lambs were treated with a single subcutaneous injection of 10mg/kg tilmicosin (Micotil) and the other half with a single intramuscular injection of oxytetracycline (Engemycin). There was no untreated control group used in this study to make a valid comparison. Treatment improved the clinical condition and daily liveweight gains were improved, but no significant differences occurred between the two treatment groups. Four more lambs died within two days of the treatment but there were no further deaths subsequently.

In Egypt, three flocks of sheep with average morbidity rates of 54% and mortality rates of 11% due to pneumonia, were treated with gentamycin (Sadiek et al., 1993). Treatment reduced the severity of clinical signs (anorexia, pyrexia, congested mucous membranes, laboured respiration, bilateral mucopurulent nasal discharge and signs of dyspnoea). Mortality rates post-treatment were not provided and no control groups were used.

In Hungary, tiamulin was used to treat lambs that had experienced pneumonia outbreaks associated with adenovirus, *pasteurella* and *mycoplasma* spp. infection (Stipkovits et al., 1985). Average weight gains 41 days post treatment were 15.8, 14.7 and 10.4 kg for lambs with tiamulin added to feed ($n = 200$), lambs injected with tiamulin ($n = 200$) and control groups ($n = 200$) respectively. On post mortem examination pulmonary changes were seen in 36%, 29% and 69% of each group and severe pneumonia in 7.6%, 5.4% and 32%. The

difference in pulmonary changes and pneumonia between either of the tiamulin treatment groups and the control group was significant ($p < 0.001$) but not between treatment groups. Mycoplasmas were isolated from 90% to 100% of nasal swabs prior to treatment and from 3 out of 20 (15%), 10 out of 20 (50%), 19 out of 20 (95%) nasal swabs post treatment from the feed group, injection group and control group respectively. This difference was significant between all groups of lambs ($p < 0.020$).

In a study by Alley and Clarke (1980), Ronidazole, oxytetracycline, tylosin and penicillin suppressed in varying degrees the development of lesions and the growth of bacteria and mycoplasmas in the lung. The dose of tylosin did not prevent consolidation of the lungs by *M. ovipneumoniae*, whereas the highest concentration of Ronidazole eliminated bacteria and mycoplasmas from the lungs and gave the greatest suppression of lesions, however, the dose produced signs of toxicity. Although penicillin markedly diminished the severity of lesions, it did not prevent either colonisation of the lung by *M. ovipneumoniae* or the development of localised lesions.

These limited numbers of field trials have shown that antibiotic treatment tends to have positive effects on the surviving animals of AP outbreaks in terms reducing the severity of clinical signs and reducing the development of pneumonic lung lesions. This effect is apparent even though some level of resistance of some pathogens of pneumonia to antibiotics has been observed *in vitro*. Animals surviving AP either recover completely or go on to develop CNP. Antibiotic treatment reduces the development of lung lesions of surviving animals of AP and it is likely the development of CNP is also suppressed.

Summary

This section has described the different forms of respiratory disease present in sheep, their aetiology and their clinical patho-physiological classifications. AP, CNP and pleurisy are the only forms of ovine respiratory disease found in New Zealand.

Accurate diagnosis of CNP and pleurisy is limited to slaughter, which places limitations on the ability to precisely identify the time of onset of disease and the temporal development in affected animals. Serology can provide evidence of infection with micro-organisms, however, this information is of limited use as these pathogens may have either proliferated

in the lung causing pneumonia or been cleared from the respiratory tract through innate defence mechanisms.

Ultrasonography has been trialled as a diagnostic method although it is limited to lesions on the lung surface as air in the lung reflects the ultrasonographic beam

Antibiotics have been used successfully in the treatment of AP and CNP in the field although *in vitro* studies have indicated resistance of *P. haemolytica*, *P. multocida*, *M. arginini* and *M. ovipneumoniae* to some antibiotics. Antibiotic treatment is essentially restricted to the treatment of AP, as in the absence of clinical signs for CNP, no knowledge of which lambs to treat provides difficulties.

2.4 Pneumonia in New Zealand

2.4.1 Prevalence

The earliest estimate of mortality rate attributable to AP in New Zealand lambs was about five percent in individual flocks (Porter, 1970). Manktelow (1970) proposed AP caused 'quite severe mortalities on individual farms although no field data was presented to support this proposition. Since then, several other authors have reported lamb mortality rates ranging from 8% to 21% and outbreaks occurring at various locations nationwide (Smith, 1975; Anonymous, 1976; Sorenson, 1976; Anonymous, 1978; Davies, 1986; Orr and Black, 1996; Orr et al., 1998; Clark et al., 2001). From the limited published reports, there appears to be no identifiable trend in AP mortality rates over time or associated with geographical location. A map of New Zealand (Figure 2.2) shows the various regional locations of pneumonia studies as discussed throughout this review.



Figure 2.2: Map of New Zealand.

Reports of CNP prevalence have varied between 21% and 93%. In a trial estimating the seasonal incidence of pneumonia in Hamilton (Waikato, Kirton et al. 1976), an average of 60% of the trial lambs showed some evidence of pneumonic lesions at slaughter over a five year period. Thurley et al. (1977) reported CNP prevalence of 78% ($n = 27$) and 57% ($n = 58$), recorded at slaughter, in a subsequent season at Wallaceville (Wellington). In the Hawkes Bay and Feilding (Manawatu), McGowan et al. (1978) demonstrated prevalence of 78 to 93% in lambs three months of age when examined post-mortem. The prevalence of lesions measured at slaughter in their older counterparts at suitable market slaughter weights was 35 to 68%.

Between March and April 1996, the prevalence of CNP among 9,400 lambs across seven slaughter plants covering all geographic regions of New Zealand was estimated by Black (1997). The case definition used in this study was lesions with red or red-grey consolidation covering more than a quarter of one anteroventral lung lobe with the presence of fibrinous plural exudates. The prevalence of this definition of pneumonia in Northland was 13% (95%CI 11, 16), Bay of Plenty 6% (95%CI 5, 8), East Coast (corresponds to Eastland in Figure 2.2) 4% (95%CI 3, 5), Wanganui 6% (95%CI 4, 7),

Marlborough 4% (95%CI 3, 5), Canterbury 4% (95%CI 3, 5) and Southland 5% (95%CI 4, 7).

In Southland, the King Country (refer Figure 2.2, Upper Wanganui/Taupo) and Northland the pneumonia prevalence of lambs randomly selected for slaughter was 21.8% (95%CI 20.0, 23.7) in Southland ($n = 1,917$), 49.2% (95%CI 46.9, 51.5) in the King Country ($n = 1,831$) and 60.3% (95%CI 57.8, 62.8) in Northland ($n = 1,485$). The prevalence of lesions in each region was significantly different from each other region (Goodwin et al., 2004).

2.4.2 Feedback to farmers from processing plants

Pneumonia is not routinely recorded by processing plants as there are no associated human health risks or direct effects on lamb carcasses. In flocks with a high incidence risk of subclinical pneumonia, farm managers may be unaware of the extent of the problem due to the lack of feedback from processing plants. Post mortem inspection by veterinarians when AP related mortality occurs on farm is currently the only source of an aetiological diagnosis. However, these are not likely to be conducted unless mortality rates are high. Pleurisy is routinely recorded by processing plants and reported to producers. Pleurisy affects carcass quality and consequently, carcasses with pleurisy are of reduced value. As pneumonia can be a precursor to pleurisy, records of pleurisy from processing plants may provide some indication of pneumonia levels. The correlation between pneumonia and pleurisy, however, is highly variable, so pleurisy is not an accurate indicator of pneumonia.

In the pig industry, programs for the utilisation of post mortem data collected at slaughter have been developed to improve disease control measures and management practices. This includes the collection of pneumonia information. In the pig industry an effective mycoplasma vaccine is often used to control pneumonia. The need for use of this vaccine may be established through feedback of pneumonia levels at slaughter to farm managers. The main limitation is that pneumonia levels recorded at slaughter only reflect the last four to six weeks of production. The ability to identify significant risk factors for pneumonia occurring through the entirety of the animal's life, therefore, is limited. In comparison, there is no efficacious pneumonia vaccine for lambs at present and only general guidelines exist for control of the disease. It is questionable therefore whether feedback of pneumonia levels at slaughter would be beneficial to sheep farm managers.

2.4.3 Discussion

There is a lack of detailed data on AP in New Zealand. Whilst it has been reported that mortality rate vary between 8% and 21% for AP outbreaks at various locations nationwide, there are no reports of average mortality rates, incidence of AP, recovery rates or the rate at which AP develops into CNP. However, due to the sporadic nature of such outbreaks this information may be difficult to obtain. CNP prevalence has been estimated in various studies. Particularly high prevalence was reported from two farms in the Hawkes Bay in November in three month old lambs of 80% and 93% (McGowan et al., 1978). The prevalence of CNP tends to decrease from the North of the North Island to the South of the South Island. This has been demonstrated in two studies. The reasons for this are unclear although one would suspect it to be related to climate. Another possible explanation is that it is related to farm management or predominant sheep breed. The study of Goodwin et al. (2004) selected flocks with a history of pneumonia. The study of Black (1997) included all flocks supplying lambs ($n = 9,400$) to seven slaughter houses nationwide, however, the period only covered two months. There is no information of CNP prevalence across the wider population of sheep to indicate averages and extremes of prevalence. The temporal pattern of CNP based on processing plant data has not been established, probably due to it not being routinely recorded. Collection of this information would be valuable to indicate how widespread CNP is. Farmers realise that pneumonia is a problem that leads to reduced productivity of lambs. Their needs are focused on the development of control strategies for the disease in the absence of an effective vaccine. Currently there is no feedback to farmers on the pneumonia status of lambs.

2.5 Economic loss due to pneumonia and pleurisy

2.5.1 The effect of pneumonia on growth rate

In New Zealand, three studies have evaluated the effect of chronic pneumonia on lamb growth rate. One of these involved experimentally induced pneumonia (Alley, 1987b) and the other two involved the naturally occurring disease under field conditions (Kirton et al., 1976; Goodwin et al., 2004).

In the Hawkes Bay, Kirton et al. (1976) showed an association between pneumonia at slaughter and live-weight gain under field conditions of 3,243 lambs born in a flock over a

five year period. The study design was restricted by sample size (one farm) making it difficult to extrapolate results to the national lamb population. However, moderate and severe pneumonia reduced carcass weight on average by 0.45 kg per lamb. The average carcass weight of lambs excluding those with moderate to severe pneumonia was 12.4 kg. If lambs were slightly heavier than average at weaning they had more extensive pneumonia at slaughter but the authors were unable to explain this finding. The overall pneumonia prevalence was 50.5%. The severity of observed pneumonia was, however, relatively low with 20% mild pneumonia, 6% moderate pneumonia, 0.5% severe pneumonia and 24% parasitic (due to *Dictyocaulus* spp.). The mean growth rate of unaffected lambs was low (45 to 112 g/day, in comparison with 161 to 205 g/day reported by other studies that were conducted at the time (McConnell and Jagusch, 1972; Joyce et al., 1976)). It seems likely there were other factors influencing lamb growth rate masking the effect of pneumonia on growth in the Kirton study. Also, the method of selection (based on weight and condition) of lambs for slaughter would have biased the results of this study in comparison to an unbiased random selection method.

A trial was conducted by Alley (1987a) in the Manawatu involving experimentally induced pneumonia. Live-weight gains and carcass weights of 40 lambs grazed under pastoral conditions were compared with those of a control group. Lambs of 120 days of age were intranasally inoculated with homogenised pneumonic lung derived from cases of naturally occurring CNP. At 30 days post-inoculation pneumonic lambs weighed on average 1.74 kg less than the controls. At 60 days post-inoculation, this difference was 2.19 kg. Carcass weights of pneumonic lambs were reduced on average by 1.5 kg over the 60-day period, 1.39 kg of which occurred in the first 30 days. No confidence intervals were presented for this study nor was the standard deviation of the reduction in carcass weight. Excluding sheep with healthy lungs from the inoculated group and excluding sheep with pneumonic lungs from the control group, provided a more accurate estimation of the effect of pneumonia. A significant correlation was found indicating that under good pasture growing conditions pneumonic animals could be expected to show a reduction of 0.8 kg per month for every 10% of lung area affected with pneumonia. Under drier weather conditions (30 to 60 days post-inoculation) the reduction in growth rate was 0.9 kg per month per 10% pneumonic lung area, probably due to a lower growth rate in all lambs due to a reduction in the quality and quantity of pasture available. Therefore, the effect of pneumonia on growth may be more severe under conditions of nutritional stress.

However, experimentally induced pneumonia may not replicate the disease in its natural state. The external validity (ability to make inference about the underlying population from this sample) of this study could, therefore, be questioned.

A similar effect of pneumonia on lamb growth rate was found under field conditions in three regions of New Zealand by Goodwin et al. (2004). Daily weight gain in the month prior to slaughter was reduced in randomly selected lambs where, at the time of slaughter $\geq 20\%$ lung surface area was affected by pneumonia. Although the study of Alley (1987a) was investigating experimentally induced disease, the reduction in growth rate due to pneumonia was comparable with the study of Goodwin et al. (2004). Lambs with pneumonia grew 65.5 g/day slower than control lambs (Alley, 1987a), similar to the 71 g/day reduction observed by Goodwin et al. (2004). Lambs in the latter study experienced a similar prevalence and severity of pneumonia as in a Scottish study of Jones et al. (1982), where pneumonic lambs grew at 70 g/day less compared with control lambs. The Scottish study was conducted on housed lambs comparing experimentally induced pneumonia with controls (Jones et al., 1982).

2.5.2 Pleurisy

At slaughter, lamb carcasses with pleural lesions are typically identified by meat inspectors and detained for trimming. In severe cases, trimming may involve part or all of the rib cage. The carcass is then re-inspected by a meat inspector and railed back into the production line.

Pleurisy is not a known public health risk, but a carcass may be downgraded if it has been detained and required removal of the rib cage due to pleurisy. Most lamb exports from New Zealand are in the form of carcasses boned into cuts, therefore, a carcass that has been trimmed due to pleurisy is devalued because the rib cage (lamb racks) is not at a suitable standard for human consumption. Our major lamb export markets (Europe, United States and Asia) currently have no specific restrictions regarding pleurisy as the New Zealand standard for post-mortem inspection is accepted by the regulatory authorities in these countries.

The financial cost of pleurisy to the meat industry is substantial through an increased workload in identifying and trimming pleural lesions in carcasses at slaughter. In addition, carcasses downgraded due to pleurisy reduce the price received by the farmer.

2.5.3 Mortality

Mortality due to AP is a source of economic loss to New Zealand farmers. Mortality rates in New Zealand have been reported between 8% and 21% with variation between seasons and individual farms (Smith, 1975; Anonymous, 1976; Sorenson, 1976; Anonymous, 1978; Davies, 1986; Orr and Black, 1996; Orr et al., 1998; Clark et al., 2001). However, these mortality rates are reported from flocks with mortality due to AP only, with little known of AP incidence or mortality attributable to AP across the wider sheep population.

2.5.4 Economic losses at the industry level

No specific economic models have been developed to estimate the cost of pneumonia to farmers or the meat industry. While an estimate of the direct cost of pleurisy to New Zealand farmers was given 29 years ago at \$1.8 million (Dysart, 1976), it is not currently applicable due to changes in lamb prices and pleurisy prevalence. For the 2002/2003 season, the national average pleurisy prevalence was 8.7% (ASURE New Zealand Ltd., P.O.Box 1141, Christchurch). Assuming this prevalence was constant throughout the country, that 65% of lambs with pleurisy end up in cutter grades (Dysart, 1976), an average lamb price of \$60 per head, a loss of \$18 per carcass if pleurisy cutter grades are incurred (S. Brown, personal communication) and 23.8 million lambs were killed, as in 2004 (MAF, 2005), the direct loss to the New Zealand farmer in 2002/2003 due to lamb pleurisy would be in the order of NZ \$24 million (US \$15 million). The economic loss due to pneumonia is more difficult to estimate.

CNP reduces the growth rate of lambs (Kirton et al., 1976; Jones et al., 1982; Alley, 1987a; Goodwin et al., 2004) leading to reduced lamb productivity and a subsequent economic loss to the farm. In order to reach target slaughter weights, lambs with pneumonia stay on the farm longer resulting in increased inputs and costs (pasture, labour, animal health treatments). This also leads to reduced returns due to target slaughter weight not being reached, or a decrease in lamb prices, as tends to occur later in the season.

The financial cost associated with pleurisy is mainly a result of increases in workload at the processing plant due to trimming and additional inspection before the carcass goes back into the production line. There is also a cost to farmers where carcasses are devalued due to trimming of pleural adhesions. Mortality causes direct financial loss to farmers through lamb mortality which may be between 8% and 21% in individual cases. However, little information is available on how often these outbreaks occur in individual flocks and the proportion of the remainder of the flock affected. Economic losses due to pneumonia (AP or CNP) have not been quantified.

2.6 Causes

Pneumonia is a disease of complex aetiology, involving interactions between a range of microorganisms (bacteria, viruses, mycoplasmas), the immunological and physiological responses of the host (Bruere et al., 2002), and environmental effects. Pneumonia develops when antibacterial defence mechanisms of the lung break down and bacterial proliferation occurs (Bruere et al., 2002). Stress and/or infections with viral or primary bacterial agents reduce the innate pulmonary immune barriers leading to infection (Brogden et al., 1998).

2.6.1 Pathogens of pneumonia

The list of possible aetiological agents for CNP and AP is identical. Pneumonia in sheep is commonly associated with *Pasteurella haemolytica*, *Pasteurella multocida*, *Mycoplasma ovipneumoniae*, *Mycoplasma arginini* and parainfluenza virus type 3. A wide range of micro-organisms, in addition to those cited, have been isolated from affected lungs.

Bacteria

Pasteurella (Mannheimia) haemolytica is thought to be an opportunistic pathogen incapable of inducing disease in the absence of a mild respiratory virus infection (Davies et al., 1980a; Davies, 1985a; Brogden et al., 1998). The organism can be isolated as a harmless commensal from the upper respiratory tract of lambs (Davies, 1987). A breakdown of barrier integrity at any level may release *P. haemolytica* from its usual commensal status in the nasopharynx and allow it to colonise and proliferate throughout the upper respiratory tract and induce tissue damage in the lung (Brogden et al., 1998).

P. haemolytica, *P. multocida* and *Escherichia coli* are the most common bacterial isolates from AP and CNP cases world-wide (Table 2.4).

Table 2.4: Bacterial isolations from cases of ovine pneumonia.

Bacteria	Countries	Reference
<i>Acholeplasma laidlawii</i>	India, Germany	(Banerjee et al., 1979; Bocklisch et al., 1989)
<i>Arcanobacterium pyogenes</i>	Nigeria, New Zealand	(Alley, 1987b; Obasi et al., 2001)
<i>Bordetella bronchiseptica</i>	USSR, New Zealand	(Khamadeev et al., 1983; Cullinane et al., 1987)
<i>Corynebacterium equi</i>	Nigeria	(Addo and Dennis, 1977)
<i>Corynebacterium pyogenes</i>	Spain	(Loizelier, 1975)
<i>Corynebacterium</i> spp.	Iran	(Tabatabayi et al., 1992)
<i>Escherichia coli</i>	Nigeria, India, Australia, New Zealand	(Kapur et al., 1974; Alley, 1975; St. George and Carmichael, 1975; Ikede, 1978; Alley, 1987b; Obasi et al., 2001)
<i>Klebsiella</i> spp.	Nigeria, Australia	(St. George and Carmichael, 1975; Ikede, 1978)
<i>Neisseria catarrhalis</i>	Nigeria, New Zealand	(Alley and Marshall, 1970; Alley, 1975; Obasi et al., 2001)
<i>Pasteurella haemolytica</i>	New Zealand, Norway, Spain, Germany, Spain, Turkey, Nigeria, Hungary, Australia, Iran	(Salisbury, 1957; Alley and Marshall, 1970; St. George and Sullivan, 1973; Alley, 1975; Loizelier, 1975; Thurley et al., 1977; Ikede, 1978; Bakke, 1982; Bocklisch et al., 1987a; Bocklisch et al., 1987b; Bocklisch et al., 1989; Alley, 1991; Tabatabayi et al., 1992; Hazirolu, 1994; Bouljihad and Leipold, 1995; Miklos, 1999)
<i>Pasteurella multocida</i>	Germany, Spain, Nigeria, USSR, Australia, Iran, New Zealand	(St. George and Sullivan, 1973; Shegidevich et al., 1983; Bocklisch et al., 1987a; Bocklisch et al., 1987b; Bocklisch et al., 1989; Tabatabayi et al., 1992; Bouljihad and Leipold, 1995; Black, 1997; Obasi et al., 2001)
<i>Spherophorus necrophorus</i>	Spain	(Loizelier, 1975)
<i>Staphylococcus</i> spp.	Nigeria, New Zealand	(Alley, 1975; Ikede, 1978; Alley, 1987b)
<i>Streptococcus</i> spp.	Spain, Iran, New Zealand	(Loizelier, 1975; Alley, 1987b; Tabatabayi et al., 1992)
<i>Streptococcus pyogenes</i>	Nigeria	(Obasi et al., 2001)

Eleven serotypes of *P. haemolytica* biotype A are recognised in New Zealand (Alley, 2002). The most common serotype isolated from pneumonic lungs is A2 (Prince et al., 1985). In New Zealand, *P. haemolytica* serotype A2 was predominant in a survey of pneumonia involving North Island slaughterhouses (Northland, Te Puke (Bay of Plenty), Wairoa (Northern Hawkes Bay), Wanganui) and South Island slaughterhouses (Malborough, Canterbury and Invercargill (Southland)) with A7, A9, A1 and A6 following in order of frequency (Black, 1997). The distribution of *P. haemolytica* serotypes was similar in all locations. The number of pneumonic lungs with *P. haemolytica* was relatively similar at six of the plants but the northernmost plant had a higher number of both *P. haemolytica* and *P. multocida* cases. As a percentage of total *Pasteurella* isolates, *P. multocida* decreased with latitude from 29 out of 92 (32%) in Moerewa (Northland) to 0 out of 70 (0%) in Invercargill (Southland). Three serotypes of *Pasteurella trehalosi* were cultured (Black, 1997). *Neisseria catarrhalis* has also been found to be common in the nasal cavity of sheep in New Zealand and is usually found in association with *P. haemolytica*. It appears to have the ability to colonise the lung in a significant proportion of cases of chronic pneumonia (Alley, 1975).

***Mycoplasma* species**

Mycoplasma ovipneumoniae and *Mycoplasma arginini* are commonly isolated in cases of sheep pneumonia.

In a British study, the combination of *Mycoplasma ovipneumoniae* and *P. haemolytica* serotype A2 experimentally induced a proliferative (atypical) pneumonia in lambs (Jones et al., 1982).

Table 2.5 shows the most common isolates of mycoplasma from cases of ovine pneumonia worldwide. The most frequently isolated mycoplasmas were *M. ovipneumoniae* and *M. arginini* with *M. bovis* and *M. agalactiae* isolated less frequently.

Table 2.5: Mycoplasmal isolations from cases of ovine pneumonia.

Mycoplasma	Countries	Reference
<i>M. ovipneumoniae</i>	Australia, Denmark, Germany, Hungary, Kenya, Norway, Sweden, Turkey, USA, New Zealand	(St. George and Sullivan, 1973; Alley et al., 1975; Alley and Clarke, 1977; Pfeffer et al., 1983; Alley et al., 1999)
<i>M. arginini</i>	Germany, India, Iran, Nigeria, USA, New Zealand	(Alley et al., 1975; Bocklisch et al., 1987a)
<i>M. bovis</i>	Germany	(Bocklisch et al., 1987a)
<i>M. agalactiae</i>	Kenya	(Mohan and Uzoukwu, 1985)
<i>Mycoplasma</i> spp.	USSR	(Khamadeev et al., 1983)

In a New Zealand survey of six to nine month-old lambs slaughtered during autumn, Alley (1975) found that all mycoplasmas recovered from the respiratory tract were isolates of either *M. ovipneumoniae* or *M. arginini*. *M. ovipneumoniae* was recovered from 48% of normal sheep and 70% of pneumonic sheep. *M. arginini* was recovered from 33% of normal sheep and 52% of pneumonic sheep.

Viruses

Viruses are rarely isolated from pneumonic lung tissue although there is serological evidence for their presence in flocks when the prevalence of pneumonia is high (Davies et al., 1982). Experimental investigations have shown that *P. haemolytica* can proliferate in the lung following infection with a number of different viruses and give rise to pneumonia. It is usually cleared rapidly from uninfected lung and few lesions develop (Davies et al., 1981). After any one of a series of virus infections that pass through a lamb flock *P. haemolytica* proliferates in the nose and can spread to the lung (Davies et al., 1983), impairing the ability of the lung to clear the bacteria.

In New Zealand, Parainfluenza type 3 (PI₃) is suspected to be involved in many outbreaks of pneumonia although adenoviruses may also be involved (Davies et al., 1980a). Two New Zealand studies (Davies et al., 1980a; Pfeffer et al., 1983) focused on antibodies to viruses and a relationship was shown between antibody titres and pneumonia prevalence. Davies et al. (1980a) investigated the pattern of antibody titres to adenovirus and PI₃ virus.

Four farms were studied in the Hawkes Bay where serum samples from groups of 11 to 14 lambs on each farm were collected monthly from August 1976 (when lambs were 1 to 3 weeks old) to July 1977 (when lambs were 45 to 47 weeks old). Antibody titres against adenovirus decreased steadily from August to April, followed by an increase until July. The frequency of new infections was the highest in April and May (Table 2.6). Antibody titres decreased steadily against PI₃ from August to February, followed by an increase until July. The frequency of new infections was the highest from March to April. Although no causal relationship could be established from this study, serological evidence of infection with PI₃ in flocks A and B was temporally related to high pneumonia prevalence in slaughtered lambs (Table 2.6). However, high pneumonia prevalence was observed in lambs slaughtered at the time of, or shortly after, evidence of flock infection with an adenovirus. The study suggests that adenovirus and PI₃ viruses may play an important role in the development of pneumonia.

Table 2.6: Relationship between virus infections and prevalence of pneumonia (Davies et al., 1980a).

Month	Farm A			Farm B			Farm C		
	New infections*			New infections*			New infections*		
	PI ₃	AV	Pn	PI ₃	AV	Pn	PI ₃	AV	Pn
Nov	0	0	-	0	0	-	0	0	1.1
Dec	0	0	4.3	0	0	7.0	0	0	3.0
Jan	0	0	-	0	0	-	0	0	-
Feb	1	0	9.9	10	0	8.3	0	0	1.8
Mar	12	0	24.8	1	5	-	3	0	-
Apr	1	2	-	0	6	32.2	10	1	-
May	0	8	-	0	0	-	0	7	9.4
Jun	0	1	22.8	0	0	39.2	0	5	-

* Number of animals with a rise in antibody titre to ≥ 1.2 . The same 14 lambs on farm A, 11 lambs on farm B and 13 lambs on farm C were examined each time

PI₃ – parainfluenza virus type 3

AV – adenovirus WV 757/75

Pn – pneumonia, percentage of slaughtered lambs with pneumonia

In the study by Pfeffer et al. (1983), involving one flock in the Hawkes Bay, the prevalence of large pneumonic lesions (CNP) detected at slaughter was associated with isolations of microorganisms. Large lesions contained significantly more *P. haemolytica* and *Mycoplasma* spp. than did small lesions or normal lungs. Prevalence of mottled lesions in the anterior lobes was low but peaked in January and May, associated with adenovirus infection and elevation of *P. haemolytica* and *Mycoplasma* spp. infection. Most lambs were infected by PI₃ between January and February and adenovirus (strain WV 757/75) between March and June. The average antibody titre to *P. haemolytica* increased by more than ten-fold between December and January and was accompanied by an increase in pneumonia. Figure 2.3 gives an illustration of this study. The pneumonia prevalence appears to follow a similar trend to nasal infection with *P. haemolytica*, however, no causal relationships can be definitively identified from this study.

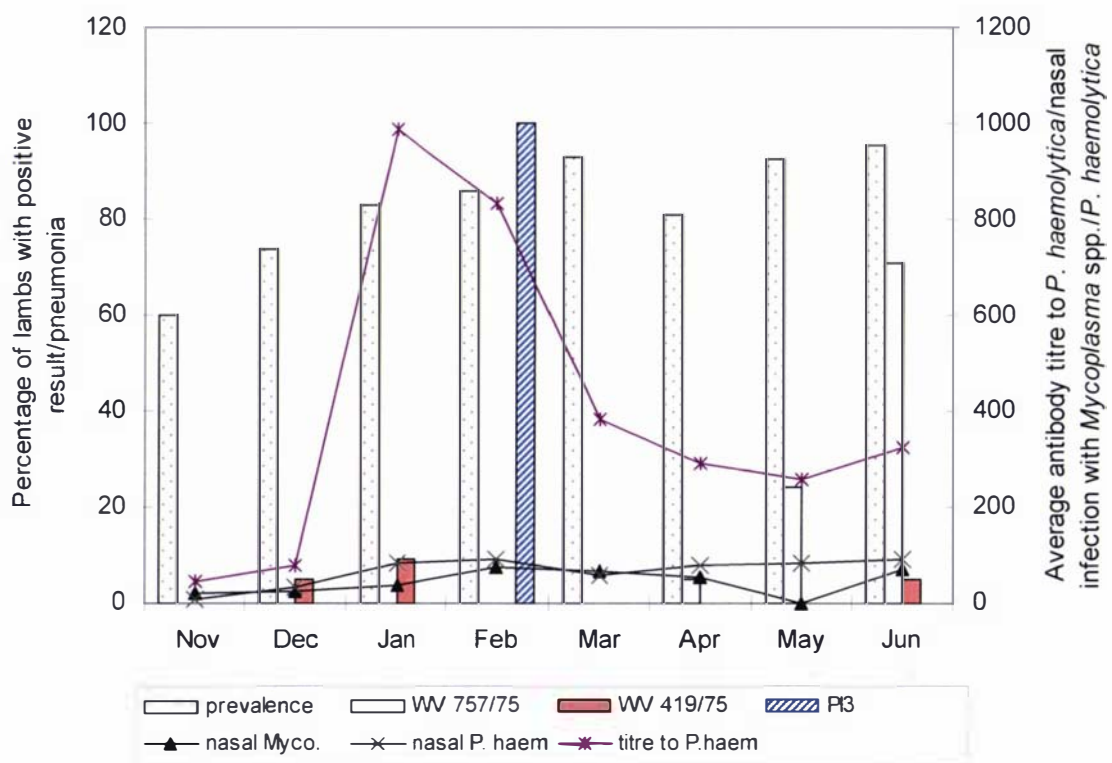


Figure 2.3: Isolation of adenovirus (WV 757/75, WV 419/75) and parainfluenza type 3 virus (PI₃) in the surveillance group of lambs, nasal isolation of *Mycoplasma* spp. (Nasal Myco.) and *P. haemolytica* (Nasal P. haem), average haemagglutinating antibody titres to *P. haemolytica* (titre to P. haem) and pneumonia prevalence (prevalence) at slaughter in random groups of lambs (adapted from Pfeffer et al. (1983)).

Viruses that have been isolated from lamb pneumonia cases in New Zealand include ovine adenovirus type 6, parainfluenza type 3 virus, bovine adenovirus type 7, respiratory syncytial virus and unidentified cell-associated agent with parainfluenza type 3 virus being the most common. Viruses are not isolated as frequently as bacteria or mycoplasmas from sheep pneumonia cases. It is thought that virus infection compromises innate defence mechanisms through epithelial damage, allowing invasion of other (often bacterial) opportunistic pathogens.

The initial site of infection for the main pathogens of pneumonia (*Pasteurella* spp., *Mycoplasma* spp. and PI₃ virus) is the upper respiratory tract (Baskerville, 1981). Transmission of infectious material between sheep is thought to be through aerosol spread. Pneumonia that has been experimentally induced through nasal inoculation of pneumonic lung homogenate is pathologically indistinguishable from naturally occurring disease (Alley and Clarke, 1979, 1980).

Summary

Pasteurella haemolytica and *P. trehalosi* are commonly isolated from cases of pneumonia in New Zealand sheep. *Neisseria catarrhalis* was suggested to have the ability to colonise the lung in a significant proportion of CNP in 1975, although no studies have investigated the role of this bacterial agent or isolated this bacteria from pneumonic cases since. *Mycoplasma ovipneumoniae*, *M. arginini* and parainfluenza virus type 3 are also common pathogens of pneumonia in New Zealand. Two field studies conducted in the 1980's investigated antibody levels and infection with microbial pathogens along with pneumonia prevalence (Davies et al., 1980a, Pfeffer et al., 1983). Although causality could not be established from these studies, they demonstrated temporal associations between infection and lamb pneumonia prevalence. A limitation of the study of Davies et al. (1980a) was infrequent monitoring of the pneumonia status of lambs. Some months were not monitored, resulting in missing information for the temporal pattern of pneumonia prevalence. In the study of Pfeffer et al. (1983), lambs were slaughtered at random every month in order to establish temporal pneumonia prevalence. The study design adopted by these authors eliminated any of the selection bias that may have been present in the study of Davies et al. which provides a better representation of the whole flock. This may be the reason why the prevalence in the Pfeffer et al. study is markedly higher. These two studies are now 22 to 25 years old. More recent studies may be required to establish the current

situation using the study design of Pfeffer et al. (1983) utilising several flocks across different regions.

2.6.2 Host

Age of the host

In the majority of cases, age at onset of CNP is the first summer of life, mostly in lambs which are 5 to 10 months old (Alley, 2002). It is thought to coincide with the period of high susceptibility to microbial infection during the time when passive immunity is waning. In a British study, colostrum derived antibodies to *Mycoplasma ovipneumoniae* and *Mycoplasma arginini* declined to minimum levels at 50 days old (Jones et al., 1979). In this study, the decrease of passive immunity and build up of active immunity to *M. ovipneumoniae*, *M. arginini* and PI₃ virus was associated with increased incidence of respiratory disease.

AP has been reported in all ages of sheep although lambs appear to be the most susceptible. The earliest record of sheep pneumonia in New Zealand was in adult sheep in the Otago and Southland districts, termed "Southland Pneumonia" (Gilruth, 1900). In the published literature since 1955, most surveys and reports indicated that lambs and hoggets were the predominant age group of affected sheep (Hartley and Boyes, 1955; Hartley and Kater, 1964; Porter, 1970; Smith, 1975; Anonymous, 1976; Sorenson, 1976; Anonymous, 1978; Davies, 1986; Allen, 1987; Sutherland, 1987; Davis, 1989; Wakelin, 1989; O'Hara, 1994; Orr, 1995; Orr and Black, 1996; Orr et al., 1998; Smits et al., 1998; Gill, 1999; Clark et al., 2001; Fairley et al., 2002). Rodger (1989) noted that ewes at lambing and lambs in the first months of life were particularly susceptible to AP, although no field-based evidence was provided to support this.

Breed

Studies investigating the susceptibility or resistance of individual breeds of sheep to pneumonia are lacking. As temperature is considered to be a risk factor for the disease it is worthy of note that Merinos are more heat tolerant than British breeds (Brown, 1974; Carles, 1983). This may be a key factor reducing their susceptibility to pneumonia for which there has been some anecdotal evidence (R. Jackson, personal communication).

Defence mechanisms

In the respiratory tract, several defence mechanisms exist to protect the animal against microbial colonisation and infection. These include the mucociliary apparatus, surfactant and surfactant proteins, alveolar macrophages and an intact epithelium (Fales-Williams et al., 2002).

The activity of the mucociliary apparatus reduces the ability of microbes to adhere and proliferate within the airways of the respiratory tract. Within the secreted mucinous and serous fluids of the airways are factors that inhibit microbial activity. These include lactoferrin, lysozyme, surfactant proteins, phospholipase A2, secretory leukoprotease inhibitor, peroxidases, bactericidal permeability-inducing factor, lysozyme, serprocidins, cathelicidins, defensins and anionic peptides (Ganz and Weiss, 1997).

Innate pulmonary defence mechanisms may be compromised due to stress or initial infections with viral or primary bacterial agents (Brogden et al., 1998). Within hours after infection, the bronchi, bronchioles and alveoli contain dense infiltrates of neutrophils, fibrin, seroproteinaceous fluid and blood. The exudate is associated with extensive parenchymal necrosis caused by bacterial toxins such as leucotoxin, lipopolysaccharide and polysaccharide and also inflammatory factors released by neutrophils and other cells of the acute inflammatory process. Neutrophil constituents that potentially contribute to the tissue damage include enzymes, oxidative radicals, cytokines and chemokines (Ackermann and Brogden, 2000).

In the lung, mast cells orchestrate both the inflammatory and immune responses (Abraham et al., 1997). They produce compounds and cytokines necessary to mount the acute phase of the inflammatory response. They phagocytose bacteria and present antigens to immune cells (Abraham et al., 1997). During the acute inflammatory response in the lung, mast cells are required to stimulate neutrophil infiltration and bacterial clearance (Abraham et al., 1996). They also contain proteases and growth factors that make them an important component in inflammatory responses such as chronic lung diseases (Inoue et al., 1996; Cairns and Walls, 1997).

Influences of stress on immune function

Physical and psychological stresses are capable of altering immune function in animals (Kelley, 1980, 1982, 1984; Albani-Vangili, 1985; Kelley, 1985; Siegel, 1985; Blecha, 1988; Minton et al., 1992; Minton, 1994). It has been accepted that stress plays an important role in the development of pneumonia which may be due, in part, to alterations in immune function. Roth and Flaming (1990) listed potential causes of immunosuppression as follows:

- Stress.
- Viral infection.
- Inadequate nutrition.
- Hormonal fluctuations.
- Exposure to environmental toxins.
- Sub-optimal immune function in very young and old animals.

Events associated with stress alter immune function through an increased secretion of glucocorticoids, endorphins, enkephalins and catecholamines. These compounds can directly alter host defence mechanisms (Roth and Flaming, 1990). Glucocorticoids stimulate gluconeogenesis and reduce inflammatory and immunological responses (Griffin, 1989). Endorphins (Gilman et al., 1982; Johnson et al., 1982) and enkephalins (Johnson et al., 1982) alter humoral or cellular immune reactivity.

There are two distinct behavioural responses to stress (Engel, 1967):

1. Flight; as a result of physiological changes due to production of catecholamines by the sympathetic-adrenal medullary system (Axelrod and Reisine, 1984).
2. Conservation, withdrawal reaction; as a result of the failure of the sympathetic-adrenal medullary system to resolve stress. This activates the hypothalamic-pituitary-adrenal cortical response (conservation, withdrawal reaction). Persistence of this response causes biological changes which may produce a pre-pathological state increasing the animals susceptibility to disease (Kagan and Levi, 1974).

The conservation, withdrawal reaction, through stimulation of the anterior hypothalamus, results in the production of CRF (corticotrophin releasing factor) and stimulates the anterior pituitary gland secretion of ACTH (adrenocorticotropins) (Harris, 1948).

The production of ACTH stimulates production of glucocorticoids (cortisol, cortisosterone) with the above mentioned effect on gluconeogenesis and the inflammatory and immunological systems.

It is generally recognised that environmental or management-associated stressors activate the pituitary-adrenal axis and that such stressors may result in reduced immunological function in animals (Coppinger et al., 1991). The effect of restraint and isolation stress was tested in groups of six lambs (Coppinger et al., 1991). The results showed that repeated application of a stressor repeatedly activated the pituitary-adrenal axis, but the ability of the adrenal gland to secrete cortisol was reduced by subsequent application of the stressor. The repeated application of restraint and isolation stress reduced some measures of T-lymphocyte function whereas single application of a stressor failed to alter immune function. Consequently, 'one-off' management or environmental stressors to which farm animals are exposed may not be sufficient to alter immunological function (Coppinger et al., 1991), although this has not been investigated in any depth.

There are few documented reports implicating management stress in increased disease susceptibility in domestic species (Axelrod and Reisine, 1984; Henry and Stephens-Larson, 1985). This is most likely due to the complex interplay between factors such as exposure to infectious agents and host response to infection. However, what is known about the effect of stress on the secretion of hormones from endocrine glands and the consequential effect on the immune system would lead to the conclusion that management stress must play a role in an animal's susceptibility to disease.

Influences of nutrition on immune function

The essential nutrients of the sheep's diet include energy (fat and carbohydrates), protein, vitamins and minerals. The nutritional status of an animal may influence the outcome of an infection. A low plane of nutrition may also impose stress on the animal with additional consequences for immune function as discussed above.

Energy and protein

In New Zealand, where sheep are predominantly pasture fed, energy is often the most important limiting nutrient in the diet. Inadequate dietary energy results in decreases in

production, reproductive failure, increased mortality rates and increased susceptibility to disease and parasites (Giminez, 1994).

Dietary protein provides amino acids which are required for maintenance of vital functions, reproduction, growth and lactation. Protein deficient diets may adversely affect immune responses of young, growing animals (Reddy and Frey, 1990).

Vitamins

Vitamins are necessary for normal growth, health and reproduction. Vitamin E has been shown to provide some degree of protection against disease through enhanced antibody titres and improved recovery from disease (Stephens et al., 1979; Tengerdy et al., 1983; Afzal et al., 1984; Reffett et al., 1988). Recent research of this effect is lacking. Diets deficient in Vitamin E may increase susceptibility to infection. The recommended level of Vitamin E in the diet is 15 International Units (IU) of Vitamin E Activity per kg of dry matter (National Research Council, 1985). The IU is defined as 1 mg of *dl*- α -tocopheryl acetate which has the biopotency of 1.5 IU of vitamin E activity. The recommendations for Vitamin E assume that dietary selenium levels are >0.05 ppm (National Research Council, 1985). Vitamin E and Selenium are integral parts of the antioxidant system present in most mammalian cells (Hoekstra, 1975) and can spare each others requirement in the diet (Mateos et al., 2005).

Macro-minerals

Macro-minerals (e.g. Ca, P, Mg, K, Na and Cl) are required in relatively large amounts in the diet. Dietary deficiencies of minerals are known to cause disease or limit productivity and can also limit the ability of the immune system to respond to antigens and potentially, deal with pathogens (McClure, 2003). Mineral requirements for production have been estimated but little work has been done on any additional requirements for immunity.

Trace elements

Trace elements are those elements required by sheep in small quantities to ensure adequate immune responses, reproduction and growth. Trace element status can influence immune function directly, but also indirectly by modulating plasma levels of hormones that regulate the development and function of host defence cells (Munoz, 2005). Selenium (Turner et al., 1985; Jelinek et al., 1988), copper (Wiener and Field, 1969; Whitelaw et al., 1979; Jones and Suttle, 1981; Yeoman, 1983; Wiener et al., 1985; Suttle and Jones, 1986) and

cobalt (Downey, 1966; MacPherson et al., 1976) more specifically have been shown to influence function of the immune system. Toxicity, however, is also possible with these elements and leads to various health issues; and in severe cases, death (Ministry of Agriculture and Food, 2003). Requirements of these nutrients for sheep are, selenium 0.1–0.2 parts per million (ppm), copper 7-11 ppm (Ministry of Agriculture and Food, 2003), cobalt 0.1–0.2 ppm (Salt Institute, 2001). Selenium is deficient in approximately 30% of areas used for farming in New Zealand and supplements are routinely given to livestock to prevent deficiency (Grace, 1995b). Cobalt is deficient in about 13% of New Zealand farmland (Grace, 1995a) and large areas of New Zealand have soils which are either low in copper or have other chemical elements that interfere with copper absorption (Fleming, 2003b). Deficiency of these nutrients may affect immune function in some areas of the country when supplementation is not provided.

2.6.3 Environment

Temperature, humidity and inclement weather have all been implicated as risk factors for sheep pneumonia. Heat and temperature variation have been indicated as predisposing factors in the development of the disease (Knowles et al 1995). Specifically, cold temperatures have been shown to increase the susceptibility of animals to respiratory infection by *P. haemolytica* (Diesel et al., 1991). It is thought that AP outbreaks tend to be associated with a period of stress which may often involve hot, dry conditions (Bruere et al., 2002). Panting and mouth-breathing (which results in inhaled air bypassing defence mechanisms in the nose) during mustering and yarding in hot, dusty conditions can aid the establishment of pathogens such as *P. haemolytica*, especially if the respiratory tract defences have already been compromised by viral or mycoplasmal infections (Bruere et al., 2002).

In Northern Ireland, rainfall and the windchill factor were found to be highly correlated to pneumonic and pleuritic lung condemnations in sheep at slaughter (McIlroy et al., 1989). McIlroy et al. (1989) showed that the prevalence of pleuritic and pneumonic lesions in sheep at slaughter was associated with rainfall and windchill factor at the time of slaughter, or one or two months earlier. No specific explanations or hypotheses were proposed for this phenomenon, only that adverse weather conditions are important precipitating stress factors for the occurrence of pneumonia. It is difficult to relate these findings to the New

Zealand situation, as the rain and windchill factor through our late summer and autumn period, when pneumonia is at its peak, is not likely to be high as it is in the United Kingdom. This is in contrast to the peak of pneumonia in the United Kingdom and continental Europe, which is in the late winter and early spring period (Alley, 1991).

2.6.4 Summary

Respiratory disease in sheep is caused by a complex interplay of several factors including microbial agents, host factors and the environment. CNP development in lambs often coincides with the decline of colostrum derived antibodies and the development of active immunity. However, as there are no live-animal diagnostic tests available in the case of pneumonia the time of disease onset cannot be predicted accurately. AP has been reported in sheep of all ages, but lambs and hoggets tend to be more commonly affected. It has been suggested that ewes at lambing are susceptible as well, but there is no field-based evidence to support this claim. Susceptibility to pneumonia has not been reported to be different between sheep breeds, however, anecdotal suggests that Merinos may be less susceptible. The immune response of the animal to infection can be compromised through stress, the presence of concurrent disease and nutritional deficiencies. Stress alters immune function by triggering increased secretion of hormones from the endocrine system. A study of restraint and isolation stress indicated that 'one-off management events may not alter immune function. However, the effect of routine management events on stress levels, immune function and pneumonia susceptibility has not been thoroughly investigated. Diets deficient in selenium, cobalt or copper may compromise immune function in animals. New Zealand soils are often deficient in these elements, so it cannot be ruled out that this may influence the level of pneumonia on some properties. Further investigation is needed to clarify this. Environment is possibly one of the most important factors influencing the development of pneumonia. AP outbreaks have often been associated with hot dry weather. High humidity is also thought to play a role. Again, this evidence is mostly anecdotal and no studies have been conducted comparing humidity and temperature levels with the pneumonia status of lambs.

2.7 Epidemiology of chronic non-progressive pneumonia and pleurisy

2.7.1 Prevalence, distribution and seasonality

CNP morbidity varies among farms with approximately 30% of slaughtered lambs affected in March and April (Manawatu, New Zealand, refer Figure 2.2) with a range of 5% to 70% lambs affected among CNP positive flocks (Bruere et al., 2002). The course of disease may be several months in duration and resolution can occur during the late autumn or winter months with little permanent lung damage.

In the United Kingdom and continental Europe, peak CNP prevalence is in late winter and early spring, compared with late summer and autumn in Australia and New Zealand (Alley, 1991). The peak period in the UK and Europe may be related to the fact that sheep are often housed over the winter period, facilitating infection of housed animals with pathogenic microorganisms. Kirton et al. (1976) suggested that heavy lambs at weaning were more affected later in life than lambs with average weaning weight. This may be due to the fact that these animals are usually older and, therefore, the first to lose passive immunity, which is thought to coincide with disease onset.

Pneumonia prevalence trials in New Zealand

McGowan et al. (1978) conducted a trial to estimate the prevalence of subclinical pneumonia among lambs on two farms in the Hawkes Bay and Manawatu region of New Zealand (refer Figure 2.2). The prevalence of lesions was recorded at slaughter from lambs selected on liveweight and body condition. A comparison was made with lesions recorded in small lambs (not yet of market size) slaughtered for necropsy.

Table 2.7 shows the pneumonia and pleurisy prevalence of small lambs from the three farms studied (McGowan et al., 1978). All farms had a high prevalence of pneumonia and pleurisy with the exception of Farm A (zero pleurisy recorded). These lambs were apparently healthy young lambs purposively selected, based on their small size and were compared to older market lambs selected for slaughter, based on reaching an appropriate slaughter weight. Any lambs showing signs of clinical illness were not included in this sample. The nomenclature these authors used, of enzootic pneumonia, is equivalent to CNP.

Table 2.7: Prevalence of enzootic pneumonia and pleurisy on necropsy in lambs less than 3 months of age (below slaughter weight) from three New Zealand sheep farms (McGowan et al., 1978).

Farm (Region)	Date	No. of lambs	%EP	%PL
Farm A (Hawkes Bay)	Nov 1975	15	93	0
Farm B (Hawkes Bay)	Nov 1975	15	80	13
Farm C (Manawatu)	Jan 1976	19	78	16

%EP and % PL - Prevalence of enzootic pneumonia and pleurisy expressed as a percentage

Table 2.8 shows the pneumonia and pleurisy prevalence of slaughter lambs on the three farms studied. The results showed that the overall pneumonia prevalence of small lambs was high compared with older market lambs originating from the same farms. No estimate of age was given for these market lambs. The method of selecting these lambs would potentially result in selection bias resulting in pneumonia and pleurisy levels that misrepresent the whole flock. These market lambs were purposively selected on body weight and condition, selecting against smaller, slower-growing lambs, which may have been more adversely affected by pneumonia.

Table 2.8: Prevalence of enzootic pneumonia and pleurisy at time of slaughter in market lambs from three New Zealand sheep farms (McGowan et al., 1978).

Farm (Region)	Date	No. of lambs	%EP	%PL
Farm A (Hawkes Bay)	Feb 1976	235	41	3
Farm B (Hawkes Bay)	Nov 1975	273	35	2
	May 1976	233	64	15
Farm C (Feilding)	Feb 1976	253	68	6
	Mar 1976	406	66	7

%EP and % PL - Prevalence of enzootic pneumonia and pleurisy expressed as a percentage

Thurley et al. (1977) reported an abrupt increase in the severity and prevalence of lesions of enzootic pneumonia after January at Wallaceville (Wellington, New Zealand) in 85 lambs. Kirton et al. (1976) demonstrated an average pneumonia prevalence of 60% between 1966 and 1970 at the Ruakura Research Station in Hamilton (Waikato), New Zealand. This included parasitic pneumonia and atelectasis. If parasitic pneumonia

(caused by lungworm) and atelectasis (lung tissue collapse) were removed, the average prevalence of CNP in this group was 26%. The average CNP prevalence for January, February and March was 12%, 24% and 43% respectively.

The prevalence of CNP with lesions greater than 3cm² was determined from slaughtered lambs from three Hawkes Bay farms (Davies et al., 1980a). The peak prevalence occurred from March to June. On Farm C, which had halfbred breeding ewes, there was a markedly lower prevalence of CNP compared with the other two farms. Peak CNP prevalence for farms A, B and C were 24.8%, 39.2% and 9.4% respectively. As mentioned in section 5.1.2, anecdotal evidence suggests that Merinos are less susceptible to pneumonia. The Merino genetics of the lambs from these halfbred ewes may have provided some protection in this case, resulting in a lower CNP prevalence.

In a study conducted in the Hawkes Bay of New Zealand (Pfeffer et al., 1983) between August 1978 and June 1979 lambs selected for slaughter each month were divided into two groups. One group was selected based on commercial selection criteria (selected group) and the other selected randomly regardless of commercial criteria (random group). Another group of 25 lambs was selected to monitor serological responses to viral infections throughout the study period. It was found that the prevalence of pneumonic and pleural lesions and devaluation of carcasses was lower in the selected group compared with the random group. The prevalence of large lesions in the anterior lobes was low in November, increased to peak levels in February, then declined to intermediate levels. The prevalence of large lesions appeared to be negatively related with the average carcass weight of lambs. Only one farm was sampled in this study limiting any inference to the wider population.

A more recent study (Goodwin et al., 2004) evaluated pneumonia prevalence on 14 commercial sheep farms in Northland, the King Country (refer Figure 2.2, Upper Wanganui/Taupo) and Southland regions of New Zealand. The prevalence of moderate to severe pneumonia (affecting > 10% lung surface area) increased from December to March from 1.4% to 10.1% lambs in Southland ($n = 1,917$), 1.2% to 25.7% in the King Country ($n = 1,831$) and 4.7% to 21.4% in Northland ($n = 1,485$) (Figure 2.4). Prevalence of any degree of pneumonia was 21.8% in lambs from Southland ($n = 1,917$), 49.2% from the King Country ($n = 1,831$) and 60.3% from Northland ($n = 1,485$) (Figure 2.4). Such

regional differences may be linked to a variety of factors including climate, location and type of farm. Different genetic lines of sheep, stocking rates, time of lambing and weaning and regional differences in farm management practices may also play a role. No data has been presented for April in Southland, however the interval between the March (23rd) and May (3rd) recordings was 41 days compared with an average interval between the other months of 32 days.

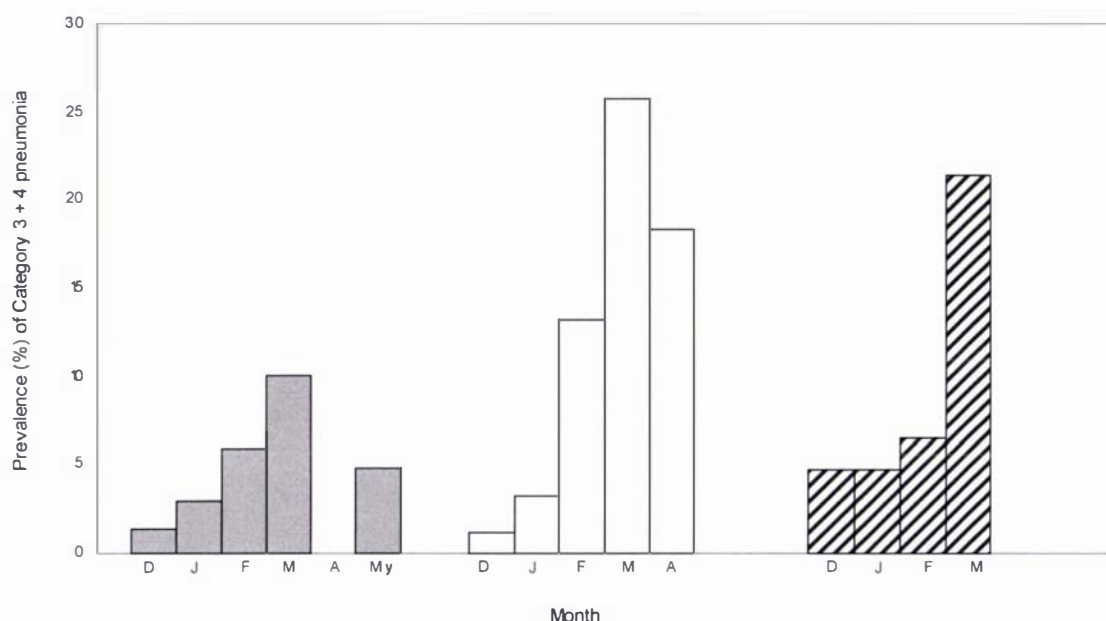


Figure 2.4: Prevalence of lambs with pneumonic lesions classified as Category 3 or 4 ($\geq 10.0\%$ lung surface affected) that were randomly selected for slaughter at monthly intervals (Group I) from Southland (■), King Country (□) and Northland (▨) in December (D) 2000; and January (J), February (F), March (M), April (A) and May (My) 2001 (Goodwin et al., 2004).

Several limitations were present in some of the above studies. Irregular sampling of lambs in the study of McGowan et al. (1978) and Davies et al. (1980a) prevented the conclusive establishment of a temporal disease pattern. Comparison of pneumonia and pleurisy prevalence between market and small lambs was difficult in the study of McGowan et al. (1978), as there was only one simultaneous slaughter date for the two groups. Overall, younger lambs had markedly higher disease prevalence. Alley (1991) suggested that pneumonic lesions may resolve over time. In a study by Gilmour et al. (1982a) involving experimental CNP, indistinguishable from naturally occurring CNP, lesion resolution

occurred after two to three months although some lesions persisted for up to seven months. Higher disease prevalence in the small lambs compared to market lambs in the study by McGowan et al. (1978) could be explained by lesion resolution in market lambs before slaughter. In addition, the small lambs selected may have sustained more extensive lesions, resulting in reduced growth rates, compared with market lambs. This, in turn, leads to bias due to selection of lambs for slaughter based on body weight and condition.

The study by Pfeffer et al. (1983) accounted for the selection bias that may exist when slaughter lambs are sampled. This was achieved by simultaneous selection of a random group and a market group of lambs for slaughter. The study of Kirton et al. (1976) was biased because sampling was only carried out over three months on only one farm. This sampling technique provided an extreme under-representation of the population of farms in this region.

Pleurisy prevalence studies in New Zealand

Most studies that have investigated the prevalence of pleurisy in New Zealand lambs have used processing plant data. This is due to the fact that this information is routinely collected and easily obtainable. The limitation of this, however, is that farm prevalence is not considered, since whole plant monthly figures tend to be the most detailed information published.

Hathaway and McKenzie (1987) recorded higher pleurisy prevalence in the North Island compared with the South Island. The study was conducted in two North Island processing plants (Moerewa (Northland) and Wairoa (Northern Hawkes Bay)) and two South Island processing plants (Smithfield, South Canterbury and Ocean Beach, Otago). Veterinarians and meat inspectors carried out the post mortem inspections of lungs. In the North Island, greater than 27% of carcasses had pleural lesions evident by September, compared with 9% in the South Island. In November, the prevalence of pleurisy in new season lambs was much lower: 1.5% for the North Island group and 0.6% for the South Island group. Chronic pleural lesions were the most dominant pathology observed. The ratios of chronic to acute types of pleurisy indicated that an increased proportion of acute lesions occur in new season lambs.

In the 1974/1975 season, Dysart (1976) reported an incidence rate of pleurisy of 3.2% ($n = 816,700$) in lambs and 19.2% ($n = 1,359,900$) in ewes. The average pleurisy incidence rate in lambs in the North Island was more than twice that of the South Island. Geographical variations followed the same trend in adult sheep, where the South Island average was 16.4% compared with the North Island average of 26.5%. In adult sheep, the pleurisy incidence rates between the two periods of measurement were relatively similar. In lambs, the pleurisy incidence rate in the period October 1975 to December 1975 was markedly lower at all locations compared with the previous period, particularly in the North Island. An assumption was made by Dysart (1976) that 65% of lambs with pleural lesions end up requiring part or all of the rib cage removed in order to pass meat inspection ('cutter grade'). Not all carcasses observed by meat inspectors as having pleurisy when they are processed, end up in cutter grades. This is because often the pleural adhesions can be removed without carcass trimming. The difference in prevalence between the South and North Island could be attributed to regional differences in climate and farm management factors.

More recent data from ASURE New Zealand Limited (P.O.Box 1141, Christchurch), indicated similar pleurisy prevalence for South Island and North Island lambs in the 2002/2003 season. The prevalence of pleurisy was 8.4% for the North Island and 8.9% for the South Island. The seasonal patterns for percentages of lambs with pleurisy at slaughter (for the main lamb slaughter period) in five regions of New Zealand are shown in Figure 2.5. The prevalence increased from December through to July without marked regional variation.

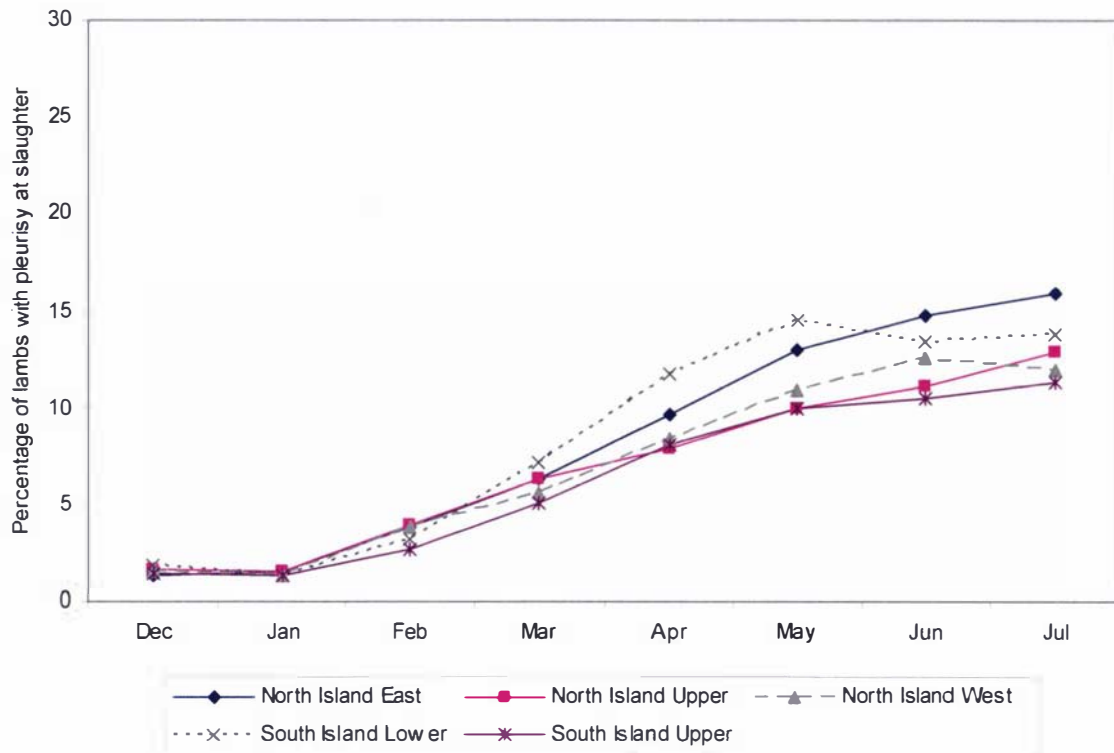


Figure 2.5: Percentage of lambs with pleurisy at slaughter between December and July 2002/2003 in five regions of New Zealand (ASURE New Zealand Ltd., P.O.Box 1141, Christchurch).

Van der Logt (1996), showed a temporal pattern of pleurisy from records of four meat processing plants in four regions of New Zealand (Bluff (Southland), Timaru (South Canterbury), Wairoa (Northern Hawkes Bay) and Moerewa (Northland)). Records from 2.5 million lambs showed that there were considerable geographical and temporal differences in pleurisy prevalence. All regions showed high levels of major pleurisy from June to September, then low levels in November and December, after which the prevalence increased to peak levels in the May to September period (Figure 2.6).

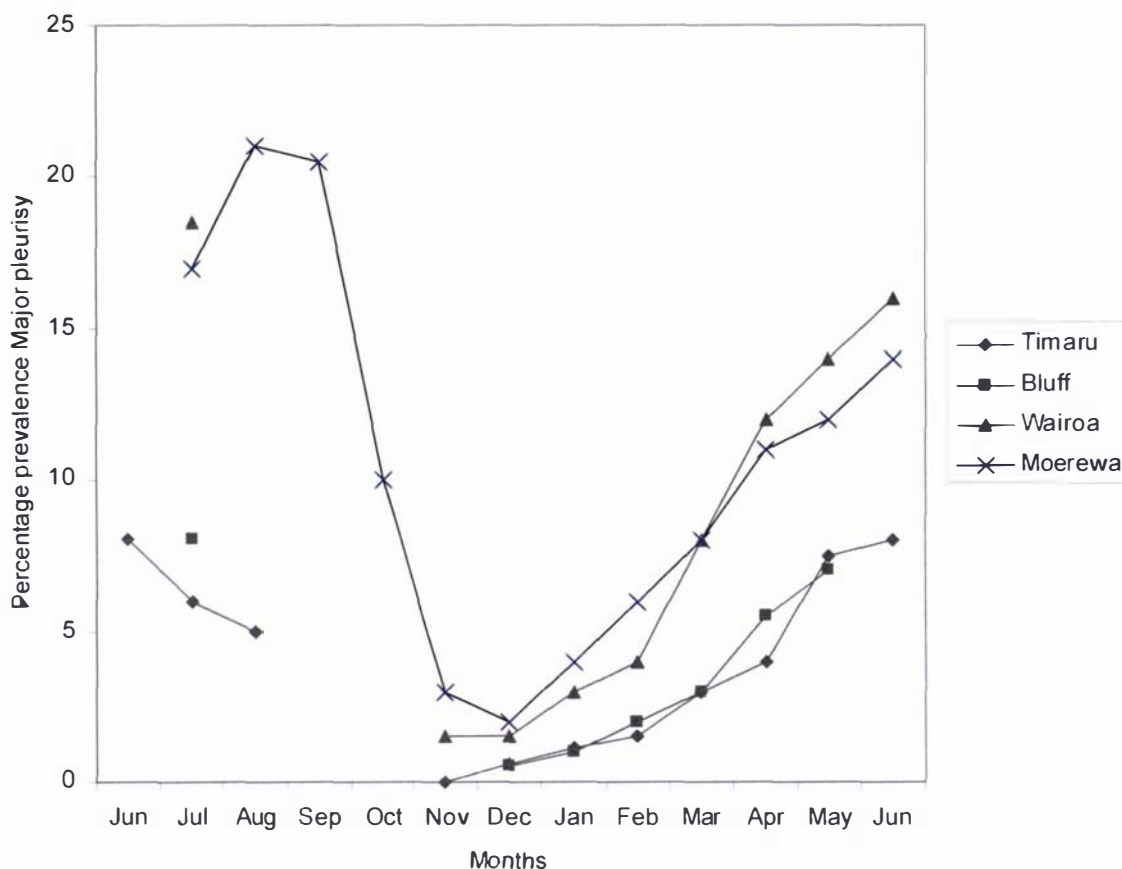


Figure 2.6: Percentage prevalence of major pleurisy at slaughterhouses in Timaru (South Canterbury), Bluff (Southland), Wairoa (Northern Hawkes Bay) and Moerewa (Northland) (Van der Logt, 1996).

Farm level pleurisy prevalence

The observed increase of pleurisy prevalence over the season (Hathaway and McKenzie, 1987, Van der Logt, 1996, ASURE New Zealand Ltd., P.O.Box 1141, Christchurch) has been attributed to the chronic, fibrotic nature of pleurisy lesions. New cases, along with the persistence of older cases, is thought to lead to the steady increase in prevalence through time (McGowan et al., 1978). The only studies that measure and compare pleurisy prevalence on multiple farms are that of McGowan et al. (1978) and Davies et al. (1980a). As mentioned previously, the irregular sampling of lambs and the lack of corresponding sampling dates between farms limits the ability to draw definitive conclusions about the accuracy of temporal disease patterns in these studies. The data is presented in Table 2.9. Farm level prevalence increased during the course of the season. The difference in pleurisy prevalence between farms was thought to be attributable to differences in

pneumonia prevalence. Confidence intervals were not presented in either study, but were able to be derived from the data presented in the study of McGowan et al. (1978). In the study of Davies et al. (1980a), however, confidence intervals were not able to be derived as the number of lambs slaughtered in each month was not presented. No indication of flock size was given in this study either.

Table 2.9: Prevalence of pleurisy at slaughter in market lambs from 3 farms from the studies of McGowan et al. (1978) and Davies et al. (1980a).

Month	Davies et al. 1980			McGowan et al. 1978		
	(% lambs with pleurisy)			(% lambs with pleurisy)		
	Farm A	Farm B	Farm C	Farm A	Farm B	Farm C
November			0.0	0.3	2.0	
December	2.5	0.0	0.3			
January						
February	5.5	2.3	0.0	3.0		6.0
March	12.3					7.0
April						
May			7.2		15.0	
June	22.8	16.3				

2.7.2 Disease dynamics within and between flocks

CNP is a multifactorial problem in sheep flocks. On some farms and in some regions CNP is an ongoing problem, indicating that environmental and host conditions are favourable for maintaining the viability of causative organisms within these farms and regions. In particular, unfavourable conditions include climate (high temperature/humidity), management stress, poor nutrition and other diseases are involved in the aetiology of CNP (Knowles et al., 1995; Adegboye et al., 1996; Cole, 1996; Martin, 1996; Alley, 2002; Bruere et al., 2002). AP has been shown to occur in sporadic outbreaks whereas CNP seems to occur every season in three to ten-month-old lambs (Alley, 1987b, 2002; Bruere et al., 2002). These flocks may be affected to variable degrees between subsequent seasons, depending on conditions.

It is not known to what extent pathogens causing pneumonia are transmitted between sheep. Transmission is thought to occur by direct contact between animals. This is facilitated by management practices when animals are crowded together for prolonged periods, such as during drenching, or when animals are fasted for shearing or crutching. There are many routes by which transmission between farms may occur. The most obvious of these is when animals, purchased from other farms, are brought onto the 'home' farm. This would especially be an issue on farms purchasing young, weaned lambs to fatten in addition to keeping lambs that were bred on the farm. It has been shown in a case-control study that as flock size increases, the risk of pneumonia also increases (Dercksen et al., 1996). It was suggested by these authors that this was due to a more successful maintenance of micro-organisms within larger flocks.

2.7.3 Risk factors for pneumonia and pleurisy

Predisposing factors for AP and CNP

As with AP, stress is thought to be a precursor for CNP, along with conditions that promote cross colonisation, such as the grouping together of animals (Alley, 1987b). Factors isolated by American and European authors as predisposing lambs to pneumonia include:

1. Heat, crowding, exposure to inclement weather, poor ventilation with high levels of moisture, handling and transport (Knowles et al., 1995).
2. Castration and docking, weaning and changes in feed, exhaustion and hunger during transportation (Cole, 1996).
3. High loads of parasites and mixing of animals from different sources (Martin, 1996).
4. Extensive stressful exercise under experimental conditions (Anderson et al., 1991) and cold temperatures (Diesel et al., 1991), have been shown to increase the susceptibility of animals to respiratory infection by *P. haemolytica*.

A risk indicator study of subclinical lamb pneumonia in the Netherlands showed that taking sheep to sheep fairs, the purchase of sheep or lambs, the lack of indoor housing and increases in flock size were associated with an increased risk of chronic pneumonia in lambs (Dercksen et al., 1996). In this study, the response rate to mailed questionnaires was 64% ($n = 550$), of which 57% were complete and suitable for analysis. The nature of a

questionnaire survey implies some limitations with regard to the interpretation of results, as such studies are designed to screen for risk factors rather than prove causation. Such a study provides an insight into events at a particular time and, therefore, suffers from the fact that cause and effect are often difficult to separate (Kelsey et al., 1986). It is often apparent from observational studies that disease incidence increases as herds or flocks get larger (Wittleberg et al., 1994). This may be either a spurious finding, or a consequence of introducing larger numbers of possibly diseased animals from other flocks. Large flocks may also maintain infection longer and be managed in ways that favour the spread of disease, compared with small flocks (Dercksen et al., 1996). A study in Northern Ireland found rainfall and windchill factor to be associated with pneumonic and pleuritic lung condemnations in sheep at slaughter (McIlroy et al., 1989). Dust has also been indicated as a likely risk factor (Davies, 1985b; Bruere et al., 2002). Firstly, there is the physical impact of dust on the respiratory tract, interfering with host defence mechanisms. Secondly, it has been postulated that dust can bind bacterial toxins that may be inhaled by animals (Urbain et al., 1999).

Pneumonia is the most important precursor for the development of pleurisy. Therefore, risk factors for pneumonia are indirect risk factors for pleurisy. Van der Logt (1996) conducted a case-control study that identified a number of risk factors for pleurisy on New Zealand lambs. On-farm factors that were associated with farms having a high prevalence of pleurisy were:

- Drenching animals at a high frequency.
- Shearing twice a year.
- High frequency of yarding after weaning.
- Motorised means of mustering.
- Poor water supply.
- A large number of lambs on the property in July.
- A high stocking density of cattle in contact with sheep.

Protective effects included using either a spray-on dip or a wand for dipping, the use of cement or concrete yards, trough water supply and cross breeding. While this study provides useful insights into factors that are associated with farms having a relatively high prevalence of pleurisy, it should be acknowledged that some (if not all) of the identified factors are simple markers, rather than being causally associated with the disease.

Studies reporting pneumonia prevalence have generally been limited to small geographical areas. They have typically involved small sample sizes. Studies utilising slaughter house data have shown that pleurisy prevalence increases from a low prevalence of 21% in November and December to peak prevalence in May to September (Van der Logt et al., 1995). Earlier studies (Dysart, 1976; Hathaway and McKenzie, 1987), indicated a higher prevalence of pneumonia in the North Island compared with the South Island, however, the most recent nationwide data suggests that the prevalence between the islands is essentially the same (ASURE New Zealand, P.O.Box, Christchurch). Two studies have reported farm-level pleurisy prevalence (McGowan et al., 1978; Davies et al., 1980a). These studies were restricted by irregular sampling of lambs and lack of corresponding dates between farms, limiting comparisons. Also, in the study of Davies et al. (1980a) sufficient detail of the number of lambs slaughtered was not provided in order to derive confidence intervals for prevalence. CNP affects some farms or regions more than others, in contrast to AP, which tends to occur more sporadically. Farms with CNP are thought to have favourable host and environmental conditions allowing the maintenance of pathogens within the flock. Crowding lambs for long periods may increase the risk of pathogen transmission between these animals. Purchasing lambs from other farms is one possible route enabling CNP spread between farms. In Ireland, windchill was a suggested risk factor for pneumonia but is an unlikely risk factor in New Zealand, as CNP occurs most commonly in the late summer and autumn when temperatures are still relatively high (Kirton et al., 1976; Alley, 1991; Goodwin et al., 2004). This is in contrast to the UK where high levels of CNP occur in the late winter and early spring. No case-control studies have been conducted to date that have investigated risk factors for pneumonia in New Zealand. A number of risk factors have been proposed for pneumonia, however, there is very little scientific evidence to substantiate them. This means the role of these factors in the development of CNP is still poorly understood.

2.8 Control of pneumonia

2.8.1 Vaccination

Trials investigating vaccination as a potential tool to control both CNP and AP have been variable. Most available vaccines against *P. haemolytica* A2 have failed to meet efficacy requirements in the field. In many studies that have been conducted a poor immune response to the sero-type specific capsular polysaccharide of *P. haemolytica* A2 has been evident (Gilmour et al., 1979; Gilmour and Angus, 1983; Adlam, 1989; Zamri-Saad et al., 1994). If antigens common to all serotypes were identified a vaccine could be developed to provide better protection.

Sabri et al. (2000) showed that the antibody response of lambs was more specific toward homologous challenge of *P. haemolytica* (e.g. lambs vaccinated and challenged with the same serotype), but generally did not cross-protect against heterologous challenge of *P. haemolytica* (e.g. lambs vaccinated with a different serotype to challenge) (Sabri et al., 2000). A controlled environment is required for challenge experiments with infectious pathogens if vaccine efficacy is to be demonstrated in small groups of fully susceptible experimental animals (Roth and Flaming, 1990). Vaccines that have been evaluated in a controlled environment have generally been successful but efficacy has been questionable in the field due to the varying extent of susceptibility and pathogen challenge. Farmers may regard vaccination as the only solution in controlling this complex disease. However, the prevention of causes other than specific pathogens may have greater benefit in controlling pneumonia in the field than vaccination.

***Pasteurella* vaccines**

Pasteurella vaccines using antigens derived from killed whole bacterial cells, or cell wall extracts, administered with and without adjuvants have been studied (Donachie et al., 1983; Gilmour et al., 1983; Wells and Robinson, 1984; Cameron and Bester, 1986; Donachie et al., 1986b; Jones et al., 1986). Some have been shown to protect sheep against challenge with virulent *P. haemolytica* organisms (Donachie et al., 1983; Gilmour et al., 1983; Wells and Robinson, 1984). *Pasteurella* vaccines are commercially available worldwide, although only one is commercially available in New Zealand at present (Table 2.10).

Table 2.10: *Pasteurella* vaccines commercially available throughout the world.

Vaccine	Country	Antigens	Reference
Ovipast Plus	NZ/UK/Spain	Serotypes of <i>P. haemolytica</i> , <i>P. trehalosi</i>	(Intervet Ltd., 2005; Intervet UK Ltd., 2005b; Laboratorios Intervet S.A., 2005)
Multivax-P	South Africa	<i>Clostridium perfringens</i> type D, <i>C. septicum</i> , <i>C. tetani</i> , <i>C. chauvoei</i> , T serotypes of <i>Mannheimia</i> (<i>Pasteurella</i>) <i>haemolytica</i>	(Intervet South Africa (Pty.) Ltd., 2005)
Ovovac-P Plus		<i>Clostridium perfringens</i> type D, <i>C. septicum</i> , <i>C. tetani</i> , <i>C. chauvoei</i> , serotypes of <i>P. haemolytica</i> and <i>P. trehalosi</i>	(Intervet UK Ltd., 2005c)
Heptavac-P Plus	UK	<i>C. perfringens</i> types B, C and D, <i>C. septicum</i> , <i>C. tetani</i> , <i>C. novyi</i> type B, <i>C. chauvoei</i> , serotypes of <i>P. haemolytica</i> and <i>P. trehalosi</i>	(Intervet UK Ltd., 2005a)
Poly Serum	US	<i>Actinomyces pyogenes</i> , <i>E coli</i> , <i>P. haemolytica</i> , <i>P. multocida</i> and <i>Salmonella</i> <i>typhimurium</i> .	(Novartis Animal Vaccines Inc., 2005)
Ovine <i>P.</i> <i>haemolytica</i> pneumonia vaccine	US	<i>P. haemolytica</i>	(Pipestone Veterinary Supply, 2005)

The following sections summarise experimental and natural challenge trial results of *Pasteurella* vaccines.

***Pasteurella* vaccine trials using experimental challenge**

Several trials have tested vaccine efficacy using *Pasteurella* vaccines on experimentally challenged lambs (Gilmour et al., 1982b; Gilmour et al., 1983; Donachie et al., 1986a; Jones et al., 1986; Chandrasekaran et al., 1991; Sabri et al., 2000). The results of the three most recent trials will be described here. Sample size calculations or the level of statistical power was not provided in any of these three studies.

A Malaysian study investigated the effect of a *Pasteurella* vaccine against experimental challenge in lambs (Chandrasekaran et al., 1991). The vaccine was an oil adjuvant vaccine incorporating strains of *P. haemolytica* type A7 and *P. multocida* types A and D. A single vaccination was administered intramuscularly. Lambs were assigned to three groups according to challenge type. Groups 1 and 3 consisted of two treatment groups each, oil adjuvant vaccine ($n = 5$) and Carovax ($n = 4$) and one control group each ($n = 4$). Group 2 had one treatment group, oil adjuvant vaccine ($n = 5$) and a control group ($n = 4$). The lambs were challenged at 4 weeks post-vaccination. They were given aerosol sprays of; Group 1 - *P. haemolytica* type 7; Group 2 - *P. multocida* type A and *P. multocida* type D and; Group 3 - *P. haemolytica*, *P. multocida* type A and *P. multocida* type D. Lung lesions were significantly reduced compared to the control group when experimentally challenged with *P. haemolytica* alone, but not with *P. multocida* or mixed challenge of *P. multocida* and *P. haemolytica*. Another *Pasteurella* vaccine (Carovax, Wellcome laboratories) was tested but was unsuccessful in suppressing lesions, regardless of the type of challenge (Chandrasekaran et al., 1991). The statistical power for comparisons between the oil adjuvant vaccine group and control group (challenged with *P. haemolytica* alone), was not presented in this study, but sufficient information was provided by the authors to calculate it at 83%, which is considered to be adequate.

In another Malaysian study, the effect of a *Pasteurella haemolytica* vaccine against experimental challenge in lambs was investigated (Sabri et al., 2000). An outer membrane protein (OMP) of *P. haemolytica* A2, A7 or A9-enriched vaccine was injected, with a booster three weeks later. Sixty nine-month-old lambs were divided into four groups, based on which outer membrane protein vaccine was used (*P. haemolytica* A2, A7 or A9), with one control group. Lambs of each group were challenged intratracheally, two weeks after the last vaccination. Five lambs in each group were challenged with inoculum containing *P. haemolytica* A2, A7 or A9, respectively. Vaccination with the outer membrane proteins of *P. haemolytica* provided a good correlation ($R^2 > 0.78$) between antibody response and extent of lung lesions following homologous challenge. In the case of heterologous challenge, only a moderate correlation ($R^2 > 0.44$) between antibody response and extent of lung lesions was evident. In this study, the prevalence of individual lambs' pneumonic lesions was not provided, but an average extent of lung lesions per group was calculated. Therefore, it is unknown if all unvaccinated lambs developed lung lesions. Sample size calculations or statistical power levels were not presented in this

study. Statistical power would have been low in this study when considering comparisons of the extent of lung lesions between treatment and control groups, mainly due to small treatment groups ($n = 5$) and relatively large standard deviations.

A Moredun Research Institute study investigated colostrum deprived lambs kept in isolation (Gilmour et al., 1991). Experimental challenge was used to test the efficacy of a vaccine containing sodium salicylate extract (SSE) of *P. haemolytica* A2 grown in iron-depleted (SSE-IRP) conditions. One injection with the vaccine was administered when lambs were three weeks old and another 28 days later. Experimental groups consisted of $n = 13$ (SSE vaccine), $n = 8$ (SSE-IRP vaccine) and $n = 7$ lambs (unvaccinated controls). On day 35, all lambs were infected with PI₃ administered intratracheally and intranasally. After seven days, lambs were exposed to an aerosol of *P. haemolytica* A2. The vaccine containing IRP was 99% protective in 8 lambs compared to 47% protection in 7 lambs vaccinated with the iron-replete vaccine antigen (Table 2.11). All control lambs died after challenge with *P. haemolytica* A2, with a mean disease score of 50.8 (a semi-quantitative assessment of clinical findings, consolidated lung lesion area, *P. haemolytica* isolation index and pleurisy score) in comparison to no A2 SSE-IRP vaccinated animals dying with a mean disease score of 0.5. No sample size calculations were provided in this study and statistical power could not be determined, since standard deviations of mean disease scores were not presented.

Table 2.11: Group mean disease scores and percentage protection of iron regulated protein vaccines in SPF lambs challenged with *P. haemolytica* A2 (Gilmour et al., 1991).

Experiment Group	Vaccine	Number in group	Group mean disease score	% Protection
1.1	A2 SSE ^b	13	26.7	47.4
1.2	A2SSE-IRP ^c	8	0.5 ^a	99
1.3	Unvaccinated	7	50.8	0

^aSignificantly different from unvaccinated group ($P < 0.01$) using the Mann-Whitney rank test

^bA2 SSE – vaccine containing Sodium Salicylate Extract of *P. haemolytica* A2 grown in an iron replete medium

^cA2 SSE-IRP– vaccine containing Sodium Salicylate Extract of *P. haemolytica* A2 grown in an iron deplete medium

***Pasteurella* vaccine trials using natural challenge**

Very few *Pasteurella* vaccine trials have been conducted under natural pathogen challenge conditions. In a study in the United States (Kiorpes et al., 1991) lambs from vaccinated ewes were investigated under field conditions. A modified-live, attenuated *P. haemolytica* vaccine registered for use in cattle, was administered intradermally to ewes in the last 30 days of gestation. The vaccination group ($n = 26$) received booster vaccinations at 2 week intervals until parturition and controls ($n = 24$) were left untreated. On day 2 and 16 of life, subgroups of lambs from vaccinated ($n = 13$) and control ewes ($n = 10$) received the same vaccine intradermally. Another two subgroups of lambs from non-vaccinated ewes ($n = 13$) and from vaccinated ewes ($n = 11$) served as controls. Lambs from vaccinated ewes showed no significant increase in direct bacterial agglutination titres, but had significantly elevated anti-leukotoxin titres compared with lambs from control ewes. The subsequent vaccination also did not appear to be protective against *P. haemolytica* infection, based on serological responses. The decline in direct bacterial agglutination due to maternal antibodies in lambs after birth was more rapid than expected. The lowest titre was reached in less than 30 days. The efficacy of the vaccine against challenge was not assessed and this brings into question the conclusion that vaccination of either ewes in late gestation, or lambs post-partum was not able to produce a protective immune response. This is based on the fact that this was an extremely underpowered study. A calculation of statistical power for this study shows that, for the most part, the statistical power was low when comparing antibody responses between groups of lambs.

Two *Pasteurella* vaccines were tested under field conditions on live-sheep shipments of lambs from New Zealand to Saudi Arabia (Black and Duganzich, 1995; Black et al., 1997). Due to the confinement of animals, the conditions under which these vaccines were tested were markedly more extreme than would be expected under pastoral grazing conditions. One vaccine contained whole cell antigens of *P. haemolytica* A2 grown under IRP conditions (Ovipast, Hoechst) and another contained *P. haemolytica* A1 cell surface and leucotoxin antigens registered in North America for young cattle (Pneumostar, Biostar). A subcutaneous injection was administered 50-60 days prior to voyage, followed by a second injection 4 to 5 weeks later (13-18 days prior to voyage). A systematically randomised sample of 10,500 male lambs was assigned to two vaccine groups and one control group. The deaths attributable to pneumonia were 90 out of 2043 (4.5%) for the control group, 78 out of 2030 (3.9%) for the IRP vaccine group and 75 out of 1932 (4.0%) for the

Leucotoxin vaccine group. There were no significant differences between pneumonia scores recorded at the abattoir between control ($n = 52$), IRP ($n = 58$) or Leucotoxin groups ($n = 50$). A subsequent study evaluated the efficacy of another *P. haemolytica* vaccine under similar conditions (Black et al., 1997), but again, no significant protection against pneumonia was observed with regard to mortality and lung pneumonia scores at slaughter. Both of these studies (Black and Duganzich, 1995; Black et al., 1997) estimated the statistical power to be at least 80%, which is the level considered sufficient to detect statistically significant differences between treatment groups.

***Pasteurella haemolytica* capsular polysaccharide**

The capsular polysaccharide (CP) of *P. haemolytica* serotype A1 is the initial contact point between pathogen and host. An immune response to CP is important in protecting the lung from bacterial infection and colonisation through activation of antibody-mediated killing and phagocytic clearance mechanisms. There is strong evidence to correlate high anti-CP antibody titres with resistance (Friend et al., 1977; Gilmour et al., 1979; Gilmour, 1980; Gilmour et al., 1980; Wilkie et al., 1980; Panciera et al., 1984; Confer et al., 1985; Confer et al., 1988; Frank, 1988; Conlon et al., 1991; Fraser, 1991; Conlon and Shewen, 1993; Littledike, 1993; Robinson and Melling, 1993). In one study, vaccines were prepared with CP and muramyl dipeptide (MDP), or a lyophilic derivative (MDP-GDP) (Brogden et al., 1995). Seven groups of five lambs were used to test the different vaccines and the immune response was measured as IgM and IgG antibody titres. Also, the extent of lung lesions was assessed 40 days post-vaccination and found to be reduced in CP and MDP or CP and MDP-GDP vaccinated groups. Enhancement of CP with MDP or MDP-GDP may be a method of utilising CP as a vaccine immunogen. The statistical power in these studies was low when comparing lung lesion extent between groups. In comparisons of IgM titres between groups the statistical power was generally adequate, but not for comparisons of IgG titres.

Vaccines against viral pathogens

Vaccines containing viral antigens have also been tested. Results and discussion of statistical power is presented for four of these trials.

Virus vaccine trials using experimental challenge

A study of a PI₃ vaccine for lambs using experimental challenge was conducted in Hungary (Köves et al., 1982). The vaccine was derived from a PI₃ virus isolated from calves affected by acute respiratory disease. The virus was then inactivated with ethylenimine and oil-adjuvated. Eight-week-old Merino lambs were injected intramuscularly twice at an interval of 10 days. There were three groups of three lambs. One was vaccinated and challenged, another not vaccinated but challenged and the other was an untreated control group. Lambs were challenged intranasally and intratracheally 105 days after the first vaccination with PI₃ virus. This challenge was repeated 24 hours later. Histopathological and serological evidence showed that the vaccine was protective (Köves et al., 1982). Sufficient detail was not provided to comment on statistical power, however, the sample groups were small ($n = 3$).

Another experimental challenge trial was conducted in New Zealand (Davies et al., 1980b). There were four groups of 20 lambs. The vaccine contained live PI₃ virus and was injected intramuscularly (IM) in group 2 and administered intranasally (IN) in group 3. Groups 1 and 4 remained un-vaccinated. After 45 days, lambs in groups 1 to 3 were challenged with PI₃ by the intranasal (IN) and intratracheal (IT) routes. *P. haemolytica* was also inoculated by the IN and IT routes 6 days later. At slaughter, 10 to 12 days post challenge, 65% of non-vaccinates, 45% of IM vaccinates and zero IN vaccinates had pneumonic lesions (Davies et al., 1980b). This indicated that IN resulted in significantly fewer ($p < 0.001$) pneumonic lesions than IM vaccination with sufficient statistical power (84%)

Virus vaccine trials using natural challenge

In a Scottish trial, a live attenuated PI₃ virus vaccine licensed for use in cattle was studied under field conditions (Rodger, 1989). The vaccine was administered intranasally at 1ml per nostril to ewes. Half of the flock on one farm was vaccinated ($n = 19$), with the remainder unvaccinated ($n = 19$). There was a significant increase in haemagglutination inhibiting antibody titres to PI₃ virus in the vaccinated group. One of the un-vaccinated

ewes died from pasteurellosis. Subsequently, all ewes ($n = 150$ to 1100) on the other seven farms were vaccinated and fewer deaths were encountered than expected due to pasteurellosis. However, no assessment of subclinical pneumonia in lambs was conducted at any stage in the study. After the first vaccination on one farm, no control animals were used for comparison, so vaccine efficacy could not be determined after the first season.

In Oregon, a study was conducted under field conditions in feedlot lambs (Hansen, 1995). Four vaccines were used in the trial:

- A modified-live virus vaccine (containing infectious bovine rhinotracheitis virus, PI₃ virus and respiratory syncytial virus).
- A vaccine containing killed strains of IBR, BVD viruses and modified-live strains of PI₃ and RSV viruses.
- A *Haemophilus somnus* bacterin.
- An experimental core-antigen product with J5 bacterin-toxoid.

Comparisons were made between the type and timing of the vaccines. There were six trials involving 4,700 lambs with an average of 300 vaccinated lambs compared to 300 control lambs. There was a positive effect when the modified-live virus vaccine was administered either 10 days, 30 days, 10 and 30 days, or 30 and 44 days prior to shipment to the feedlot. The positive effect was measured in terms of pneumonia mortality rate and percentage of lungs with lesions. When lambs were vaccinated 10 or 30 days before shipment to the feedlot the efficacy of vaccine was 61% to 63% for mortality and 57% to 58% for pneumonic lesions. The efficacies of the modified-live, killed vaccine and the core-antigen product were not statistically different from the non-vaccinated controls.

Comparison of bacterial and viral vaccines

Although information about efficacy is required for vaccine registration in the United Kingdom, United States, and Australia (CVM, 2005; NRA, 2005; VMD, 2005), it is not required in New Zealand (ACVM, 2005). The studies presented in this section (2.8.1) have reported the efficacy of *Pasteurella* and PI₃ virus vaccines under both experimental and field conditions. However, statistical power is often not at an adequate level. There have only been two reported field studies of *Pasteurella* vaccines which occurred on live-lamb shipments (Black and Duganzich, 1995; Black et al., 1997), indicating the lack of documented trial work in pastoral farming conditions. PI₃ vaccines, by comparison, have

often been tested under pastoral farming conditions and have shown promising results. On the whole, PI₃ vaccines were more effective than *Pasteurella* vaccines against pneumonia, perhaps due to the poor immunogenicity of some isolates of *P. haemolytica* A2. Most of these trials have tested vaccines to target a small number of microbial species and strains. A wide range of micro-organisms are capable of causing pneumonia, so a move towards broader spectrum vaccines may prove more successful in controlling disease. Moreover, most experimental challenge studies involving *Pasteurella* spp. had extremely low statistical power in terms of revealing vaccination effects.

2.8.2 Antimicrobial peptides

Antimicrobial peptides are naturally occurring immunogens that are part of the immune system in animals. Their antimicrobial properties are generally broad-spectrum for Gram-positive bacteria, Gram-negative bacteria and fungi. Synthetic antimicrobial peptides have potential use in treatment or prevention of respiratory infection as direct antimicrobial agents. In addition, an animal's production of antimicrobial peptides may be stimulated through vaccination, e.g. at times of stress when they are most likely to develop pneumonia.

To test the efficacy of antimicrobial peptides in the treatment of bacterial infection, a model of AP in lambs was established using the ovine respiratory pathogen *P. haemolytica*. In one study, a single bronchial instillation of 0.5 mg myeloid antimicrobial peptide (SMAP29) reduced the concentration of bacteria in bronchoalveolar lavage fluid and consolidated pulmonary tissues (Brogden et al., 2001). In another study, a single bronchial instillation of 0.5 mg anionic peptide reduced pulmonary inflammation and the concentration of *P. haemolytica* in infected lung tissue (Kalfa et al., 2001). The authors suggested the *in vitro* and *in vivo* effectiveness of SMAP29 and that anionic peptides may have applications in the treatment or prevention of pulmonary infections.

The field of antimicrobial peptides in animals is expanding and substantial advances are expected in the near future, where genes encoding antimicrobial peptides may be discovered. Conventional animals or transgenic animals may be used as a source of antimicrobial peptides. Antimicrobial peptides have immuno-enhancing activities which

could be used to augment immune responses to antigens in vaccines for disease prevention (Brogden et al., 2003).

2.8.3 Management

Management practices that are thought to increase the risk of pneumonia include tail docking, castration, crowding, handling, transport and weaning (Knowles et al., 1995; Cole, 1996). Such practices cause stress, and stress can lead to increased secretion of stress related hormones which, in turn, increases susceptibility to infection. Many of these practices are unavoidable under commercial farming conditions in New Zealand. It is still poorly understood how management-related stress leads to the development of pneumonia in lamb flocks, due to a lack of field studies.

Other management practices that should be avoided as much as possible to help control pneumonia include: sudden changes in diet; mixing animals from different sources; excessive heat; poor ventilation; parasitic infestation and exposure to low temperatures. In New Zealand, pneumonia tends to occur in the late summer/early autumn. It seems likely, therefore, that high rather than low temperatures pose the highest risk. Blaxter (1967) presented an upper critical temperature of 25°C for growing lambs, above which heat stress supposedly occurred from inadequately regulated heat. Temperatures above 25°C are not uncommon in the summer and late summer in New Zealand. In addition, if lambs are mustered during this period, their body temperature may increase through exercise, handling or confinement in close proximity to other animals in yards or shearing shed. Recording and classifying such events and comparing them with lamb pneumonia at slaughter may reveal these as risky practices.

Hot, dry weather often precedes outbreaks of AP (Bruere et al., 2002). Poor ventilation is not a likely risk factor for pneumonia in New Zealand, as animals are not routinely housed indoors. However, in the event of crutching or shearing when lambs are housed overnight, ventilation quality may be important. Internal parasite infestation may increase susceptibility to pneumonia, possibly augmented by high levels of drench resistance (Hughes et al., 2004; Hughes et al., 2005).

A case-control study (Van der Logt, 1996), identified a number of risk factors that, if avoided, may reduce pneumonia and pleurisy in lambs. These included:

- Drenching lambs at a high frequency.
- Shearing lambs twice.
- Frequently yarding lambs after weaning.
- Using motorised means of mustering.
- Using a lake for water supply.
- Having a large number of lambs on the property in July.

This study was based on a questionnaire and as such the data were likely to be subject to confounding. It seems that if lambs are yarded after weaning infrequently the potential for cross colonisation of potential pathogens between lambs will be reduced. Drenching lambs at a low frequency may have a similar effect, as they spend a minimum of time in the yards. Practices that were protective included the use of a wand for dipping or a spray-on dip, concrete rather than soil yards, access to a trough water supply and cross breeding. The use of concrete yards may reduce the development of dust when animals are crowded.

Bruere et al. (2002) advised that stress be minimised from the time of weaning in November or December until May and June, to reduce the number of yardings (especially under hot and dusty conditions) and to maintain optimum stock health during that period. Maintenance of stock health can be achieved by systematic animal health care, especially with regard to parasite control.

If the above mentioned management practices were definitively identified as increasing the risk of pneumonia, it would be highly possible that sheep flocks could be better managed to reduce the disease. These possible factors need to be validated in further studies to support the development of control options for farmers. One of the difficulties in assessing the effect and role of these factors is that pneumonia can only be diagnosed accurately at the time of slaughter.

2.9 Outline and aims of the thesis

This thesis addresses several key questions regarding frequency, causes, consequences and control of chronic progressive pneumonia of lambs in New Zealand. These questions take account of seasonal and spatial patterns of pneumonia prevalence, management related factors at farm-level contributing to the development of pneumonia, economic loss associated with lamb pleurisy and pneumonia and efficiency of vaccination to reduce the economic cost of pneumonia. We base our analyses on lamb pneumonia as detected at slaughter which, predominantly consists of CNP but some recovered AP would also be present.

The chapters, their titles and objectives are as follows:

Chapter 3, Hierarchical model of pneumonic lesions in lambs at slaughter and investigation of spatial patterns of pneumonia prevalence: The aim of this chapter is to investigate spatial and temporal prevalence of lamb pneumonia in New Zealand. This is based on slaughter data gathered from a large sample of lambs from farms in three regions over a ten-month period.

Chapter 4, Case-control study of lamb pneumonia: This chapter consists of a case-control study with the aim of identifying management practices and characteristics of the production system that may increase the risk of pneumonia in lambs. It compares flocks with a high prevalence of moderate to severe pneumonia to flocks with no moderate to severe pneumonia diagnosed at slaughter. A path model was used for more in-depth investigation of the inter-relationships between hypothesised management factors and a high prevalence of pneumonia at farm level.

Chapter 5, Efficacy of Ovipast Plus® vaccine for pneumonia of lambs under field conditions in New Zealand: In this chapter we evaluate the efficacy of Ovipast Plus® in preventing sub-clinical effects of pneumonia on average daily weight gain and lung lesions under commercial farming conditions.

Chapter 6, Economic effect of chronic non-progressive pneumonia and pleurisy in New Zealand lambs: The aim of this chapter is to provide an estimate of economic loss to the New Zealand sheep industry due to pneumonia and pleurisy based on field studies and current data.

Chapter 7, General Discussion: The aim of this chapter is to discuss the significance of the findings presented in this thesis. Also to review the merit and limitations of studies performed for the thesis and outline the need and objectives for further research.

Hierarchical model of pneumonic lesions in lambs at slaughter and investigation of spatial patterns of pneumonia prevalence

3.1 Introduction

Chronic non-progressive pneumonia (CNP) and acute pneumonia (AP) are endemic conditions of New Zealand lambs. Both CNP and AP lead to substantial production loss as a result of reduced growth rates, a predisposition to pleurisy and reduced carcass value. Growth rates are reduced when pneumonic lung lesions are evident, in comparison with lambs that have no visible lesions at slaughter (Jones et al., 1982; Alley, 1987a; Goodwin et al., 2004). The only accurate diagnosis for pneumonia in lambs is examination of lungs at slaughter however, pneumonia is not routinely recorded at processing plants as there is no direct effect on the value of the lamb carcass. Currently, no live-animal diagnostic tests are available for pneumonia in lambs. Control of these diseases is difficult because: (1) the condition can only be detected by *post mortem* inspection of lungs at the time of slaughter, and (2) the time lag between application of interventions and the identification of responses to those interventions.

It has been assumed that pneumonia is a widespread problem in New Zealand lambs although there is little quantitative data to support this (Kirton et al., 1976; Alley, 1987b; Davies, 1987; Goodwin et al., 2004). Reports of CNP prevalence in New Zealand sheep vary between 21% and 93% (Kirton et al., 1976; Thurley et al., 1977; McGowan et al., 1978; Pfeffer et al., 1983; Goodwin et al., 2004). The wide variation in estimates of CNP prevalence is probably due to the small number of flocks selected for inclusion in the cited studies. This, in addition to purposive selection of studied flocks, means that these estimates should not be regarded as representative of the New Zealand sheep population. Although broad-scale, regional differences in pneumonia prevalence as measured at

slaughter have been identified (Black, 1997; Goodwin et al., 2004), variations in flock-level disease risk at finer spatial scales are largely unknown.

The objectives of this study were to: (1) evaluate the ability of meat inspectors to correctly classify pneumonic lesions in slaughtered lambs into three categories of severity; (2) quantify the influence of processing plant and month on the proportion of each flock being diagnosed with pneumonia at slaughter; and (3) investigate the data for any residual, spatially correlated risk of pneumonia after controlling for flock-level risks for disease.

3.2 Materials and methods

Data collection

This was a cross-sectional longitudinal observational study of pneumonia in lambs at slaughter. The eligible population was comprised of flocks located in each of the Canterbury, Manawatu, and Gisborne regions of New Zealand (Figure 3.1). The study population was comprised of members of the eligible population that supplied lambs to single processing plants in each region (Canterbury 837 flocks; Manawatu 724 flocks, and Gisborne 680 flocks). For the purpose of this study we define a farm as the physical location where sheep are resident, a flock as the collective group of sheep from a single farm, and a mob as a group of lambs from a single flock submitted as a single unit for slaughter.

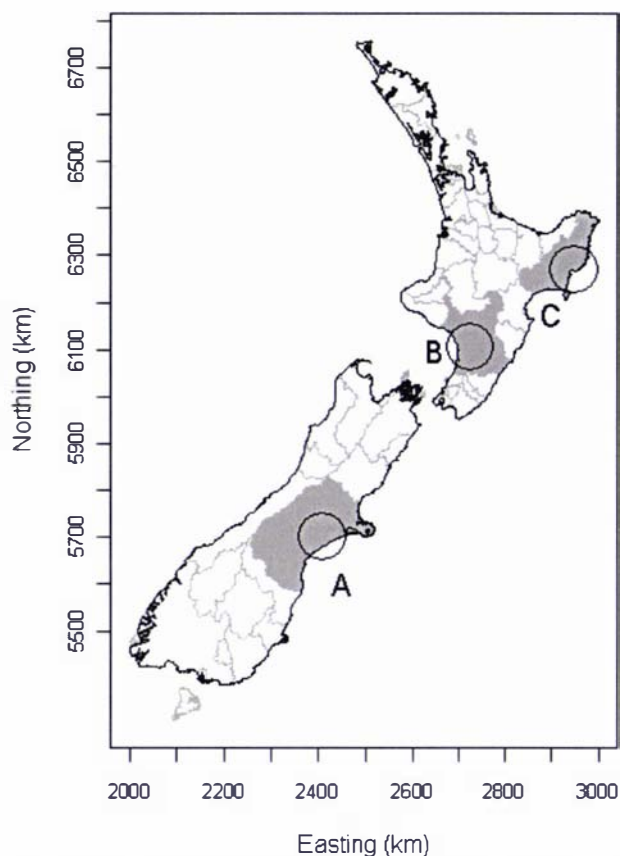


Figure 3.1: Map of New Zealand with shaded areas indicating the selected study areas: (a) Canterbury, (b) Manawatu, and (c) Gisborne. Circles represent areas where farms were selected for the spatial analyses described in the text.

Data were collected by meat inspectors of ASURE New Zealand Ltd. from 1 December 2000 to 30 September 2001 (inclusive). Pneumonia status was assessed for every lamb slaughtered and processed at each plant throughout the study period. For each lamb, lungs were visually assessed and classified by meat inspectors into one of the following categories: no pneumonia, minor pneumonia (less than 10% of total lung surface area affected) and moderate to severe pneumonia (greater than 10% of total lung surface area affected). There was no differentiation between CNP and AP. To ensure consistency of lung scores between meat inspectors and processing plants, training sessions were conducted in each plant at the start of each data collection period. The date of commencement of data collection was different for each plant on account of logistics surrounding data collection. Data collection commenced on 1 January 2001 in Canterbury, 1 December 2000 in the Manawatu, and 1 February 2001 in Gisborne.

Validation of lung scoring

At each plant, a validation study was conducted over a 21 – 24 hour period during the fifth month of data collection. To validate pneumonia diagnoses by meat inspectors the principal author assessed the lungs using the classification categories described above. The sensitivity and specificity of meat inspector diagnosis of pneumonia was evaluated for each plant using the principal investigator's diagnosis as the gold standard. The same method was used to calculate the sensitivity and specificity of moderate to severe pneumonia diagnosis. No pneumonia and minor pneumonia were pooled to form the negative category.

Estimates of inspector sensitivity (that is, the conditional probability of a positive lung score) and specificity (the conditional probability of a negative lung score) allowed the true prevalence of pneumonia to be calculated as follows (Rogan and Gladen, 1978):

$$\text{True prevalence} = \frac{\text{Apparent prevalence} + (\text{Specificity} - 1)}{\text{Sensitivity} + (\text{Specificity} - 1)} \quad \text{(Equation 1)}$$

Data management and analysis

Part I

The following details were collated for each mob of lambs presented for slaughter: slaughter date, the number of lambs slaughtered, and the number of lambs with each of the defined pneumonia scores. Farms that supplied less than 50 lambs ($n = 329$) throughout the study period were excluded from the analysis. The supply of lambs in February cannot be considered to be representative due to national strikes by MAF veterinarians, causing plants to be closed down for 4 – 5 days in some cases.

Part II

A 2-level mixed-effects binomial logistic regression model was applied to the data using the proportion of lambs with moderate to severe pneumonia per mob (grouped by flock) as the outcome variable. Only mobs with ≥ 30 lambs were included, however, if mobs of <30 lambs were slaughtered within 1 week of each other, these were pooled together to form one mob. Explanatory variables included region as a categorical variable with three levels (Canterbury, Manawatu, Gisborne), month of slaughter as a categorical variable with nine levels (January through to September) and a flock (i) and mob (j) identifier. The outcome variable was comprised of the number of lambs within a mob with pneumonia as the

numerator and the number of lambs within the mob as the denominator. The equation for the multilevel model was as follows:

$$\text{logit}(\pi_{ij}) = \text{intercept} + \text{region}_{ij} + \text{month}_{ij} + u_i + v_{ij} + \varepsilon_{ij} \quad \text{(Equation 2)}$$

Random effect terms for flock and mob are denoted by u_i and v_i , respectively with $u_i \sim \text{iid } N(0, \sigma^2)$ and $v_{ij} \sim \text{iid } N(0, \tau^2)$. An iterative generalised least squares approach using a first order marginal quasi likelihood was used to produce initial values for a Bayesian model of pneumonia probability with flat (uninformed) prior distributions using Markov chain Monte Carlo (MCMC) methods in MLwiN version 2.01 (Rasbash et al., 2004). Analyses were undertaken to determine the appropriate number of iterations of the Markov chain Monte Carlo sampler to reliably estimate the posterior distribution of the model parameters. An estimate of the total number of iterations required ($n = 1,000,000$) was given by the Raftery-Lewis quantile diagnostic (Raftery and Lewis, 1992). For parameter estimation, we ran the Markov chain Monte Carlo sampler for 1 million iterations after discarding the first 100,000 ‘burn in’ samples. Plots of the autocorrelation and partial autocorrelation functions for each parameter showed that the chain was adequately close to independently identically distributed data.

In this study, our interest was to estimate the degree of similarity of outcomes at the mob and flock levels as expressed by the intra-class correlation coefficient (ICC) (Snijders and Bosker, 1999). This was calculated as the variance of the random effect terms at the mob and flock level as a proportion of the total random effect variance. The ICC provides a measure of correlation between outcomes at different levels of the hierarchy. For example, mob ICC is the correlation of pneumonia levels of lambs within a mob, compared with that of different mobs from the same flock. Flock ICC is the correlation of pneumonia levels of lambs within a flock compared with other flocks. The purpose of the multilevel model was to identify sources of variation in pneumonia prevalence at the mob-level (e.g. duration of growth period, lamb liveweight) and the farm-level (e.g. management policy, sheep breed etc), once region and month of slaughter had been accounted for.

Part III

The objectives of this part of the analysis were to select members of the study population with a high prevalence of pneumonia (case flocks) and compare the spatial distribution of case flocks with those flocks with a low prevalence of pneumonia (control flocks). A second objective was to examine the flock-level residuals from the multilevel model (described in Part II) for the presence of second order spatial autocorrelation. Residual, spatially correlated risk – if present – would suggest that environmental risks (e.g. temperature, elevation, and/or humidity) were associated with the presence of disease.

Geographical data

The national farm database, AgriBase (AgriQuality, 2004) was queried to provide centroid coordinates of farm blocks. Study flocks were matched to AgriBase by farm name to provide an identification number and associated coordinates.

Flock selection

For the spatial analyses, the data set was restricted to include flocks that supplied more than 30 lambs over the entire season that were located within a 50 km radius of each processing plant (Canterbury $n = 292$, Manawatu $n = 271$ and Gisborne $n = 261$). Our reason for selecting according to proximity to processing plants was to ensure that all or most lambs were supplied to the respective plants. A small number of flocks ($n = 7$) were excluded from the analysis due to missing coordinates, as they had not been allocated AgriBase identification numbers.

Definition of case and control flocks

The units of interest were flocks that supplied lambs to data collection processing plants in Canterbury, Manawatu and Gisborne for December 2000 to September 2001. Case flocks were defined as those in the 80th percentile of moderate to severe pneumonia prevalence for each region. Control flocks were defined as those with no apparent moderate to severe pneumonia.

Extraction mapping

Analyses were conducted to determine if the spatial distribution of case flocks differed from that of the controls. To improve interpretation of the two distributions, kernel density surfaces were constructed using a bandwidth defined by adaptive smoothing (a weighting

factor dependent on the number of flocks in the neighbourhood of each point). The spatial incidence risk function was then calculated as the ratio of the density of case flocks to the density of both case and control flocks. The quartiles of this relative risk surface were plotted as contours to show the distribution of case flocks per case and control flocks per 100 square kilometres.

Cluster analysis

The spatial scan statistic implemented in SaTScan Version 4.0.3 (Kulldorff, 1999) was used to identify the presence of spatial clusters of case flocks occurring within each region. Using this method the number of case flocks in each region was assumed to follow a Poisson distribution. The spatial scan statistic creates circular windows at the centre of each farm with a radius from 0 – 50% of the total area. The null hypothesis was that the incidence of case flocks was constant across each region and the alternative hypothesis was that there was an increased risk of case flocks in each circular window. Monte Carlo simulation was used to test the null hypothesis against the alternative hypothesis. A significant, spatial cluster of case flocks was said to exist if the likelihood ratio of a given window was among the highest 5% of simulated maximum likelihood ratios.

Examination of residuals

Standardised flock-level residuals from the multilevel model (Part II) were calculated and covariance in the residual values as a function of distance was assessed using omnidirectional variograms (Isaacs and Srivistava, 1989). An omnidirectional variogram shows the semivariance between pairs of observations as a function of their Euclidean distance. The semivariance is half the variance of the differences between all possible points spaced a constant distance apart (Watson, 1997). Envelopes for the variograms were based on 999 Monte Carlo permutations of the data, whereby case and control labels were randomly allocated to each farm location. Spatial dependence was deemed to be present given a relationship between distance and semivariance, and if some or all of the empirical variograms lay beyond the bounds of the lower and upper simulation envelopes.

3.3 Results

Part I

Canterbury was the largest processing plant providing data from over one million lambs (Figure 2). The Manawatu processing plant supplied data from 472,057 lambs and Gisborne 302,616 lambs. The pattern of lamb supply through consecutive months was similar for the Manawatu and Gisborne. In Canterbury, the number of lambs supplied decreased markedly from January. The effect of the strikes by MAF veterinarians is evident in February by the lower than expected number of lambs killed that month for all regions (Figure 3.2).

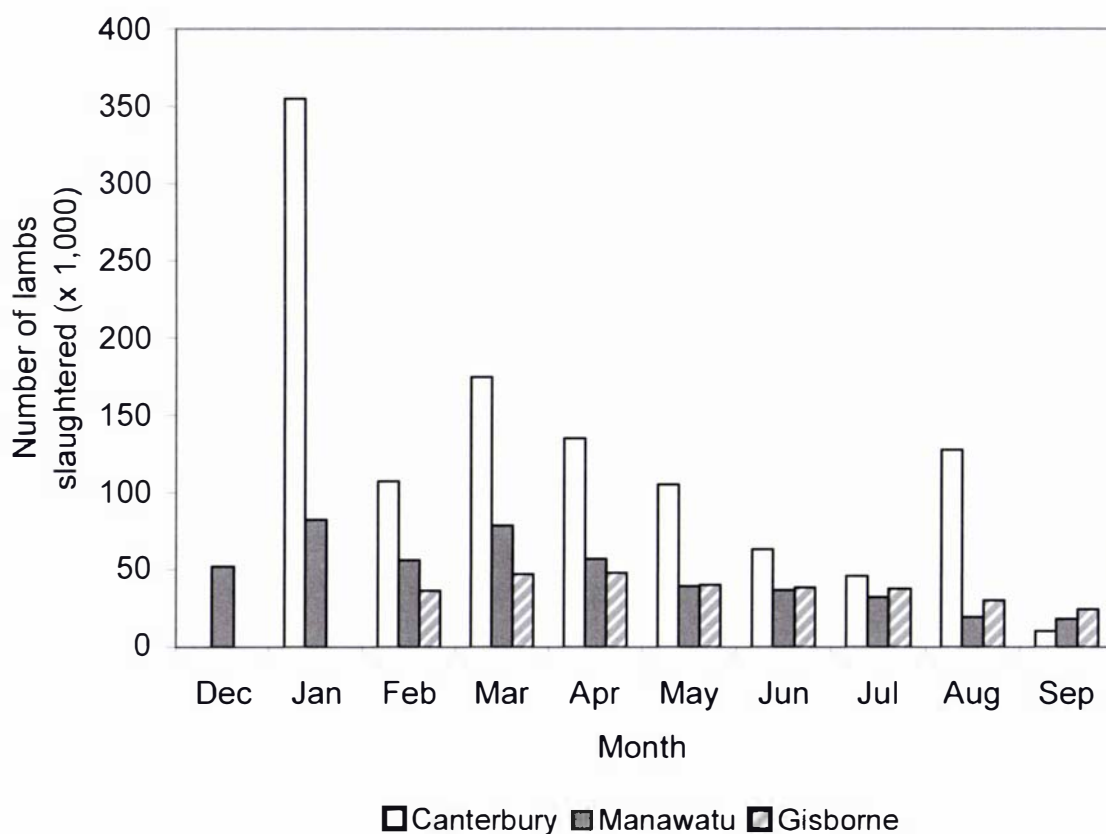


Figure 3.2: Pneumonic lesions in lambs slaughtered in three regions of New Zealand, December 2000 to September 2001. Number of lambs slaughtered per month at the Canterbury, Manawatu, and Gisborne plants.

Validation of meat inspector diagnosis of pneumonia occurred between May and June 2001 (Table 3.1). In total 9137, 4332 and 2276 lungs were sampled from the Canterbury, Manawatu and Gisborne processing plants. The difference in the total number of lungs sampled per 21 – 24 hour period reflected the number of lambs processed by each plant.

Table 3.1: Date, duration and number of lungs sampled for validation of pneumonia data from Canterbury, Manawatu and Gisborne between May 1st and June 8th 2001.

Processing plant	Date	Length of validation (hours)	Number of lungs sampled
Canterbury	10 May 2001	6	2,232
	11 May 2001	6	2,775
	21 May 2001	6	2,121
	22 May 2001	6	2,009
Total		24	9,137
Manawatu	26 Apr 2001	6	1,092
	27 Apr 2001	6	968
	30 Apr 2001	6	1,100
	1 May 2001	3	551
	2 May 2001	3	621
Total		24	4,332
Gisborne	5 Jun 2001	6	616
	6 Jun 2001	6	609
	7 Jun 2001	6	680
	8 Jun 2001	3	371
Total		21	2,276

Meat inspector sensitivity was low for both moderate to severe pneumonia and total pneumonia (mild to severe), but especially low for minor pneumonia in the Manawatu and Gisborne plants (Table 3.2). Meat inspector specificity was high. The results indicate that the level of pneumonia in this population of lambs was under-estimated. That is, a significant proportion of lungs with pneumonic lesions were misclassified as negative.

Table 3.2: Validation sensitivity and specificity (with 95% confidence intervals), of inspector diagnosis of minor, moderate to severe and total pneumonia in Canterbury, Manawatu and Gisborne.

Region	Sensitivity (95%CI)	Specificity (95% CI)
<i>Minor pneumonia</i>		
Canterbury	0.157 (0.145, 0.168)	0.910 (0.901, 0.917)
Manawatu	0.028 (0.021, 0.038)	0.974 (0.967, 0.980)
Gisborne	0.054 (0.041, 0.072)	0.980 (0.972, 0.987)
<i>Moderate to severe pneumonia</i>		
Canterbury	0.172 (0.136, 0.214)	0.979 (0.976, 0.982)
Manawatu	0.173 (0.142, 0.210)	0.923 (0.913, 0.932)
Gisborne	0.155 (0.093, 0.247)	0.991 (0.985, 0.994)
<i>Total pneumonia (minor and moderate to severe)</i>		
Canterbury	0.201 (0.189, 0.214)	0.903 (0.894, 0.912)
Manawatu	0.152 (0.137, 0.168)	0.930 (0.916, 0.941)
Gisborne	0.085 (0.068, 0.104)	0.978 (0.969, 0.985)

Canterbury had the highest mean number of lambs supplied per farm along with the highest true total pneumonia prevalence (Table 3.3). Due to lower sensitivity of minor pneumonia diagnosis, true minor pneumonia prevalence was higher in the Manawatu and Gisborne compared with Canterbury, even though the apparent minor pneumonia prevalence was higher in Canterbury.

Table 3.3: Descriptive statistics of number of mobs, number of lambs, means of true minor, true moderate to severe and total pneumonia prevalence per flock, grouped by region with 95% confidence intervals.

Plant	Parameter	Number	Mean	95% CI
Canterbury	No. mobs	3839	2	
	No. lambs	1,124,883	506	
	Mean minor pneumonia prevalence (%)		23	21.9, 24.4
	Mean moderate to severe pneumonia prevalence (%)		10	9.7, 11.1
	Mean total pneumonia prevalence (%)		29	28.1, 30.9
Manawatu	No. mobs	2788	2	
	No. lambs	472,057	278	
	Mean minor pneumonia prevalence (%)		40	38.0, 42.6
	Mean moderate to severe pneumonia prevalence (%)		13	11.5, 13.6
	Mean total pneumonia prevalence (%)		22	20.6, 23.5
Gisborne	No. mobs	1649	2	
	No. lambs	302,616	306	
	Mean minor pneumonia prevalence (%)		34	30.7, 36.4
	Mean moderate to severe pneumonia prevalence (%)		7	5.6, 7.6
	Mean total pneumonia prevalence (%)		24	21.4, 26.0

The true prevalence of pneumonia peaked earlier in Gisborne compared with Canterbury and Manawatu (Figure 3.3). Canterbury and Manawatu had a similar pattern of prevalence through the data collection period, although the prevalence in Canterbury was greater than recorded for the Manawatu.

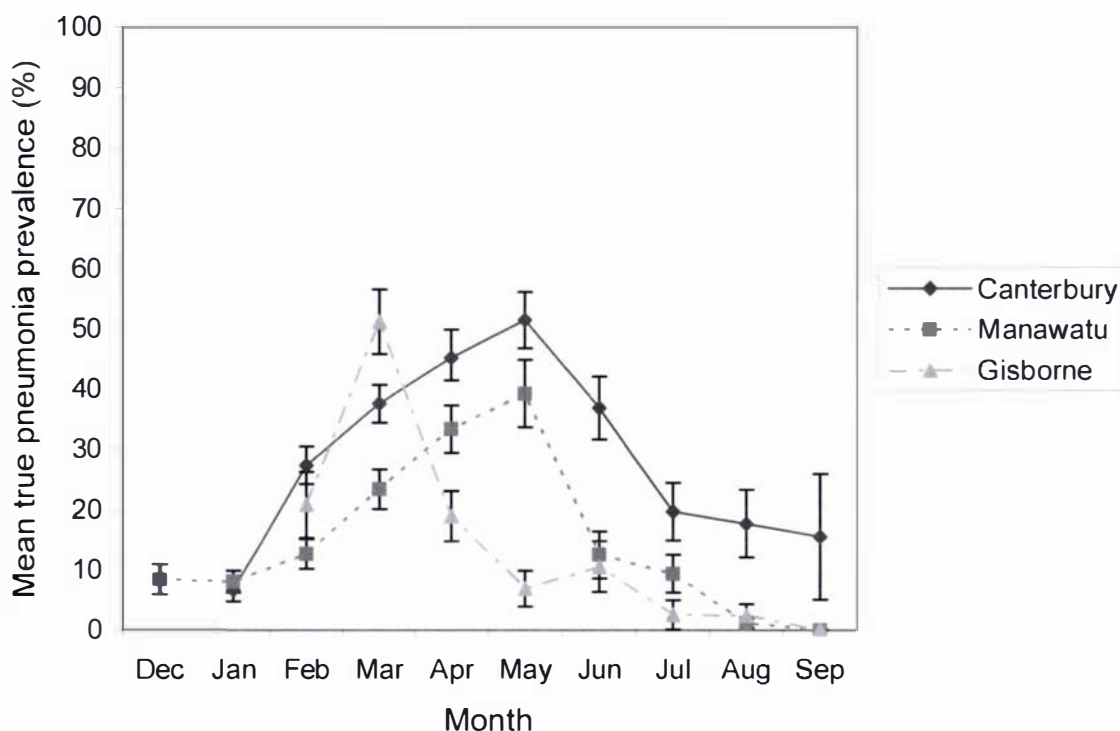


Figure 3.3: Pneumonic lesions in lambs slaughtered in three regions of New Zealand, December 2000 to September 2001. Mean monthly true pneumonia prevalence (with 95% confidence intervals) for lambs slaughtered at the Canterbury, Manawatu, and Gisborne plants.

Part II

Table 3.4 shows regression coefficients, variance estimates, and odds ratios of the multilevel model. The variance estimates of the random effect terms at the mob and flock levels were 1.83 (SE = 0.06) and 0.73 (SE = 0.06), respectively. The proportion of lambs with moderate to severe pneumonia differed between plants. The odds of moderate to severe pneumonia in Gisborne was 0.33 times (95% CI = 0.28, 0.40) that of the odds of moderate to severe pneumonia in Canterbury. The odds of moderate to severe pneumonia in the Manawatu was 0.74 times (95% CI = 0.64, 0.85) that of the odds of moderate to severe pneumonia in Canterbury. The odds of moderate to severe pneumonia from March to May was between 11.0 and 13.7 times that of the reference month, December.

Table 3.4: Logistic regression model of the effects of processing plant and month on proportion of moderate to severe pneumonia in lambs at mob and flock-level from Canterbury, Manawatu and Gisborne between December 2000 and September 2001.

Variable	β	S.E.	LRS p-value ^a	Odds Ratio (95% CI) ^b
Intercept	-7.095	0.16		
Fixed Effects				
<i>Plant</i>				
Canterbury	Ref			1.0 (1.0, 1.0)
Manawatu	-0.304	0.07		0.7 (0.6, 0.9)
Gisborne	-1.099	0.09	<0.001	0.3 (0.3, 0.4)
<i>Month</i>				
December	Ref			
January	0.552	0.16		1.7 (1.3, 2.4)
February	1.557	0.16		4.7 (3.5, 6.5)
March	2.602	0.16		13.5 (9.9, 18.4)
April	2.619	0.16		13.7 (10.1, 18.7)
May	2.394	0.16		11.0 (8.0, 15.1)
June	1.371	0.17		3.9 (2.8, 5.5)
July	0.999	0.18		2.7 (1.9, 3.9)
August	0.231	0.21		1.3 (0.8, 1.9)
September	-0.958	0.29	0.091	0.4 (0.2, 0.7)
Random effects				
Flock	0.726 ^c	0.06		
Mob	1.828 ^c	0.06		

^a P value of each whole factor from likelihood ratio statistic.

^b Interpretation: lambs slaughtered in March 13.5 (95% CI 9.9, 18.4) times more likely to have pneumonia than those slaughtered in December (the reference category).

^c Variance component.

The intra class correlation coefficient (ICC) was calculated using a latent variable approach assuming the binary outcome arose from an underlying continuous distribution. The level 1 variance was on the logit scale and was equal to $\pi^2/3$, as shown in the following equations at the flock level (Equation 3) and mob level (Equation 4).

$$\text{Flock ICC} = \frac{0.726}{1.828 + 0.726 + 3.142^2 / 3} \quad \text{(Equation 3)}$$

$$\text{Mob ICC} = \frac{1.828}{0.726 + 1.828 + 3.142^2 / 3} \quad \text{(Equation 4)}$$

Flock ICC was 12.4% and mob ICC was 31.3%. Mob ICC measures the correlation of moderate to severe pneumonia prevalence of lambs within mobs, compared with that of lambs between different mobs from the same flock. Likewise, flock ICC measures the correlation of moderate to severe pneumonia prevalence of lambs within a flock, compared with lambs from different flocks.

Part III

Table 3.5 provides descriptive data for the flocks selected for the spatial analysis by region. The mean number of lambs supplied per flock was highest in Canterbury with similar numbers in Manawatu and Gisborne. The mean true moderate to severe pneumonia prevalence was highest in the Manawatu (12%, 95% CI 11.9 – 12.1%), followed by Canterbury (9%, 95% CI 9.0 – 9.1%), and Gisborne (5%, 95% CI 4.9 – 5.1%). The mean true total pneumonia prevalence was highest in Canterbury (27%, 95% CI 26.9 – 27.1%), followed by Manawatu (21%, 95% CI 20.9 – 21.2%) and Gisborne (18%, 95% CI 17.9 – 18.1%).

Table 3.5: Number of study flocks selected for spatial analysis supplying lambs to data collection processing plants, mean (standard deviation) number of lambs supplied per flock, true moderate to severe pneumonia prevalence and true total pneumonia prevalence in Canterbury, Manawatu and Gisborne.

Region	Flocks	Mean number of lambs (SD)	True prevalence (SD) of moderate to severe pneumonia	True prevalence (SD) of total pneumonia
Canterbury	292	344 (851)	9% (13)	27% (32)
Manawatu	271	235 (572)	12% (22)	21% (30)
Gisborne	261	231 (225)	5% (14)	18% (33)

SD – Standard deviation

Figure 3.4 shows the spatial distribution of the case and control flocks in the three study regions. The processing plants were located close to Ashburton (Figure 3.4a), Feilding (Figure 3.4b) and Gisborne (Figure 3.4c). The density of case and control flocks was greatest around these centres, indicating that it was highly likely that flock managers supplied most, if not all, of their lambs to the respective processing plants.

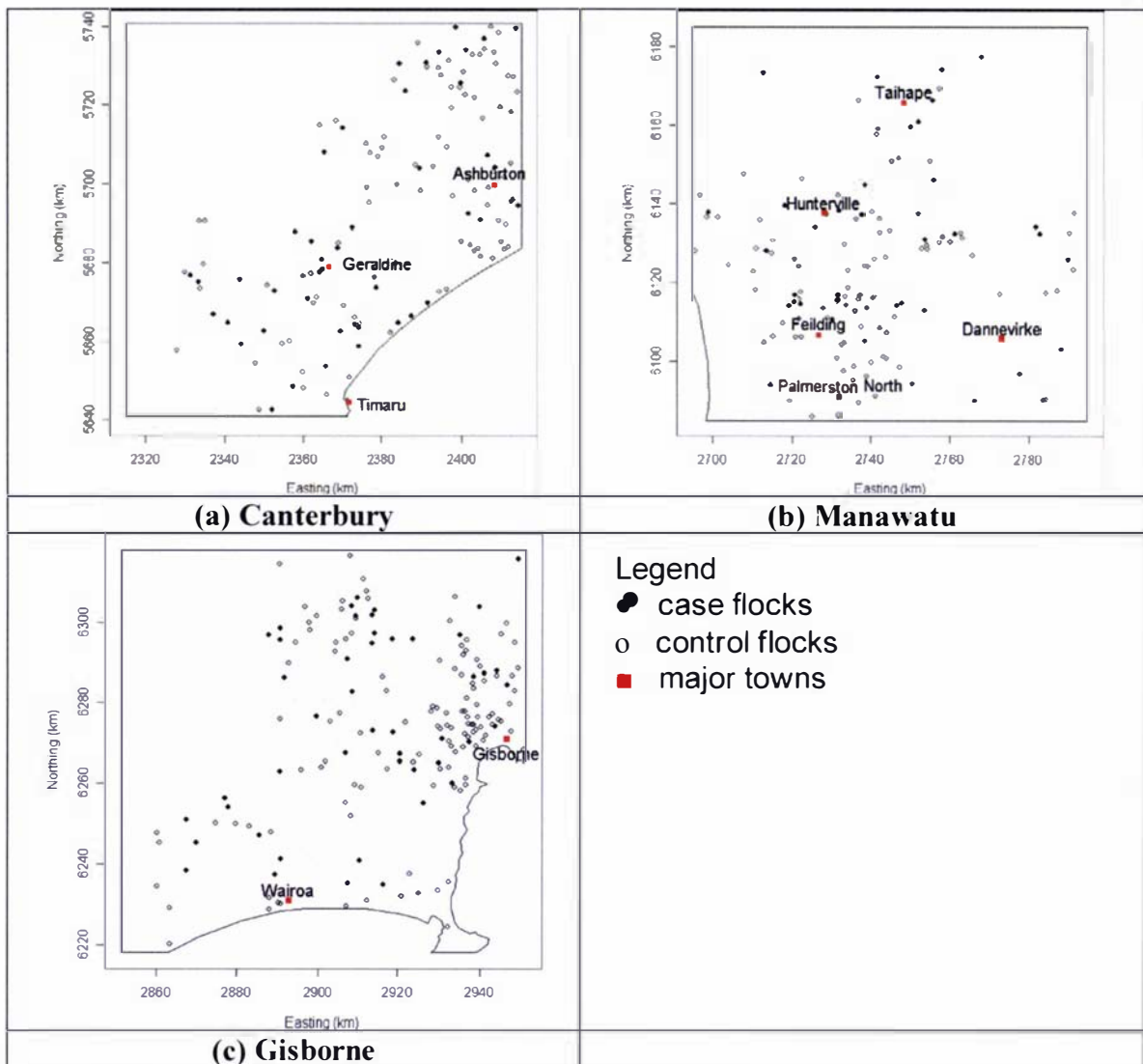


Figure 3.4: Pneumonic lesions in lambs slaughtered in three regions of New Zealand, December 2000 to September 2001. Point maps showing the location of case and control flocks in: (a) Canterbury, (b) the Manawatu, and (c) Gisborne.

In Figure 3.5 quartiles of the spatial incidence risk function are plotted, showing the distribution of case flocks per 100 case and control flocks per kilometre. These show locations within the study regions where the spatial incidence risk of flock pneumonia prevalence was high (75th percentile) and low (25th percentile). In Canterbury there was a

high spatial incidence risk of flock pneumonia prevalence south west of the township of (Figure 3.5a). In the Manawatu there was a high spatial incidence risk south of Dannevirke, and to the east and south of Taihape (Figure 3.5b). For Gisborne an area of high spatial incidence risk was northwest Wairoa and Gisborne (Figure 3.5c). Results from the SaTScan analysis identified a cluster of case flocks in Canterbury that was significant at the alpha level of 0.05 ($n = 5$, $p = 0.025$). There were no clusters identified at the alpha level of 0.05 in the Manawatu or Gisborne.

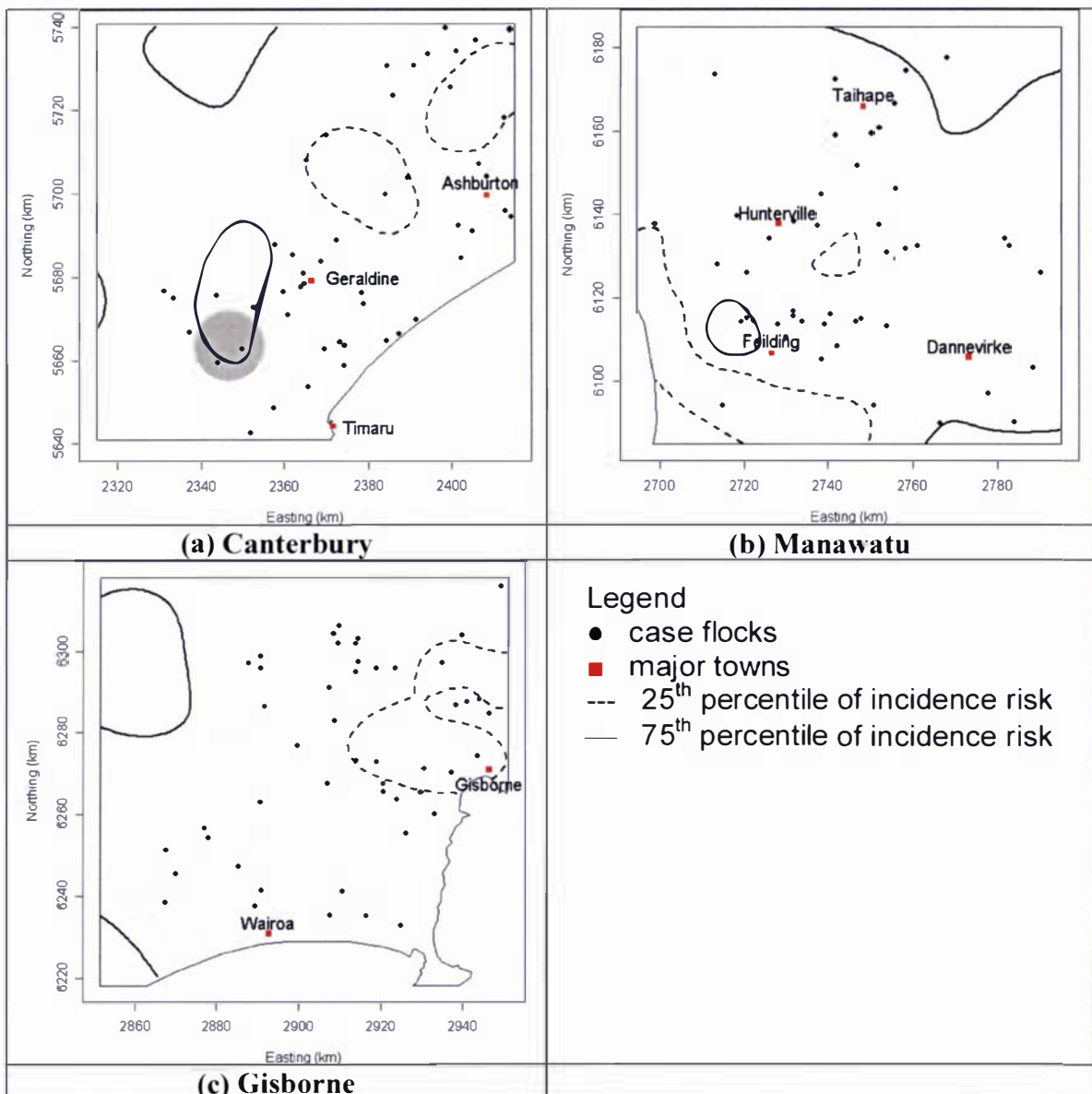


Figure 3.5: Pneumonic lesions in lambs slaughtered in three regions of New Zealand, December 2000 to September 2001. Contour plots showing the spatial incidence risk of moderate to severe pneumonia for flocks in: (a) Canterbury, (b) the Manawatu, and (c) Gisborne. In (a) the shaded circular area identifies the location of the significant cluster of case flocks, identified using the spatial scan statistic.

Binned omnidirectional variograms computed from the flock-level standardised residuals from the multilevel analyses are shown in Figure 3.6. The plots show that once the flock-level explanatory variables had been accounted for, there was no residual second order spatial autocorrelation in pneumonia probability in any of the study regions. This is indicated by the lack of relationship between semivariance and distance, and each empirical variogram is located wholly within the upper and lower boundaries of the permutation-based envelopes.

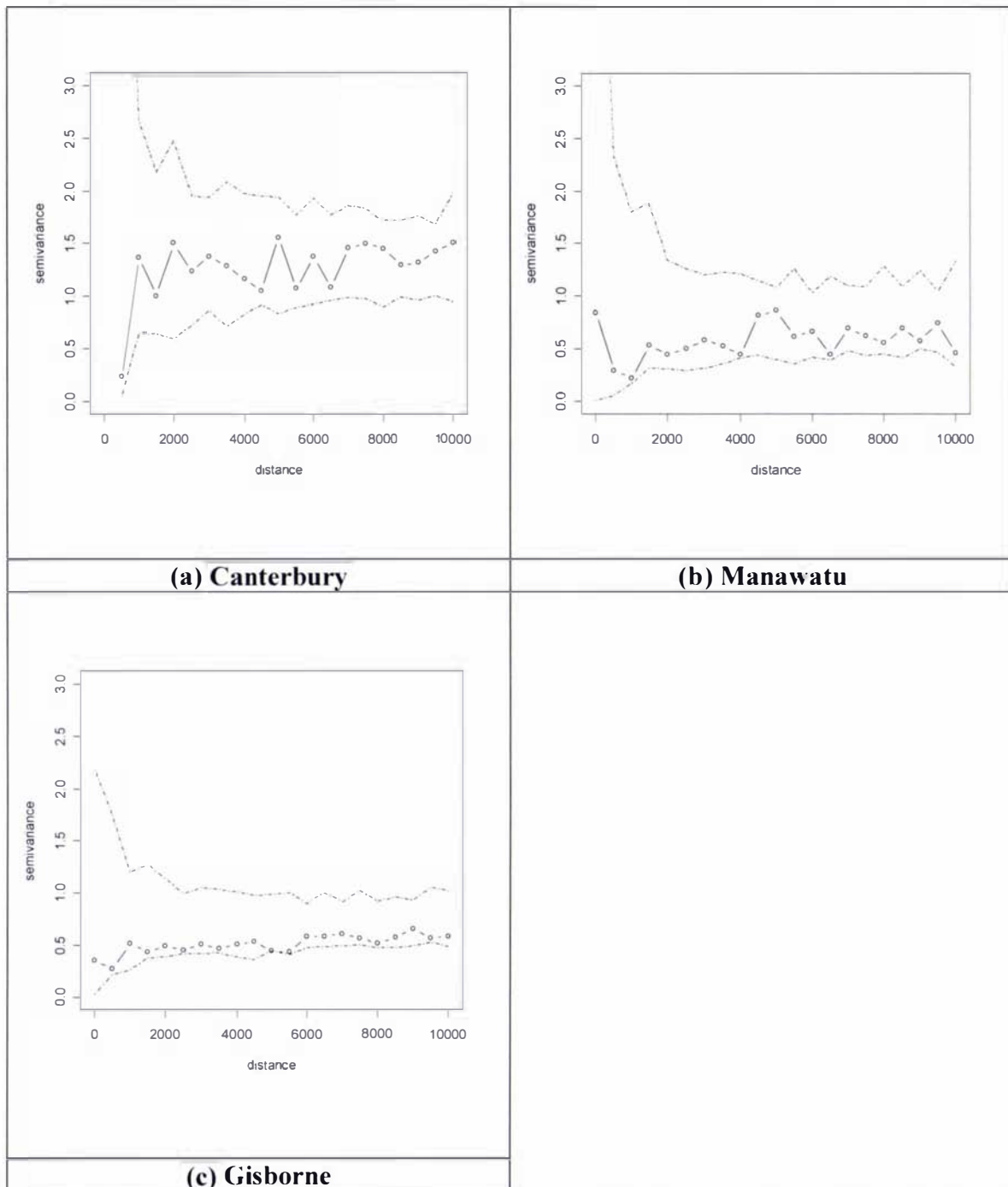


Figure 3.6: Pneumonic lesions in lambs slaughtered in three regions of New Zealand, December 2000 to September 2001. Binned omnidirectional variograms computed using the standardised residuals from the multilevel model for flocks in: (a) Canterbury, (b) the Manawatu, and (c) Gisborne.

3.4 Discussion

This was a cross-sectional observational study of 1,899,556 lambs submitted for slaughter from three New Zealand slaughter plants (Canterbury, the Manawatu, and Gisborne) between December 2000 and September 2001. The supply pattern of lambs over the study period was similar among the three regions, with the exception of Canterbury, in January, where the proportion of lambs supplied was twice that of Manawatu (there were no records for Gisborne in January). In Gisborne, a larger proportion of lambs were supplied later in the season compared with Canterbury and the Manawatu. This was perhaps due to less intensive sheep farming systems associated with steeper terrain in the Gisborne region. No data were available for Canterbury in December, or for Gisborne in December and January, due to the inability to implement data collection and inspector training in more than one region simultaneously. December and January are typically months of low pneumonia prevalence (Davies et al., 1980a; Pfeiffer et al., 1983; Goodwin et al., 2004), and it is our belief that prevalence estimates for Canterbury and Gisborne should not have been unduly biased because of this.

Only one other study has made regional comparisons of pneumonia prevalence in New Zealand involving a large number of flocks. In 1997, Black estimated the prevalence of pneumonic lesions in lambs ($n = 9,400$) in 7 regions throughout New Zealand. In this study a lamb was classified as pneumonic if greater than one quarter of one antero-ventral lung lobe had red/grey consolidation and fibrinous plural exudates were present. Regional differences were not identified in this study since data were collected over a one month period. In this study we believe data are more representative of the underlying population, as all flocks supplying these plants were included over an extended period (10 months) and a substantial number of lambs were monitored (1.8 million compared with 9400 in the study of Black, 1997). The multilevel model described in this study showed moderate to severe pneumonia prevalence varied among regions, with significantly lower levels in the Manawatu and Gisborne, compared with Canterbury.

It has previously been assumed that pneumonia is a widespread problem in New Zealand sheep flocks. Descriptive statistics from the current study support this assumption, where the true mean pneumonia prevalence of a large sample of flocks ($n = 2241$) was 26% (95% CI 25%, 27%).

The temporal pattern of moderate to severe pneumonia prevalence was similar in the Manawatu and Canterbury, although the Canterbury prevalence was slightly higher from February onwards. In Gisborne, the peak of moderate to severe pneumonia prevalence occurred abruptly, rising from 9% in February to 18% in March. In the two other regions the peak of pneumonia prevalence showed a steadier increase from December and January to May. It is likely that some characteristic of the environment or farm management system could be responsible for this peak (such as steeper terrain, higher temperatures, earlier lambing/weaning dates), though insufficient data were available in this study to investigate these possibilities further. It is equally likely, that the peak of pneumonia prevalence could have been a spurious result, but this possibility cannot be confirmed without evaluating pneumonia prevalence over multiple seasons.

The validation of meat inspector diagnosis demonstrated, due to low sensitivity, that a significant amount of pneumonic lesions present at slaughter were not detected. The detection of moderate to severe pneumonia was more reliable than that of minor pneumonia, as reflected by the sensitivity of these diagnoses (Table 3.2). A low sensitivity of pneumonia diagnosis (0.26) in pigs at slaughter has also been reported (Elbers et al., 2003). This suggests that visual assessment of pneumonic lesions by meat inspectors at slaughter is an inaccurate diagnostic tool and the development of a more objective method for diagnosing pneumonia at the time of slaughter would provide greater accuracy. In a study of pleurisy diagnoses by meat inspectors at four processing plants throughout New Zealand, Van der Logt (1996) found that the sensitivity of detecting major pleural lesions was higher compared with minor pleural lesions. In the current study, apparent pneumonia prevalence was adjusted according to the calculated sensitivity and specificity values from a validation of meat inspector diagnosis. Due to the low sensitivity of pneumonia diagnosis, the estimate of apparent prevalence substantially under-estimated the true prevalence. A significant amount of slaughter lines (49.8%) had an apparent prevalence of zero hence the true prevalence was also zero. Some of these were false negative diagnoses due to the low sensitivity resulting in an under-estimated true prevalence. The formula adjusting apparent prevalence is applicable for small deviation of sensitivity and specificity from unity or when either sensitivity or specificity is close to one (Rogan and Gladen, 1978). When test sensitivity is very low, true prevalence estimates can numerically become greater than 100%. In this study, true prevalence was greater than 100% for 2% of the

mobs in categories of moderate to severe pneumonia, and for 9% of the mobs for total pneumonia. However, we believe the resulting bias was small and acceptable. The 95% confidence intervals calculated for true prevalence were under-estimated in this study due to the uncertainty of sensitivity, specificity and apparent prevalence. The work of Rogan and Gladen (1978) did not consider the combined uncertainties about apparent prevalence, sensitivity and specificity. Thus we could not provide adjusted estimates of variability for true prevalence.

Another source of bias occurred as meat inspectors would have been more conscientious than usual during the validation period, on account of the validation personnel present. As a result, it is likely that the sensitivity of diagnosis outside of the validation period was actually lower than that calculated, resulting in an underestimate of true pneumonia prevalence. Ideally, the validation should have been conducted without the inspectors' knowledge. This was not possible as the operator carrying out the validation was known to the inspectors from the training period before data collection commenced.

ASURE New Zealand Ltd. do not have contractual agreements to monitor and report the presence of pneumonia in slaughtered lambs, but were willing to carry out data collection for this study without reimbursement. While this was a cost effective way for obtaining details of lung condition for a large number of lambs, the disadvantage was that incentive to perform the task to a high standard was not present. We conclude that meat inspector diagnosis of pneumonia in lambs is a potentially useful surveillance tool, providing sensitivity and specificity of diagnosis are evaluated in order to estimate the true prevalence. Individual inspectors may have to be evaluated, due to the high subjectivity of the diagnosis, to enhance the accuracy of true prevalence estimates. This would ideally occur on several occasions through the season. Such evaluations would need to be conducted without inspector's knowledge to reduce bias. More frequent validation periods and additional training sessions may help to increase the sensitivity of diagnosis. If the validation were conducted at times of lower pneumonia prevalence the sensitivity of diagnosis is likely to have been higher resulting in overestimates of true prevalence.

The intra class correlation coefficient derived from a multilevel analysis provided a measure of the correlation between observations from the same hierarchy in the data. There were two hierarchies or levels in this study; mob-level and flock-level. Greater

variation in lamb pneumonia prevalence occurred between mobs within flock (variance = 1.83) than between flocks (variance = 0.73). This indicates that lamb pneumonia assessed at the mob level at slaughter is not a reliable representation of pneumonia patterns from a flock, after adjusting for processing plant and month. Therefore, feedback of pneumonia levels from processing plants to producers is unlikely to be worthwhile due to the large variability of pneumonia levels between mobs. While we are relatively confident our prevalence estimates are robust at the regional level (due to the large number of lambs included in those estimates), the sensitivity of diagnosis was probably much more variable at mob level (due to low number of lambs in several mobs) and was therefore a possible explanation for increased variation in pneumonia prevalence at mob level compared to farm level. Consequently, the relatively high ICC at mob level could have been caused by the lack of accurate lung scoring at the processing plants. However, it appeared difficult to overcome this system immanent problem, considering that continuous training of meat inspectors on-the-job might be hard to realise. Another drawback of recording pneumonia at processing plants is that these lambs are purposively selected for slaughter (based on liveweight and body condition), so pneumonia levels are unlikely to reflect the true pneumonia status of the flock. In the absence of live-animal diagnostic tests, the most accurate estimate of pneumonia prevalence of a flock would be selection of random samples of lambs for slaughter.

Nationwide strikes by MAF veterinarians in February may have resulted in a biased selection of mobs presented for slaughter during this phase of the study. Selection bias is the error of distorting a statistical analysis due to the methodology of how the samples are collected. The February estimates of pneumonia prevalence may not have been accurate, although, the period was only short (4 – 5 days). The result of the strike was that lambs scheduled for slaughter at that time, would have had a delayed slaughter date, as would all other lambs scheduled for slaughter subsequent to the strike until the back log was cleared.

Pneumonia prevalence may be determined by flock-level factors able to be controlled by farm managers, or by environmental factors (such as climate and geography), which are generally not able to be controlled. Contour plots (Figure 5) showed that the incidence risk of pneumonia throughout each study region was not constant. Cluster analyses identified a significant cluster of high prevalence flocks in the Canterbury study region. This significant cluster of case flocks was identified based on raw data, without controlling for

possible confounders. Binned variograms for each region showed that second order spatial autocorrelation in the distribution of case flocks was not present after adjusting for the fixed and random effects in the multilevel analysis (Figure 6). These findings indicate that within a region, factors operating at the flock level are more important determinants of pneumonia prevalence compared with environmental factors. Differences in pneumonia prevalence found between regions in the multilevel analysis (Table 3.4) may have been attributable to climatic differences. However, showing an association between climate and pneumonia prevalence is problematic because pneumonia status can only be assessed at slaughter, whereas climatic variables may be assessed daily for every month of the growing period.

A limitation of these spatial analyses is that farm centroid co-ordinates were used as location indicators for flocks. The distance between farm centroids, therefore, is dependent on farm size. An alternative method would be to use an area or polygon where discrete areas are spatially referenced by an adjacency matrix defining each neighbouring area.

3.5 Conclusions

We present analyses from an extensive database of lamb pneumonia levels recorded by meat inspectors at slaughter in three New Zealand regions throughout 2000 and 2001. Validation of diagnosis showed sensitivity to be low and specificity high, therefore, the true pneumonia prevalence of the population was under-estimated. Multilevel analysis of the data identified a significantly lower odds of moderate to severe pneumonia in Manawatu and Gisborne lambs compared with Canterbury lambs and a significantly higher odds of pneumonia in lambs slaughtered from March to May, compared with those slaughtered in December. Greater variation of pneumonia levels occurred between mobs within flocks, than between flocks. The higher ICC at mob level than at flock level suggested that due to greater variation occurring within flocks, meat inspector diagnosis of pneumonia at slaughter would not reliably represent true flock pneumonia levels unless sensitivity of diagnosis was higher. A significant cluster of case flocks was found in the Canterbury region based on the raw data, but no spatial autocorrelation was evident between case flocks in any region after adjusting for the fixed (processing plant, month)

and random (clustering at mob and flock level) effects of the multilevel model. In conclusion, factors operating at the flock level, within the control of farm managers, seem to have a more important influence on lamb pneumonia prevalence than environmental effects such as climate and geography.

Case-control study of lamb pneumonia

4.1 Introduction

In New Zealand sheep are traditionally grazed on pasture throughout the year, often with supplements of hay or silage in the winter. Ewes are mated in autumn and lamb in spring with lambs being weaned at approximately 100 days of age. Chronic non-progressive pneumonia (CNP) is a common, sub-clinical disease of lambs in New Zealand leading to substantial production loss through reduced growth rate and a predisposition to pleurisy. The latter often leads to a devaluation of lamb carcasses at processing plants. Acute pneumonia (AP) occurs sporadically and often results in mortality, but impaired production due to persisting CNP also occurs. Pneumonia is a multi-factorial disease believed to involve a range of microbial agents, host factors, farm management practices, and environmental factors (Bruere et al., 2002). The complex causal factors for pneumonia are poorly understood and effective control measures not well defined.

Vaccination and antibiotic treatment are options to control pneumonia in lambs, but both have limitations. Vaccination has only been partially effective because the microorganisms involved in the disease process are extremely variable both in species and strains. Vaccine trials under controlled conditions usually involve experimental challenge, while trials under natural challenge conditions have either not been conducted or failed to show protective efficacy probably due to the large variation in the microflora involved in the pathogenesis of pneumonia (Alley and Marshall, 1970; Alley, 1975; Davies et al., 1980a; Davies, 1985a; Davies and Jones, 1985; Pfeffer, 1986; Cullinane et al., 1987; Black, 1997; Alley et al., 1999). Trials investigating the efficacy of antibiotics have typically involved sheep with acute pneumonia (Alley and Clarke, 1980; Gilmour et al., 1982c; Stipkovits et al., 1985; Appleyard and Gilmour, 1990; Gilmour et al., 1990; Sadiq et al., 1993; Sargison and Scott, 1995). In New Zealand, Alley and Clarke (1980) showed that the treatment of acute pneumonia in lambs with antibiotics suppressed the development of pneumonic lesions (Alley and Clarke, 1980), resulting in partial recovery

and persistent sub-clinical disease. The efficiency of antibiotics to reduce the duration and spread of CNP in lamb flocks is limited by the difficulty to detect the disease in live animals. Other reasons limiting the value of antibiotic use include antibiotic residues in meat, development of antibiotic resistance and high cost.

Preventive measures related to farm management practices suggested in the literature for the control of pneumonia are largely based on first principles and anecdotal evidence (Davies, 1985b; Alley, 1991; Brogden et al., 1998; Bruere et al., 2002). These include the prevention of contact between ewes and weaned lambs in common pens at night, avoiding contact between hands and the nasal area of lambs when drenching (Alley, 1991), avoiding yarding and mustering under hot and dusty conditions (Davies, 1985b; Alley, 1991; Bruere et al., 2002), minimising stress for lambs and hoggets, minimising driving distance, use of sprinkler systems in yards to reduce dust in the yards, controlling dogs when they are not working around sheep that are yarded (Bruere et al., 2002) and maintaining a high general health standard (Davies, 1985b; Bruere et al., 2002). Little is known about the impact of these various management practices on pneumonia.

This study uses a case-control design by comparing management practices of farms with high pneumonia prevalence to farms with low pneumonia prevalence. To our knowledge, no case-control studies were reported as yet that have evaluated the effect of farm management practices on CNP in New Zealand lambs. The identification of both hazardous and advantageous management practices is the first step in the development of control measures to reduce the incidence of lamb CNP. The aim of the current study was to examine the association between management practices and lamb pneumonia using a case-control design.

4.2 Materials and Methods

Case-Control flocks

Sampling and analysis was done at flock level. Flocks were selected from data collected by meat inspectors of ASURE New Zealand Ltd. at processing plants in three regions (Canterbury, Manawatu and Gisborne), examining slaughter lambs from December 2000 to May 2001. The lungs of every lamb processed were scored for pneumonia by meat inspectors at each plant ($n = 1,305,838$ lambs in 6,940 slaughter lines from a total of 2,154

flocks). In Manawatu and Gisborne at meat inspection, pneumonia tickets were put on carcass hooks and data entered into a database at carcass weighing. In Canterbury, the pneumonia scores went directly into a database via a touch screen at meat inspection. The majority of pneumonia diagnosed at slaughter was presumed to be CNP although some residual lung lesions from recovered AP may also have been present. Each lung was classified into one of three categories: no pneumonia, mild pneumonia (< 10% of lung surface area affected) and moderate to severe pneumonia (\geq 10% lung surface area affected). To ensure consistency of classification across processing plants ASURE New Zealand Ltd. meat inspectors were provided with reference photographs before December 2000, the start of the data collection period.

The eligible flocks were those that supplied lambs to single processing plants in Canterbury ($n = 702$ flocks), Manawatu ($n = 1,066$ flocks) and Gisborne ($n = 386$ flocks) from December 2000 to May 2001. The study flocks were eligible flocks supplying ≥ 100 lambs in total (regardless of the number of slaughter lines), to Canterbury ($n = 593$ flocks), Manawatu ($n = 795$ flocks) and Gisborne ($n = 251$ flocks) processing plants between December 2000 and May 2001.

A histogram of lamb pneumonia prevalence was plotted of all eligible flocks. A lower threshold of $\geq 3\%$ flock prevalence of moderate to severe pneumonia prevalence was visually determined to define case flocks. This was equivalent to the 75th percentile of flock prevalence while zero prevalence flocks included the 33rd percentile of all flocks in the ASURE database. To increase the statistical power of the study the target ratio of control to case flocks was 2:1. Control flocks had zero moderate to severe pneumonia prevalence. The distribution of the total lambs supplied for control flocks was matched approximately to the equivalent case flock distribution, to make the populations as similar as possible, in order that appropriate comparisons could be made. A limited number of control flocks compared to case flocks in Canterbury resulted in a ratio of control to case flocks of 1:1. In Manawatu and Gisborne, the ratio of control to case flocks was 3:1. Region was therefore included in all multivariate analyses to control for confounding. Flocks with moderate to severe pneumonia up to 3% were excluded from the study.

Farm Questionnaire

A questionnaire of farm characteristics and management practices was compiled. It was tested by mailing it to 10 farm managers who were then interviewed face to face. Following slight changes for ease of filling in the questionnaire it was mailed to 492 farm managers whose flocks fitted the selection criteria for case ($n = 192$) or control flocks ($n = 300$). The questionnaire (Appendix 1) included the variables summarised in Table 4.1.

Data analysis

Composite analysis

Variables were individually compared to the case-control status of a flock using chi-squared tests for categorical and independent samples t-tests for continuous variables. Variables significant at $p \leq 0.250$ were included in further multivariate analysis using logistic regression with case (1) or control flock (0) as the dependent variable. Region, stocking rate, and farm area used for grazing sheep were included in a base model as likely confounders. Other variables were added to the base model in a forward selection process; at each step, models were compared using the log-likelihood ratio test of the larger versus the smaller model (Hosmer and Lemeshow, 2000) if $p \leq 0.05$. Finally, variables that were initially not associated with the case-control status ($p > 0.250$), and therefore excluded from the stepwise selection process, were added to the best model to re-evaluate their relationship to the case-control outcome. Odds ratios and 95% confidence intervals were calculated from final model coefficients.

Path Analysis

Path analysis was used to test hypothesised relationships among risk factors in order of time and between risk factors and the outcome (case-control status). Risk factors were ordered in three subsequent event clusters: (i) from mating to lambing, (ii) from lambing to weaning, and (iii) from weaning to slaughter. A path coefficient or odds ratio indicates the direct effect of a variable on the next variable in order of time until the outcome was reached. Thus, a network of cause and effects was constructed. For example, variables not significant in the composite analysis might have indirect effects on the outcome, by their effects on other variables that were directly associated with the outcome. Management events were ordered in time from ewe mating to the sale of their offspring, with each variable having the opportunity to be represented in the path model as a dependent or independent variable. A null path model was initially constructed including all

hypothesised relationships between variables in the data. Individual hypothesised relationships in the null path model were then tested by a series of regression analyses (linear, logistic and ordinal) depending on the nature of the dependent variables, in chronological order of the farm management events. Variables were retained in the final path model at $p \leq 0.05$. Exogenous variables (that is those not hypothesised as a cause, but having potential confounding effects: region, ewe breed, stocking rate and farm area) were included in all models.

4.3 Results

Composite analysis

The response rates of questionnaires from 300 control flocks and 192 case flocks were 60.3% ($n = 181$) and 68.8% ($n = 132$), respectively. The difference between response rates was marginally significant ($p = 0.058$). A summary description of the variables in the questionnaire is shown in Table 4.1. Table 4.2 shows descriptive and univariate statistics for continuous variables significant at $p \leq 0.250$. Of those, variables significant at $p \leq 0.05$ were related to flock size (number of ewes, number of lambs weaned and sold), duration of weaning, time of year lambs were sold, average slaughter age of lambs and lamb shearing (Table 4.2). Likewise, Tables 4.3a and 4.3b show statistics of categorical variables significant at $p \leq 0.250$. Categorical variables significant at $p \leq 0.05$ were related to flock replacement policy, sheep breed, farming enterprise, hogget mating, supplementary feeds for pregnant ewes, vaccination of ewes prior to lambing and lamb disease, feed source and grazing system between weaning to slaughter.

Table 4.1: Summary description of variables from a retrospective questionnaire (for 2000/2001 season) mailed to study flocks in 2002.

Section	Details
Farm details	Total area, sheep grazing area, no. paddocks for sheep, farm enterprise (sheep, beef, cropping, deer, dairy grazing, other), % land area used per enterprise
Labour on farm	Average number of people working on farm per annum
Flock size	Numbers of sheep wintered in 2000
Sheep breeds	Fine wool breeds, Romneys (and Romney crosses), other breeds
Sheep categories	Sex (male/female), age (lamb, hogget, ewe)
Farm topography	Flat, flat-rolling, mixture of flat and hill country, moderate-steep hill country
Ewe mating	
Dates and weights	Dates of mating and average ewe weight (if recorded), by age class
Scanning	Pregnancy scanning percentages by age class
Feed types to pregnant ewes	Pasture, hay, silage, grain, crop or other and months fed
Ewe shearing	Dates shorn in 2000 by age class
Ewe vaccination	5 in 1, Androvax, Eweguard, Campylobacter, Salmonella, Toxoplasma
Lambing	
Grazing management	Shifts every 2-5 days, 6-10 days, >10 days but not set stocking or set stocking
Shelter availability	Nil, low, moderate, high
Stocking density	Single bearing, multiple bearing, or all ewes (ewes/ha)
Tailing	
Tailing dates	Start and finish dates by ewe age class
Tailing/castration methods	Rubber rings, hot iron, knife, crypt, burdizzo, other Percentages ram lambs castrated, crypt orchid, or entire
Health treatments to lambs	Scabby mouth, fly, internal parasite, Vitamin B12, clostridial vaccine, other
Tailing to weaning	
Stocking density	Single bearing, multiple bearing, or all ewes (ewes/ha)
Water sources	Running, surface, dam, underground, dam, bore, spring, other
Health treatments to lambs	Internal parasite drench, Vitamin B12, other
Weaning	
Numbers and dates	Number/percentage of lambs weaned and dates, average weights (if recorded)
Treatment events	Crutching, shearing, drenching, dipping, vaccination, fly treatment, other
Lamb dipping method	Wand, pour-on, shower, spray, race
Duration	Hours lambs spent in yards and/or shed
Post weaning	
Lamb purchases	Number of lambs purchase and number of sources purchased from Numbers bought per month
Lamb selling	Number of lambs sold in 2000/2001 by month and destination
Internal parasite drenching	Frequency (4 weekly, 5 weekly, 6 weekly, other)
Fly strike treatment	Methods (spray, shower, pour-on, wand, race, spot treatments)
Shearing and crutching	Dates of shearing and crutching of lambs
Feed types available	Perennial ryegrass/clover pasture, annual ryegrass/clover pasture, crop, other
Grazing management	Break feeding, shifts daily, 2-5 days, 6-10 days, >10 days, set stocking
Mustering lambs	Motorbike, truck, tractor, horse, foot, other
Use of dogs	Dog use for shifting lambs, in yards/shed on lambs
Water sources	Running, surface, dam, underground, dam, bore, spring, other
Shelter availability	Nil, low, moderate, high
Type of sheep yards	Not covered, partially covered, totally covered
Health problems	Abnormal death, ill-thrift, scours, nasal discharge, cough, fly strike, facial eczema, scabby mouth, lame, staggers, pneumonia (month, severity, % flock)
Ewe replacement policy	Bred on farm or not (age of purchase, sources purchased from)
Ewe replacement purchases	Age of purchase, sources of purchase
Ram buying-in practices	How many studs replacement sires and/or terminal sires purchased from
Pneumonia in older sheep	Age class, number of deaths, time of year

Table 4.2: Descriptive and univariate statistics of continuous variables grouped by time period (significant at $p \leq 0.250$) for case and control flocks.

Variable	Cases (n, mean, SD)			Controls (n, mean, SD)			p
<i>Time independent:</i> Number of paddocks	132	42	30	177	35	30	0.051
<i>Mating to Lambing</i>							
Mixed age ewes scanning %	63	158.3	16.7	82	152.9	18.3	0.065
2-tooth ewes scanning %	47	146.6	17.2	50	141.0	20.3	0.148
Number of 2-tooth breeding ewes	132	505	493	181	339	410	0.072
Number of mixed age breeding ewes	132	1738	1435	181	1448	1357	0.002
Total breeding ewes	132	2020	1760	181	1890	1800	0.026
Average days ram out with ewes	127	54.9	25.3	171	58.6	23.3	0.196
<i>Lambing to Weaning</i>							
Lambing percentage	128	117.9	17.9	176	115.4	19.4	0.240
<i>Weaning</i>							
Number of lambs weaned	112	2807	2296	146	2157	1709	0.010
Hours in yards at weaning	124	8.0	6.9	167	5.9	5.9	0.005
Hours in shed at weaning	42	9.3	5.9	58	7.0	6.4	0.065
Hours in yards/shed at weaning	127	10.9	9.4	176	7.9	7.8	0.003
<i>Post weaning to slaughter</i>							
Number of lambs bought in December	132	186	949	181	64	396	0.122
Number of lambs bought in January	132	130	661	181	37	142	0.068
Number of lambs bought in April	132	13	61	181	45	253	0.160
% lambs bought in December	132	9.3	25.3	181	4.2	16.5	0.031
% lambs bought in June	132	0.9	4.3	181	0.3	2.4	0.138
Number of Lambs sold	132	2471	2301	181	1751	1470	0.001
% lambs on hand July 1/lambs weaned	128	27.1	72.1	176	17.8	31.3	0.129
% lambs sold per month:							
October	132	1.5	5.3	181	2.8	7.5	0.081
November	132	5.0	9.2	181	8.9	13.8	0.006
December	132	10.2	13.2	181	15.1	16.5	0.006
January	132	15.0	12.2	181	21.7	18.3	0.000
February	132	16.1	12.1	181	13.9	13.5	0.148
March	132	23.3	14.8	181	15.8	15.5	0.000
April	132	16.6	13.1	181	13.8	18.2	0.128
May	132	12.3	14.5	171	8.1	11.6	0.005
Average slaughter age of lambs	125	180.5	26.0	171	168.2	32.7	0.001
Average shearing date for lambs	105	408	50.1	124	388	43.4	0.001
Average crutching date for lambs	78	23 Jan	59.5	104	10 Jan	54.2	0.148
Average age of lambs when shorn	129	119.6	71.7	176	95.1	73.6	0.004
Percentage lambs sold Oct to Feb	130	52.2	24.5	181	37.7	27.3	0.000
Percentage lambs sold Mar to May	130	47.8	24.4	181	27.2	24.4	0.000

Table 4.3a: Control and case flock frequency (n) and odds ratios (OR) with 95% confidence intervals (95% CI) for categorical time independent mating to lambing variables ($p \leq 0.250$).

Variable	Levels	Controls (n)	Cases (n)	OR (95% CI)
<i>Time Independent</i>				
Region	Canterbury	83	90	reference
	Manawatu	74	28	0.35 (0.21, 0.59)
	Gisborne	24	14	0.54 (0.26, 1.11)
Ewe replacements	Bred on farm	107	107	3.45 (1.96, 6.07)
	Not bred on farm	69	20	reference
	Missing	5	5	
Ewe replacements	Bought as mixed age ewes	53	17	0.36 (0.19, 0.65)
	Not bought as mixed age ewes	128	115	reference
Replacement ewes bought from	0 sources (not bought)	133		
			113	reference
	1 source	16	10	0.73 (0.32, 1.68)
	2 sources	13	5	0.45 (0.16, 1.31)
	≥ 3 sources	19	4	0.25 (0.82, 0.75)
Terminal sire rams bought from	0 sources (not bought)	125		
			105	reference
	1 source	26	5	0.23 (0.09, 0.62)
	≥ 2 sources	22	17	0.92 (0.46, 1.82)
Breeding ewe type	Missing	8	5	
	Fine wool type	20	2	reference
	Romney and crosses	90	73	8.11 (1.84, 35.85)
	Other	66	53	8.03 (1.80, 35.91)
Ram type	Missing	5	4	
	Fine wool type	4	1	reference
	Romney and crosses	32	36	4.50 (0.48, 42.37)
	Coopworth and crosses	8	10	5.00 (0.46, 54.04)
	Suffolk and crosses	20	3	0.60 (0.05, 7.35)
	Other	90	63	2.80 (0.31, 25.65)
Farming enterprise	Missing	27	19	
	Sheep	114	100	reference
	Beef	23	6	0.30 (0.12, 0.76)
	Deer, dairy grazing, other	11	1	0.42 (0.18, 0.97)
	Cropping	11	7	0.88 (0.44, 1.75)
Sheep yards used	Missing	22	18	
	Not covered	118	65	reference
	Covered	63	67	1.93 (1.22, 3.05)

Table 4.3a continued: Control and case flock frequency (n) and odds ratios (OR) with 95% confidence intervals (95% CI) for categorical time independent mating to lambing variables ($p \leq 0.250$).

Variable	Levels	Controls (n)	Cases (n)	OR (95% CI)
<i>Mating to Lambing</i>				
Hogget ewes	Not mated	140	88	reference
	Mated	41	44	1.78 (1.09, 2.95)
Pregnant ewes	Not fed haylage	133	74	reference
	Fed haylage	43	54	2.26 (1.38, 3.69)
	Missing	5	4	
Pregnant ewes	Not fed crop	120	69	reference
	Fed crop	56	59	1.83 (1.15, 2.93)
	Missing	5	4	
No. pregnant ewe feed sources	0	92	43	reference
	1	41	34	1.77 (0.99, 3.17)
	≥ 2	43	51	2.54 (1.47, 44.37)
	Missing	5	4	
Breeding ewes	Not vaccinated	61	31	1.00
	Vaccinated before lambing	115	97	1.66 (1.00, 2.76)
	Missing	5	4	
Dogs	Not used with lambs	28	28	reference
	Used with lambs	152	104	0.68 (0.38, 1.22)
	Missing	1	0	

Table 4.3b: Control and case flock frequency (n) and odds ratios (OR) with 95% confidence intervals (95% CI) for categorical variables from lambing to slaughter ($p \leq 0.250$).

Variable	Levels	Controls (n)	Cases (n)	OR (95% CI)
<i>Lambing to Weaning</i>				
Castration method	Rubber rings	46	30	reference
	Crypt or burdizzo	38	39	1.57 (0.83, 2.99)
	None (left entire)	83	51	0.94 (0.52, 1.65)
	Missing	14	12	
Lambs at tailing	Not treated against fly	108	89	reference
	Treated against fly	73	43	0.69 (0.43, 1.11)
Lambs at tailing	No internal parasite drench	153	120	reference
	Internal parasite drench	28	12	0.50 (0.24, 1.04)
Running water available	Absent	32	31	reference
	Present	144	97	0.70 (0.40, 1.21)
	Missing	5	4	
<i>Weaning</i>				
Lambs at weaning	No ectoparasite treatment	97	85	reference
	Ectoparasite treatment	84	47	0.63 (0.4, 1.01)
Lambs at weaning	Not shorn	154	102	reference
	Shorn	23	28	1.84 (1.00, 3.37)
	Missing	4	2	
Lambs at weaning	Not mineral drenched	169	116	reference
	Mineral drenched	4	8	2.91 (0.86, 9.9)
	Missing	8	8	
Lambs at weaning	Not given B12 supplement	154	119	reference
	Given B12 supplement	22	9	0.52 (0.23, 1.18)
	Missing	5	4	

Table 4.3b continued: Control and case flock frequency (n) and odds ratios (OR) with 95% confidence intervals (95% CI) for categorical variables from lambing to slaughter ($p \leq 0.250$).

Variable	Levels	Controls (n)	Cases (n)	OR (95% CI)
<i>Post weaning to slaughter</i>				
Disease in lambs	No abnormal deaths	176	124	reference
	Abnormal deaths	5	8	2.27 (0.73, 7.11)
Disease in lambs	No ill-thrift	163	100	reference
	Ill-thrift	18	32	2.9 (1.55, 5.44)
Disease in lambs	No nasal discharge	155	123	reference
	Nasal discharge	26	9	0.44 (0.20, 0.97)
Diseases in lambs	0	110	65	reference
	1	38	36	1.60 (0.93, 2.78)
	≥ 2	33	31	1.59 (0.89, 2.83)
Lamb feed sources	Not fed perennial ryegrass	17	19	reference
	Fed perennial ryegrass	164	113	0.62 (0.31, 1.24)
Lamb feed sources	Not fed annual ryegrass	120	96	reference
	Fed annual ryegrass	31	36	1.82 (1.05, 3.13)
Lamb feed sources	Not fed crop	130	86	reference
	Fed crop	51	46	1.36 (0.81, 2.21)
Lamb grazing	Not 6-10 daily shifts	139	92	reference
	6-10 daily shifts	42	40	1.44 (0.87, 2.39)
Lamb grazing	Not >10 days	97	62	reference
	>10 daily shifts	84	70	1.30 (0.83, 2.04)
Lamb grazing	Not set stocking	132	111	reference
	Set stocking	49	21	0.51 (0.29, 0.90)
Lamb grazing	Set-stocking	49	21	reference
	>10 daily shifts	77	66	2.00 (1.09, 3.67)
	6-10 daily shifts	35	31	2.07 (1.02, 4.18)
	1-5 daily shifts or break-feeding	18	13	1.56 (0.64, 3.79)
	Missing	2	1	
Lamb water sources	No bore water available	142	95	reference
	Bore water available	39	37	1.42 (0.84, 2.38)

Eight variables remained significant in the final logistic regression model (Table 4.4). Due to missing data in questionnaires, a total of 301 flocks were included in the final model. The rate of exclusion was not significantly different between control (5/181, 2.8%) and case (7/132, 5.3%) flocks ($p = 0.248$). Odds ratios for continuous variables are presented in Table 4.4 per standard deviation of that variable. Region and ewe breed were both significant variables in the final model. However, as fine wool breeds were only present in Canterbury, breed and region were combined in one variable with seven levels. In Canterbury, flocks with Romney ewes were 12.02 times more likely to be case farms compared to flocks with fine wool type breeding ewes. Two of the strongest risk factors for pneumonia included shearing lambs on the day of weaning (OR 7.26) and breeding ewe replacements on-farm (OR 4.30). Risk factors with a smaller impact on lamb pneumonia included the number of lambs sold (OR 2.00 per 1,896 sold), and an increased percentage

of lambs sold between March and May (OR 1.52 per 27.1% lambs sold). Protective factors in order of magnitude included injecting lambs with Vitamin B12 at the time of tailing (OR 0.37), injecting lambs with Vitamin B12 at weaning (OR 0.37), and set stocking lambs after weaning (OR 0.42). A significant interaction occurred where the percentage of lambs sold from March to May increased if ewe replacement were bred on-farm. A positive interaction also occurred between the number of lambs sold and the percentage sold from March to May.

Table 4.4: Odds ratios (95% confidence interval, CI) of the final logistic regression model for flock-level management factors on lamb pneumonia (control flock: 0% moderate-severe pneumonia; case flock: $\geq 3\%$ moderate-severe pneumonia).

Variable	Levels	p	Odds ratio	95%CI
Ewe breed type and region	Fine wool breeds	-	1.00	-
	Romney (Canterbury)	0.005	12.02	2.09, 63.13
	Other breed types (Canterbury)	0.766	1.31	0.22, 7.82
	Romney (Manawatu)	0.396	2.33	0.33, 16.35
	Other breed types (Manawatu)	0.022	7.46	1.33, 41.95
	Romney (Gisborne)	0.688	0.68	0.10, 4.58
	Other breed types (Gisborne)	0.847	0.80	0.08, 8.04
Number of lambs sold [†]		0.007	2.00	1.21, 3.43
Lambs set stock grazed post weaning	Present	0.021	0.42	0.20, 0.88
	Absent	-	1.00	-
Lambs given Vitamin B12 at tailing	Present	0.005	0.37	0.19, 0.74
	Absent	-	1.00	-
Lambs given Vitamin B12 at weaning	Present	0.014	0.37	0.10, 0.77
	Absent	-	1.00	-
Lamb shearing	Not shorn	-	1.00	-
	Shorn at weaning	0.000	7.26	2.75, 19.21
	Shorn after weaning	0.324	1.39	0.72, 2.67
Percentage lambs sold from March to May		0.009	1.52	1.11, 2.08
Sheep flock breeds own replacement ewes [‡]	Present	0.000	4.30	2.09, 8.87
	Absent	-	1.00	-

-2 Log Likelihood test statistic 293.277; 16 df; $p < 0.001$

[†] Interpretation: If for example, a flock sold 3792 lambs compared to another flock selling 1896 lambs, the first flock was $3792/1896 = 2.00$ times more likely to be a case flock

[‡] Interpretation: compared with sheep flocks that do not breed their own ewe replacements, after adjusting for other variables in the model, sheep flocks that breed their own ewe replacements are 4.3 times more likely to be case flocks

Path analysis

No effects were significant in the path model that occurred between mating and lambing. This period was therefore omitted from Figure 4.1. Shearing lambs at weaning was a risk factor for pneumonia compared to shearing lambs after weaning, or not shearing lambs at all. When lambs were shorn at weaning, they spent more time in the yards on the day of weaning. The time lambs spent in yards on the day of weaning (not a significant risk factor for case flocks) was related to shearing lambs at weaning (a significant risk factor for case flocks) and was therefore a significant indirect path to the case or control flock outcome. Lambs shorn at weaning were weaned later in the season than lambs not shorn at weaning, and lambs were far more likely shorn at weaning in Manawatu and Gisborne than Canterbury.

Set stock grazing of lambs after weaning was a protective factor for pneumonia and was more likely on flat farms than those with flat to rolling topography. The other classifications of topography (mixture flat and hill country, moderate to steep hill country) were not significantly associated with set stocking. Flocks in which lambs were bought after weaning were not as likely set stock grazed as flocks not buying lambs.

Lambs from flocks breeding their own ewe replacements (risk factor for pneumonia) spent longer in the yards on the day of weaning suggesting that they were more likely to be shorn at weaning although this relationship was not directly significant. These flocks were also less likely to purchase lambs, had an increased average slaughter age of lambs, sold a reduced number of lambs and were more likely to have an ill-thrift problem in lambs.

Flocks given Vitamin B12 supplementation at tailing were less likely to be case flocks and no other variables were significantly related to this treatment. At higher stocking rates it was more likely that lambs would be given Vitamin B12 supplementation at weaning which was a protective factor for pneumonia.

In Canterbury, ewes of Romney breed and other breeds were more likely to be case farms than those with fine wool breeds. Romney ewes and ewes of other breeds had higher lambing percentages than fine wool ewes in Canterbury. The average lambing date was earlier for ewes in Manawatu (21 August) and Gisborne (28 August) than those from Canterbury (8 September). Lambs from flocks with a later average lambing date had an increased average slaughter age. As would be expected, flocks with later average lambing

dates had an increased percentage of total lambs sold between March and May which was a risk factor for case flocks. The average slaughter age of lambs had a strong positive relationship to the percentage of lambs sold in March to May. The average age of lambs at slaughter was increased if weaned lambs were purchased, and this provided an indirect path to the case-control outcome through an increased percentage of lambs sold late in the season. The total number of lambs sold was a risk factor for case flocks and was affected by other indicators of flock size (number of ewes, sheep grazing area and lambing percentage).

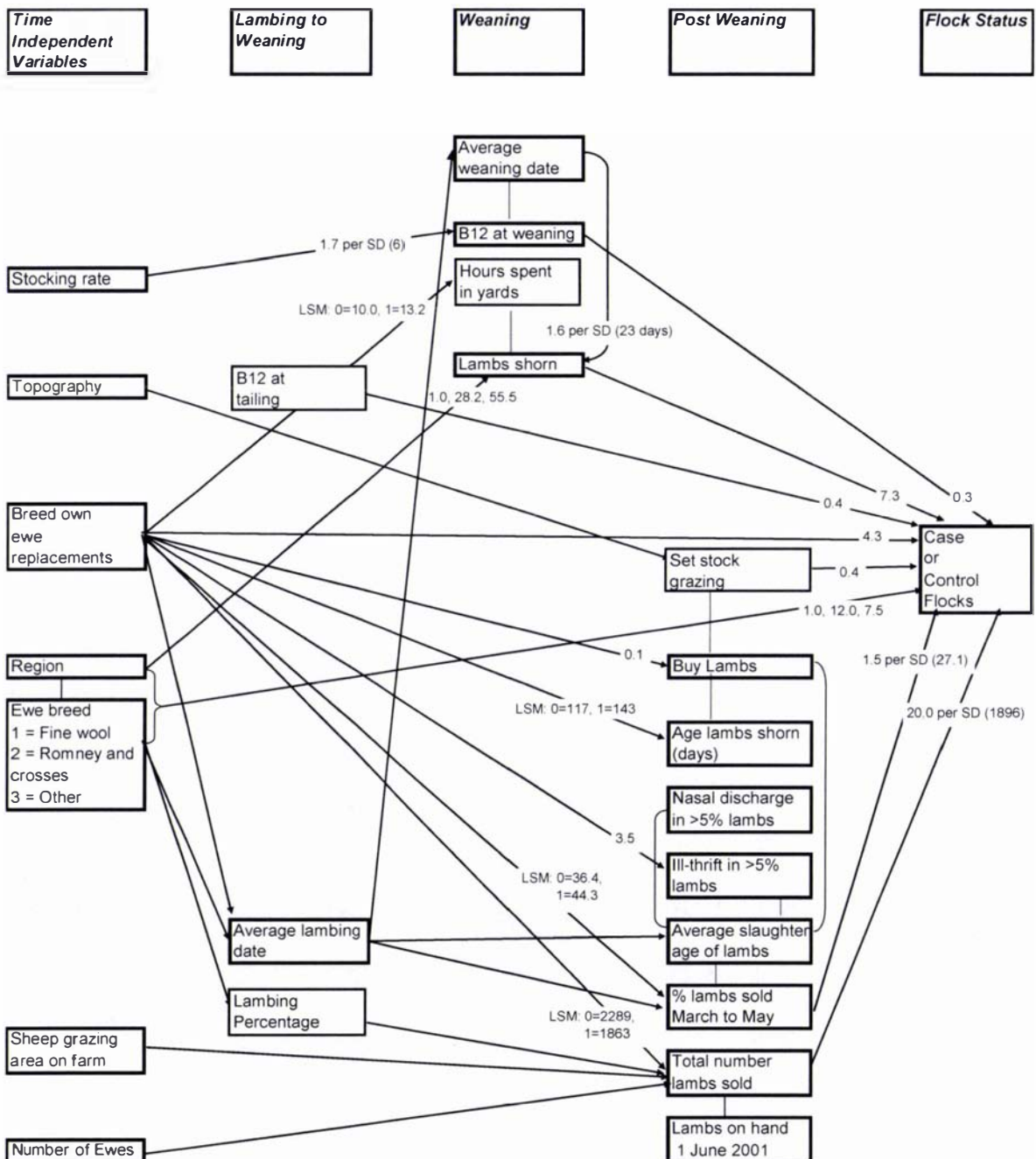


Figure 4.1: Case-control study of lamb pneumonia in three regions of New Zealand, December 2000 to May 2001. Path model showing inter-relationships between variables listed in chronological order with significant direct or indirect paths to case or control flock.

Breed own ewe replacements – properties that breed ewe replacements for flock.

Control or Case Flock – Control flock with no apparent moderate to severe pneumonia or Case Flock with $\geq 3\%$ moderate to severe pneumonia.

LSM – least square mean

4.4 Discussion

Advantages of case-control studies are that they are quick, cheap and that multiple potential exposures can be evaluated simultaneously. However, the classification of control flocks was a potential source of bias in this study because the sensitivity of meat inspector diagnosis was low (Goodwin-Ray et al., 2006b). Lungs with pneumonic lesions were misclassified as negative and therefore, some flocks were misclassified as control flocks. The selection method of lambs for slaughter also created a potential bias as farmers select lambs by weight and body condition, hence poorly conditioned lambs with pneumonia were less likely to be sent for slaughter than well developed lambs. Thus some flocks with a moderate pneumonia problem early in the season may not have been detected as a case flock. This was supported by the significantly increased average slaughter age of lambs in case flocks. As this was a retrospective case-control study there was a potential for information bias as farm managers had to recall events from the previous season. This was especially relevant for questions that required specific information such as mating, tailing, weaning dates, stocking density and numbers of ewes mated for which comprehensive records were usually not available. It was unlikely, however, that such information bias was different between case and control farmers (i.e. non-differential), as all questions were related to general farm management and not directly related to lamb pneumonia. The inferences in our study were therefore, at worst, conservative and perhaps missed existing effects, but probably did not overestimate significant associations.

The strength of our analysis was that data from only 4% of study flocks were excluded from the final model due to missing values. Most excluded farms did not have breeding ewes (finishing farms only) while the remainder were breeding only, or breeding and finishing flocks. The significant risk factor of flocks breeding their own ewe replacements was not applicable to finishing-only farms. Valid inferences were still available for finishing-only flocks for other variables.

In the Netherlands, a case-control study of subclinical lamb pneumonia showed that taking sheep to sheep fairs, purchasing sheep, and an increased flock size were associated with increased risk of occurrence of pneumonia (Dercksen et al., 1996). The suggestion was that mixing of animals from different flocks may be a potential risk through taking sheep to sheep fairs and purchasing sheep. An increased risk with increased flock size has also

often been found in epidemiological studies (French et al., 1994; Wittleberg et al., 1994; Healy et al., 2004). Dercksen et al. (1996) related this observation to either direct effects of the number of animals on disease introduction, spread and maintenance of infections within the flocks, or different management in large and small herds.

Commercial flocks in New Zealand do not commonly take sheep to fairs or shows. Therefore, these factors did not contribute to the risk of lamb pneumonia in our study. Purchasing sheep and increased flock size, however, may be potential risks for pneumonia in New Zealand sheep flocks. The composite analysis failed to identify the number of breeding ewes as a risk factor for lamb pneumonia, while larger slaughter mobs increased the risk. The path analysis showed the relationship between the number of breeding ewes and number of lambs to be significant, as would be expected. Therefore, flock size was a significant risk factor for case flocks in our study, with a relatively large effect (OR 2.04 per SD (1896)). The purchase of sheep was not significant in the composite analysis, but was significant in the path analysis. Purchasing weaned lambs increased the average slaughter age of lambs, and this, in turn, increased the percentage of lambs sold late in the season and the risk of pneumonia. This may be due to an increased exposure to pneumonia pathogens for lambs from these flocks. The path model also showed that flocks purchasing lambs were less likely to graze lambs using set stocking, a protective factor against pneumonia. Therefore, the path model revealed that lamb purchase was indirectly associated with an increased risk of pneumonia at slaughter, while this was not detected by the composite model.

A case-control study in New Zealand investigated pleurisy in lambs (Van der Logt, (1996)). Pneumonia and pleurisy have different effects on the respiratory tract but are often correlated: pneumonia predisposes lambs to pleurisy (McGowan et al., 1978; Davies, 1985a; Pfeffer, 1986). Van der Logt's study (1996) indicated drenching at a high frequency, shearing twice, high frequency of yarding after weaning, motorised means of mustering, a lake for drinking water supply, a large number of lambs on the property in July and the concentration of cattle were important risk factors for pleurisy. Protective effects included the use of a spray-on or wand for dipping, the use of cement or concrete yards, the use of troughs for drinking water and cross breeding. Only one of these effects was found to be significantly related to lamb pneumonia in our path analysis: a large number of lambs on farm late in the finishing season (June, in this study), had a strong positive effect on the number of lambs sold (risk factor for case flocks). This is not

surprising as poor growth due to pneumonia will lead to a relatively large number of lambs present late in the finishing season. Our questionnaire did not ask for the frequency of yarding after weaning, the number of cattle, or the use of cement or concrete yards. There were no significant differences in using motorised means of mustering, lamb drenching frequency, dipping method, water supply or shearing lambs twice between case and control flocks in this study.

Shearing of lambs at weaning was the strongest risk factor for pneumonia in this study. Several interrelated factors may explain the increase in risk at this time. Firstly, an increase of stress on lambs through weaning, fasting, crowding together, heat and handling may make them more susceptible to pneumonia. Weaned lambs are required to be fasted (no food or water) for at least 12 hours prior to shearing (OSH, 2004). Fasting of sheep prior to shearing ensures that soiling of wool is reduced (from close confinement of sheep in pens), easier handling by shearers and that sheep are more comfortable when being shorn. Physical and psychological stressors are capable of altering immune function in animals (Kelley, 1980, 1982, 1984; Albani-Vangili, 1985; Kelley, 1985; Siegel, 1985; Blecha, 1988) through an increased secretion of glucocorticoids, endorphins, enkephalins and catecholamines, all of which alter host defence mechanisms (Roth and Flaming, 1990). Therefore, the stressors acting at this time may temporarily exert a debilitating effect on the lamb's immune function, increasing their susceptibility to infection. Secondly, shearing at weaning also increased the time that lambs spent in the yard or shed in close confinement, resulting in high contact rates, thus an increased risk of transmission of pathogenic micro-organisms compared to lambs not shorn at weaning. This assumes that pneumonia is transmissible between lambs. Several studies on the transmission of CNP support this assumption (Alley and Clarke, 1979; Davies et al., 1982; Gilmour et al., 1982b; Jones et al., 1982; Jones et al., 1986; Jones et al., 1989; Gilmour et al., 1990; Kamil et al., 1994).

In the current study, flocks in Canterbury with mostly (e.g. >75%) Romney ewes (OR 12.0) and other breeds (OR 7.5) were more likely to be case flocks than flocks with predominantly fine wool breeds (Merino, Merino-Romney crossbreds, Corriedale). Therefore, lambs from Romney based breeding ewes may be more susceptible to pneumonia than those from other breeding ewe types. This comparison was only valid in Canterbury, as there were no flocks with a majority of fine wool ewes in Manawatu or

Gisborne. The confidence intervals for these odds ratios were wide due to a limited number of case ($n = 2$) and control farms ($n = 20$) that had mostly fine wool breeding ewes. Merinos are more heat tolerant than British breeds (Brown, 1974; Carles, 1983). Anecdotal evidence has suggested that Merinos are less susceptible to pneumonia (R. Jackson, personal communication), presumably through their increased heat tolerance. There may have been a true breed effect in the current study, or the effect could be related to different management of flocks with fine wool breeds. However, in the analysis of this study we adjusted for area of farm (hectares) and stocking rate (ewes per hectare), which would have taken account of the more extensive farms (e.g. larger area, lower stocking rate) where these breed types are commonly kept.

Several possibilities exist as to why there was an increasing pneumonia risk in flocks that breed their own ewe replacements. Firstly, from the path model it was apparent that flocks breeding their own ewe replacements had an increased percentage of lambs sold between March and May, which increased the risk for pneumonia. This could be explained by the fact that later in the season breeding flocks were likely to cull a portion lambs, initially bred as replacements, in order to only keep superior quality hoggets through the winter. One of the likely reasons to cull those lambs was poor growth due to pneumonia. Secondly, from the path model, lambs from flocks breeding their own replacements spent longer in the yards at weaning probably caused by extra time required for shearing. This direct relationship however was not significant in the path model but explained by an indirect route to shearing lambs at weaning through these flocks having a later average lambing and weaning date, which made flocks more likely to shear lambs at weaning. Univariate statistics provided support for this indirect route as 9% of flocks that did not breed replacements shorn lambs at weaning compared to 20% of flocks that did. It is typical that flocks breeding their own ewe replacements would shear only lambs of the ewe replacement breed and other lambs (usually earlier maturing 'terminal sire' breeds) would not be shorn, accounting for this relationship. Thirdly, the presence of a larger number of young, susceptible lambs on farm during times of peak pneumonia prevalence might have resulted in a higher number of diseased lambs than in flocks that did not breed their own ewe replacements. The path model suggested that the effect of breeding ewe replacements was in-part due to increased average lambing and weaning dates, increased likelihood of shearing lambs at weaning and an increased percentage of lambs sold late in the season.

Flocks selling lambs at the end of the finishing season (March to May) were more likely to be case flocks than those selling lambs earlier. Due to the chronic non-progressive development, CNP was likely to persist until slaughter whenever the disease was contracted. Recovery and complete resolution of lung lesions was unlikely to occur within the short 5-9 month growth period. Spending more time on-farm extended the time of exposure for lambs resulting in higher pneumonia prevalence at slaughter. On the other hand, retarded growth due to pneumonia extended the time lambs spent on farm because farmers tended to select lambs for slaughter based on liveweight and body condition, while retaining lambs with retarded growth due to pneumonia. Whatever the sequence of events, marketing late in the season resulted in increasing pneumonia prevalence at slaughter.

The injection of lambs with Vitamin B12 at both tailing and weaning were protective factors. Vitamin B12 is essential for the synthesis of proteins and for the metabolism of fats and carbohydrates. Cobalt is required for the production of Vitamin B12, which occurs in the ruminant stomach. Fisher and MacPherson (1986) reported that cobalt deficiency increased sheep susceptibility to bacterial infections. There may be a protective effect of Vitamin B12 on bacterial pneumonia but only in areas with cobalt deficient soils. However, it is possible that the significance of Vitamin B12 treatment could be a spurious result or a non-casual effect. It could also be a proxy variable for more conscientious, risk-averse farmers. It is therefore advisable to investigate the efficacy of preventing CNP by Vitamin B12 supplementation with a randomised clinical trial.

Set stocking as opposed to rotational grazing after weaning was associated with reduced pneumonia, possibly through a lower contact rate between lambs and decreased opportunities for cross colonisation of potential pathogens. These factors, in turn, may have an impact on lambs' susceptibility to pneumonia. If lambs are grazed in a rotation the frequency of shifts and associated stress on lambs is increased, which may increase the risk of pneumonia. Set stock grazing improves individual animal performance through the opportunity for animals to select a large proportion of their diet and a reduced exposure to internal parasites, but often at the cost of optimum pasture utilisation and quality. Rotational grazing encourages optimum pasture growth and quality and greater productivity per unit of land area. Set stocking was associated with reduced pneumonia prevalence despite a reduced pasture quality compared to rotational grazing methods.

4.5 Conclusions

This study has identified several farm-level management practices associated with flocks having high levels of pneumonia detected at slaughter. These include: (1) shearing lambs at weaning, (2) having ewe breeds other than fine wool breeds in Canterbury, (3) increased flock size and (4) breeding ewe replacements. An increased proportion of lambs sold late in the season was also a significant risk factor, but likely to be a consequence rather than cause of pneumonia. The effect of breeding ewe replacements was in-part due to increased average lambing date, weaning date, increased likelihood of shearing lambs at weaning and a greater percentage of lambs sold late in the season. Contact with other flocks through the purchase of lambs post weaning was indirectly associated with an increased risk of pneumonia. Protective factors included: (1) set stock grazing lambs post weaning and, (2) Vitamin B12 treatment of lambs at tailing and at weaning. Knowledge of these areas of risk and protection provides better focus for control efforts and provides direction for future investigative work. Possible intervention studies would better evaluate the effects of shearing lambs at weaning, fine wool breeds, set stock grazing of lambs and Vitamin B12 treatment.

Efficacy of Ovipast Plus® vaccine for pneumonia of lambs under field conditions in New Zealand

5.1 Introduction

Lamb pneumonia in New Zealand is a widespread problem leading to reduced growth rate, pleurisy and mortality in acute cases. Chronic non-progressive pneumonia (CNP), a sub-clinical form of pneumonia, results in a reduced growth rate in lambs (Alley, 1987b, a; Goodwin et al., 2004), and predisposes lambs to pleurisy. In combination, the diseases result in a large economic loss to the New Zealand sheep industry. Acute pneumonia (AP) occurs sporadically and often results in mortality but recovery with impaired production due to persisting CNP also occurs. Pneumonia is a multifactorial disease involving interactions between the host (immunological and physiological), multiple agents and the environment.

Pasteurella (Mannheimia) haemolytica is considered to be the main bacterial agent responsible for lung damage in pneumonia in sheep (Alley, 2002). *Mycoplasma ovipneumoniae* is also considered to play a role in the aetiology of lamb pneumonia in New Zealand, but is regarded as only mildly pathogenic (Alley, 1975; Ionas et al., 1985; Alley et al., 1999; Alley, 2002). *Mycoplasma arginini* has also been suggested as a common isolate from pneumonia cases (Alley, 1975), however, there have been no further studies on the role of this micro-organism in the aetiology of pneumonia since 1975. Parainfluenza virus type 3 and adenovirus have also been implicated to play a role in the development of lamb pneumonia in New Zealand, although they are not often isolated from pneumonic lungs (Davies et al., 1977; Thurley et al., 1977; Davies et al., 1980a; Davies et al., 1982; Davies et al., 1983; Davies et al., 1986c). Viruses are thought to compromise the ovine respiratory tract facilitating secondary bacterial infection. The aetiology of pneumonia is important in the consideration of antigens to include in vaccines.

This would include micro-organisms and strains of micro-organisms isolated at the highest frequency from pneumonia cases in the field.

P. haemolytica appears to be the main pathogen involved in pneumonia cases in New Zealand. In total, eleven serotypes of biotype A are recognised (Alley, 2002). A survey of 9,400 lambs across seven New Zealand slaughter houses indicated *P. haemolytica* serotype A2 to be predominant at all locations with A7, A9, A1 and A6 following in decreasing order of frequency (Black, 1997). Three *P. trehalosi* serotypes were also cultured. A possible method of pneumonia control in New Zealand would be to vaccinate against these main pathogens isolated although a more current assessment of aetiology may be required.

Most published work on *P. haemolytica* vaccines for sheep have involved experimental infection in small numbers of animals (Jones et al., 1986; Chandrasekaran et al., 1991; Sabri et al., 2000), resulting in little evidence of significant protection under field conditions with a greater number of animals (Davies et al., 1986b; Black et al., 1997). Very few vaccine trials have been conducted under field conditions, as naturally occurring disease is difficult to predict and control, leading to variable and sometimes contradictory results. Ovipast Plus® is a vaccine for pneumonia in sheep which is currently available in New Zealand. The initial efficacy trial of this vaccine involved experimental conditions. To our knowledge, few trials under field conditions have been conducted on this vaccine. The vaccine includes antigens of *P. haemolytica* and *P. trehalosi* serotypes.

The initial trial of Ovipast Plus® was conducted at Scotland's Moredun Research Institute (Gilmour et al., 1991). Experimental challenge was used to test the efficacy of a vaccine containing sodium salicylate extract (SSE) of *P. haemolytica* A2 grown in iron-depleted (SSE-IRP) conditions. One injection with the vaccine was administered when lambs were three weeks old and another 28 days later. Experimental groups consisted of $n = 13$ (SSE vaccine), $n = 8$ (SSE-IRP vaccine) and $n = 7$ lambs (unvaccinated controls). On day 35, all lambs were infected with PI₃ administered intratracheally and intranasally. In another seven days, lambs were exposed to an aerosol of *P. haemolytica* A2. The vaccine containing IRP was 99% protective in 8 lambs compared to 47.4% protection in 7 lambs vaccinated with the iron-replete vaccine antigen. Protection was defined as the percentage of the group mean disease score (the sum of clinical findings, consolidated lung lesion

area, *P. haemolytica* isolation index and pleurisy score) of the vaccine group compared to that of the control group. All control lambs died after challenge with *P. haemolytica* A2, with a mean disease score of 50.8 (the sum of clinical findings, consolidated lung lesion area, *P. haemolytica* isolation index and pleurisy score) in comparison to no A2 SSE-IRP vaccinated animals dying with a mean disease score of 0.5.

Ovipast Plus® has been registered in New Zealand since 1992, without conclusive evidence of its efficacy under commercial farming conditions. It is unknown to what extent the vaccine has been used by commercial sheep farmers since then. Vaccination with Ovipast Plus® has been suggested to reduce on-farm mortalities due to acute pneumonia.

The purpose of the current trial was to evaluate the efficacy of Ovipast Plus® in preventing adverse effects of sub-clinical pneumonia on the average daily weight gain of lambs or pneumonic lung lesions at slaughter under commercial farming conditions.

5.2 Materials and Methods

Farms and Animals

Seven commercial sheep flocks in the lower North Island of New Zealand with a history of lamb pneumonia were enrolled in the trial. Flocks were selected that were known to have high pneumonia prevalence from an earlier trial ($n = 2$) and a database of lung scores collected from processing plants for the purpose of this research programme ($n = 5$). These flocks were in the 80th percentile of moderate to severe pneumonia prevalence ($\geq 10\%$ lung surface area affected), which included flocks with a pneumonia prevalence of 68% and higher.

The farms were located in King Country (refer Figure 2.2, Upper Wanganui/Taupo) ($n = 3$), Taihape (Upper Manawatu) ($n = 1$), Feilding (Manawatu) ($n = 1$), Waverly (Wanganui) ($n = 1$) and Wairarapa ($n = 1$). Two of these sheep flocks had experienced acute pneumonia outbreaks several years prior to the 2002/2003 season, although mortality rates were not recorded. The farms were between 240 and 600 hectares farming Romney based sheep with seasonal lambing (July to September). Cattle were also grazed on these farms

consisting of mostly hill country, although some had a mixture of both flat and hill country.

Sample size

A sample size of 2,576 placebo lambs and 2,576 vaccinated lambs was selected at 80% power of observing an existing difference and 99% confidence in a statistically significant difference (i.e. a 1% probability that the observed difference occurred by chance alone). A weighted average of average daily weight gains (ADG) across all pneumonia categories (Goodwin et al., 2004) was assigned to placebo lambs (135g/day). An increase in ADG of 10g/day for vaccinated lambs was considered as clinically important, as it would offset the cost of vaccination. A sample size was calculated under the assumption of independence, using a two-sided t test with alpha ($\alpha = 0.01$) and beta ($\beta = 0.20$) error constraints, then doubled due to expected intra-flock correlation of ADG. The calculated sample size was 5,152 placebo lambs and 5,152 vaccinated lambs.

Trial design

A randomised block design was used for the clinical trial carried out in the 2002/03 growing season. In individual flocks, subgroups of 10 lambs were put in a handling race at one time. Treatment and placebo was alternated between these subgroups. Within 6 weeks after weaning, 4,597 lambs were vaccinated with Ovipast Plus® and 3,922 were re-vaccinated 4-6 weeks after the first vaccination. The corresponding numbers of lambs for the placebo group were 4,577 injected initially and 3,897 re-injected at identical time intervals to the vaccinated lambs. The first vaccination occurred between October 22nd and December 11th 2002. Lambs were individually identified with ear tags and grazed together on the same pastures. All ear tags were the same colour in order to blind the farmer to vaccination groups and eliminate possible bias that might have occurred when the farmer selected lambs for slaughter. Selection of lambs for slaughter was in accordance with farm manager's preferences relating to condition, size and weight. Typically in New Zealand lambs are weaned at approximately 100 days of age and slaughtered around 140 to 200 days of age.

Measurements

Vaccine efficacy was based on the continuous outcome 'average daily gain' (ADG), and the categorical outcome 'presence of pneumonic lesions at slaughter'.

Lambs were weighed using an aluminium FastWeigh® sheep crate with an integrated load cell system connected to a TRU-TEST® indicator. Lambs were weighed on four occasions as follows:

1. When the first vaccination was administered (W1).
2. At approximately 11 weeks post vaccination 1 (W2).
3. At approximately 23 weeks post vaccination 1 (W3).
4. 1-3 days prior to slaughter (WS).

The ADG was calculated by the difference in weights divided by the number of days between weights. Thus, the ADG for the first growth period was $(W2-W1)/\text{number of days}$, for the second growth period was $(W3-W2)/\text{number of days}$, and for the overall growth period was $(WS-W1)/\text{number of days}$. ADG was not calculated between WS-W3 as limited numbers of lambs remained after the date W3 was recorded, with the exception of one flock. There were 1050 ewe replacement lambs included in the trial, from two flocks; however, no WS was recorded for these as they were not slaughtered.

At the processing plant, visual assessments of pneumonic lesions were matched to lambs ear tag number. Pneumonia was classified by research personnel as one of 5 pneumonia categories (Category 0, no pneumonia; Category 1, <5%; Category 2, 6–9.9%; Category 3, 10–19.9%; and Category 4, $\geq 20\%$ total lung surface area affected by pneumonia). Tissue samples of all pneumonic lungs with category ≥ 3 were collected during meat inspection by ASURE New Zealand Ltd. inspectors using knives (sterilised in boiling water between samples) and frozen at -80°C for bacteriology. Additional tissue samples were fixed in 10% buffered formalin for histopathology. At the conclusion of the study, tissue samples were selected which provided a uniform distribution of slaughter dates, with the number of samples being relevant to numbers of lambs processed per flock.

Bacteriology and Histopathology

Bacteriology was performed by Anne Midwinter and Lynn Rogers. Lung samples were plated onto blood agar and MacConkey agar and incubated for 24 to 48 hours at 37°C . Characteristic colonies of *P. haemolytica* and *P. trehalosi* were looked for. Gram stained smears were made from all samples. Biochemical tests performed to identify presence of

P. haemolytica and *P. trehalosi* included oxidase production, indole production, H₂S production in triple sugar iron agar and catalase production.

Histopathology of lung samples was carried out by Maurice Alley on four of the seven flocks, including three of those that sent the most lambs to the processing plant. Samples were embedded in paraffin and cut and stained with haematoxylin and eosin for histopathological examination. The histopathological classifications of disease for analysis were: Group 1, early and mild CNP; Group 2, bronchopneumonia, collapsed lung parenchyma, moderate CNP with bronchopneumonia and moderate to severe CNP and; Group 3, Recovering CNP.

Statistical Analysis

A general linear model was used to test the effect of vaccination, flock and month of slaughter on ADG of lambs between the first and second weights (W1 to W2), second and third weights (W2 to W3), and between the first and pre-slaughter weights (W1 to WS). The response variable was ADG for the period of interest with fixed effects of flock, month of slaughter and vaccination, and an interaction term between flock and vaccination. If there was a significant increase in ADG ($p \leq 0.05$) for vaccinated lambs compared to placebo lambs, vaccine efficacy (VE%) was calculated per flock as follows;

$$VE\% = \left(\frac{ADG_{vac} - ADG_{plc}}{ADG_{plc}} \right) \times 100\% \quad \text{(Equation 1)}$$

Where: ADG_{vac} = ADG for vaccinated lambs

ADG_{plc} = ADG for placebo lambs

A logistic regression was used to test the effect of vaccination, flock and month of slaughter on pneumonia, defined as pneumonia categories 3 and 4 (moderate to severe), while pneumonia categories 0 to 2 (none to mild) were the reference group. An interaction term was tested between flock and vaccination. On account of this interaction term being significant vaccine efficacy (VE) was calculated per flock as follows;

$$VE = 1 - RR \quad \text{(Equation 2)}$$

Where: RR = relative risk and is less than one if vaccine has a protective effect.

All analyses were performed using SPSS version 12.0.1 for Windows (SPSS Inc, Chicago IL, USA). Null hypotheses of the vaccine being in-eficacious were rejected if p was less than 0.05.

5.3 Results

Our planned sample size was 5,152 per group but 4,597 placebo and 4,577 vaccinated lambs were actually enlisted in the study (Table 5.1). The number of lambs lost to follow-up between the first and second vaccination was due to some lambs being sold during this period, lost ear tags and double-ups of tag numbers. Lambs lost to follow-up between the second vaccination and slaughter was due mostly to the presence of 1,050 ewe replacement lambs in two flocks which were not slaughtered and sales of lambs to other processing plants, or to sale yards due to dry weather, but also due, in part, to lost ear tags and double-ups of tag numbers. The reasons for limiting numbers of lambs between W3-WS included two flocks which only had ewe replacement lambs left after W3, two flocks which sold remaining lambs 1-3 days post W3 (therefore W3 equalled WS), one flock where remaining lambs were sold to livestock sales 2-3 weeks after W3 (no WS could be recorded), along with one of the flocks which had sold all lambs before W3 was measured.

Table 5.1: Frequency of the number of lambs (placebo, vaccinated and total) for the planned sample size, those enlisted in the trial (W1) by flock and region, those present at vaccination 2 (W2), those with average daily weight gain (ADG (g/day)) records and those with pneumonia scores and the number of lung lesions cultured and examined for histopathology.

Group or Analysis	Placebo	Vaccinated	Total
Planned sample size	5,152	5,152	10,304
Enlisted lambs – vaccination 1 (W1)			
Flock 1 – South Taranaki	586	556	1,142
Flock 2 – Manawatu	304	304	608
Flock 3 – King Country 1	843	846	1,689
Flock 4 – King Country 2	471	467	938
Flock 5 – Wairarapa	400	400	800
Flock 6 – King Country 3	995	1,003	1,998
Flock 7 – Rangitikei	998	1,001	1,999
Total enlisted lambs	4,597	4,577	9,174
Lambs at vaccination 2	4,151	4,214	8,365
ADG: W2-W1 (0-11 weeks post vaccination 1)	3,606	3,422	7,028
ADG: W3-W2 (11-23 weeks post vaccination 1)	1,508	1,411	2,919
ADG: WS-W3 (23 weeks post vaccination 1 to slaughter)	162	132	294
ADG: WS-W1 (vaccination 1 to slaughter)	2,062	2,020	4,082
Lamb lungs scored for pneumonia	2,596	2,454	5,050
Lung lesions cultured	77	88	165
Lung lesions examined for histopathology	30	49	79

The crude ADG of lambs from the first vaccination to slaughter ((WS - W1)/number of days) was 175.1 g/day (95% CI 173.4, 176.8), with ADG of 175.3 g/day (95% CI 172.9, 177.7) and 175.0 g/day (95% CI 172.6, 177.4) for placebo ($n = 2,062$) and vaccinated ($n = 2,020$) lambs, respectively ($p = 0.850$). ADG between W1 and WS in flocks ranged from 91g/day in flock 4 to 205g/day in flock 7 (Table 5.2). With the exception of flock 4, the ADG between W1 and WS was greater than 150g/day in all flocks.

Table 5.2: Descriptive statistics of average daily gain (ADG,(g/day)) calculated from the difference between the weight taken at vaccination 1 (W1) and the final pre-slaughter weight (WS) in vaccinated and placebo lambs from 7 commercial sheep flocks.

Flock	Group	Number of lambs	Mean ADG	Standard Deviation	Minimum	Maximum
1	Placebo	146	150	41	74	252
	Vaccine	161	153	48	70	291
2	Placebo	38	189	32	101	266
	Vaccine	52	185	35	63	278
3	Placebo	274	198	41	101	291
	Vaccine	283	194	42	107	318
4	Placebo	207	91	34	27	239
	Vaccine	185	92	33	38	235
5	Placebo	267	152	53	54	285
	Vaccine	276	150	48	57	282
6	Placebo	352	168	56	78	338
	Vaccine	288	168	58	58	336
7	Placebo	778	205	38	109	345
	Vaccine	777	203	39	70	371

While a significant negative effect of vaccination on ADG was observed in the first growth period (W1 to W2) in flocks 3 and 6 (Figure 5.1), no significant differences were observed in the second period (W2 to W3) or overall (W3 to WS). However, a significant interaction between vaccination and flock indicated that vaccine was efficacious (VE = 27%) in flock 4 in the second growth period (W2 to W3) (Figure 5.2).

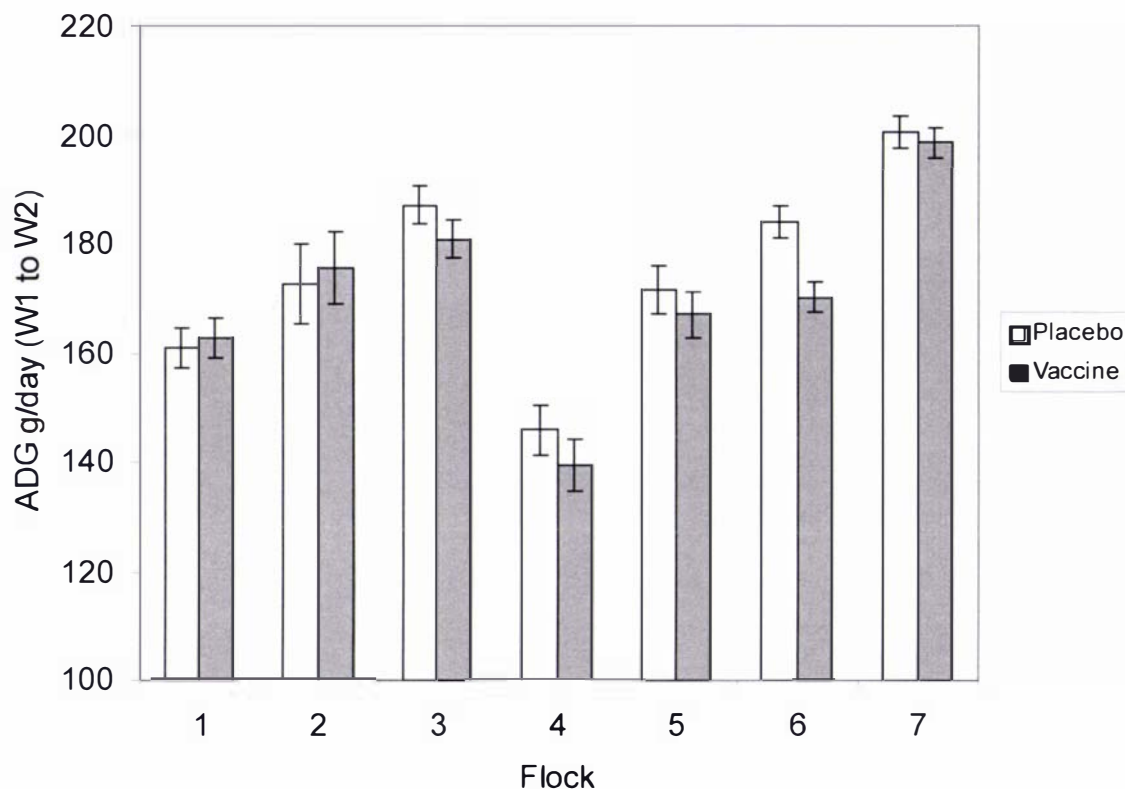


Figure 5.1: Clinical trial of Ovipast Plus® vaccine in seven commercial lamb flocks in the lower North Island of New Zealand, 2002/2003. Least square means of ADG (g/day) of lambs in the first growth period (W1 to W2: 0–11 weeks post vaccination 1) by flock and vaccination group (error bars show 95% confidence intervals).

In the second growth period (W2 to W3), the overall crude ADG in flocks ranged from 42.7 to 77.2 g/day. There was no statistically significant difference in ADG between vaccinated lambs and placebo lambs in this period, when flock and vaccination group was accounted for in the model (Figure 5.2). All lambs in Flock 2 had been sold before W3, therefore this flock did not contribute to ADG in this growth period. The interaction term between flock and vaccination group was not statistically significant ($p = 0.120$). At the flock level the difference between ADG of placebo and vaccinated lambs was significant in flock 4 ($p = 0.004$), but not for other flocks ($p > 0.510$).

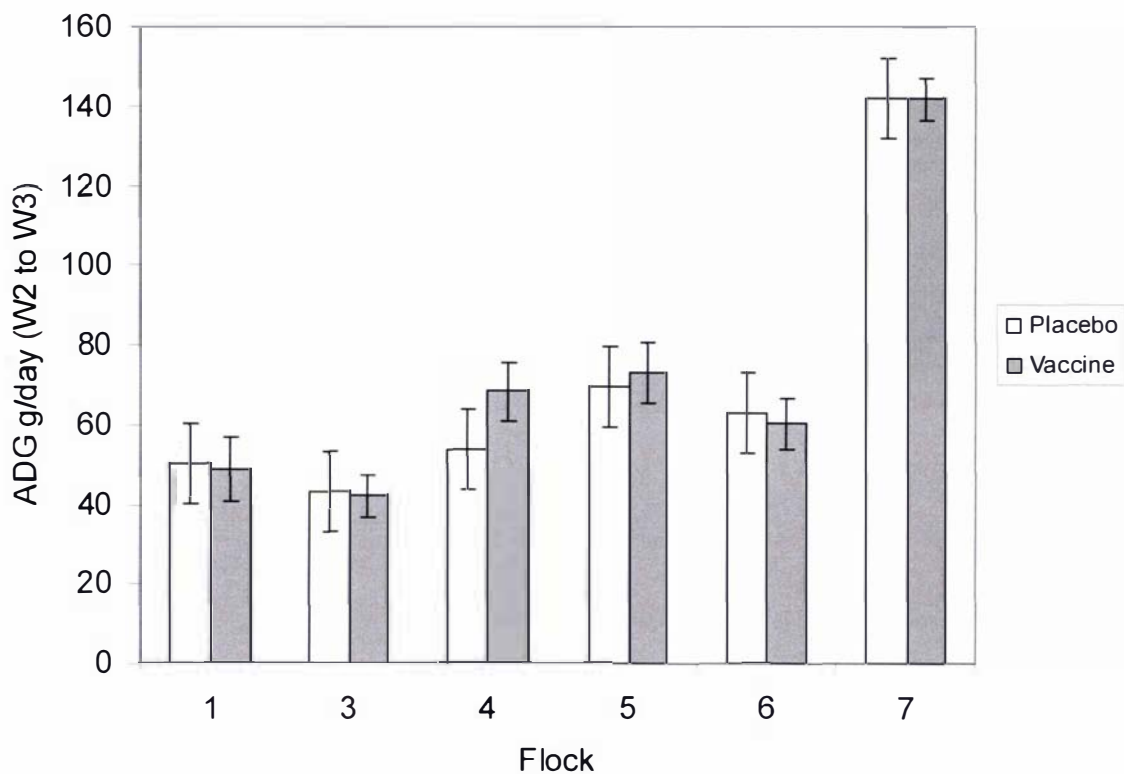


Figure 5.2: Clinical trial of Ovipast Plus® vaccine in seven commercial lamb flocks in the lower North Island of New Zealand, 2002/2003. Least square means of ADG (g/day) of lambs in the second growth period (W2 to W3: 11–23 weeks post vaccination 1) by flock and vaccination group (error bars show 95% confidence intervals).

There was no statistically significant effect ($p = 0.755$) of vaccination on ADG of lambs from the first vaccination (W1) to slaughter (WS), when flock and month of slaughter were included in the model (Figure 5.3). There was no statistically significant interaction of flock by vaccination group.

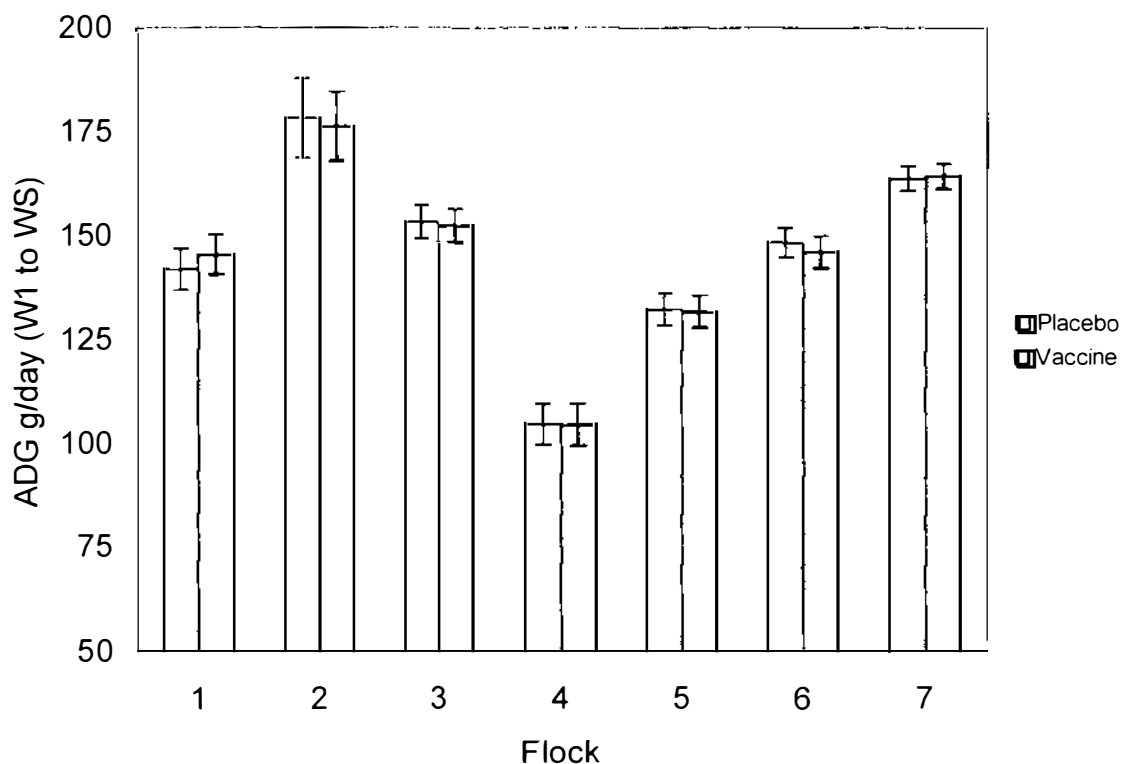


Figure 5.3: Clinical trial of Ovipast Plus® vaccine in seven commercial lamb flocks in the lower North Island of New Zealand, 2002/2003. Least square means of ADG (g/day) of lambs in the overall growth period (W1 to WS: vaccination 1–slaughter) by flock and vaccination group (error bars show 95% confidence intervals).

Figure 5.4 shows that as pneumonia category increased, ADG of lambs from the overall growth period (W1 to WS) decreased when the month of slaughter and flock of origin were taken into account. There were statistically significant ($p \leq 0.05$) differences between category 0 and all other categories, and between categories 1 and 4. Compared to category 0, the ADG for lambs in category 4 was 16 g/day lower.

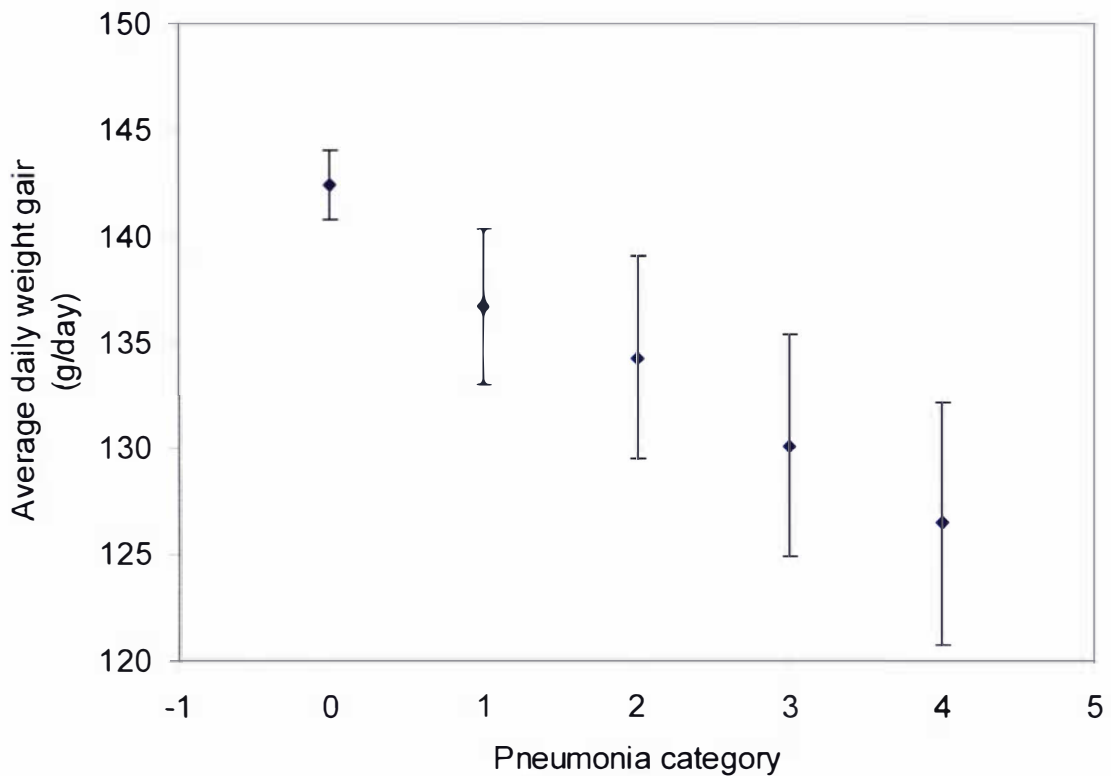


Figure 5.4: Clinical trial of Ovipast Plus® vaccine in seven commercial lamb flocks in the lower North Island of New Zealand, 2002/2003. Least square means (♦) (and 95% CI) of weight gains (g/day) of lambs from vaccination 1 to slaughter according to pneumonia category (Category 0, no pneumonia; Category 1, <5%; Category 2, 5-9.9%; Category 3, 10-19.9%; and Category 4, ≥20% lung surface area affected).

There was a wide range in the weighted average slaughter date for lambs (13 February to 22 June, 130 days) for the seven trial flocks (Table 5.3). Four trial flocks (Flocks 2, 3, 6 and 7) had an average slaughter date within a month of each other, between February 13 and March 17. Two trial flocks (4 and 5) had comparatively late average slaughter dates, in June.

Table 5.3: Number of placebo and vaccinated lamb's lungs scored at slaughter for pneumonia and weighted average slaughter dates from seven trial sheep flocks.

Flock	Placebo lambs	Vaccinated lambs	Weighted average slaughter date
1	192	196	7/04/2003
2	74	103	24/02/2003
3	346	364	17/03/2003
4	278	250	13/06/2003
5	311	316	22/06/2003
6	562	383	13/02/2003
7	833	842	27/02/2003
Total	2596	2454	15/03/2003

The overall prevalence of pneumonic lesions of lambs was 53.8% (1,396 out of 2,596) (95% CI 51.9, 55.7%) in placebo and 57.0% (1,400 out of 2,454) (95% CI 55.1 – 59.0%) in vaccinated lambs ($p = 0.019$). There was no significant difference ($p = 0.110$) between the percentage of placebo and vaccinated lambs in the five pneumonia categories (Table 5.4).

Table 5.4: Percentages of placebo ($n = 2,596$) and vaccinated lambs ($n = 2,454$) in five pneumonia categories.

Pneumonia Category	Category Description	Placebo lambs	Vaccinated lambs
0	Not-affected	46.2%	43.0%
1	<5% affected tissue	33.1%	33.8%
2	5-9.9% affected tissue	10.1%	11.0%
3	10-19.9% affected tissue	6.5%	7.8%
4	$\geq 20\%$ affected tissue	4.1%	4.4%

The effect of vaccination on the proportion of lambs with pneumonia affecting greater than 10% of lung surface area, was not significant ($p = 0.684$) after adjusting for the effects of flock of origin and month of slaughter (Table 5.5). The adjusted relative risk for vaccination was not significant (1.04, 95% CI 0.86, 1.25). An interaction term was considered between flock of origin and vaccination, but was not statistically significant for any flock ($p > 0.432$).

Table 5.5: Adjusted relative risk for the effect of vaccination on moderate to severe pneumonic lesions ($\geq 10\%$ lung surface area affected), adjusted for flock of origin and month of slaughter (95% CI = 95% confidence interval).

Variable	Degrees of freedom	p	Relative risk	95% CI of relative risk
Vaccination	1	0.684	1.04	0.86, 1.25
<i>Month of slaughter</i>				
January	reference			
February	1	0.000	3.77	2.19 - 6.50
March	1	0.000	11.53	6.77 -19.65
April	1	0.000	13.74	7.21, 26.17
May	1	0.000	19.73	10.56, 36.88
June	1	0.000	5.72	2.18, 14.99
July	1	0.005	3.71	1.50, 9.18
August	1	0.560	1.35	0.49, 3.70
<i>Flock</i>				
Flock 1	reference			
Flock 2	1	0.826	1.127	0.39, 3.28
Flock 3	1	0.000	8.217	4.42, 15.29
Flock 4	1	0.000	5.220	2.55, 10.70
Flock 5	1	0.000	3.204	1.77, 5.78
Flock 6	1	0.853	0.927	0.41, 2.07
Flock 7	1	0.000	12.683	7.05, 22.82

Nagelkerke $R^2 = 0.219$; 14 df; $p < 0.001$

There was no significant difference ($p = 0.884$) between isolation of *P. haemolytica* and *P. trehalosi* between placebo and vaccinated lambs because the incidence of isolation was 1.2% higher in vaccination lambs (Table 5.6). The sample size was large enough to detect a difference of 22% between placebo and vaccinated lambs with 80% power and $p \leq 0.05$.

Table 5.6: Prevalence of isolation of *P. haemolytica* or *P. trehalosi* from pneumonic lung lesions of placebo and vaccinated lambs from five commercial sheep flocks in New Zealand ($p = 0.884$).

Isolation of <i>P. haemolytica</i> and <i>P. trehalosi</i>	Placebo lambs	Vaccinated lambs	Total
Negative	35	39	74
Positive	42	49	91
Total	77	88	165
Percent positive	54.5%	55.7%	

There was no statistically significant difference ($p = 0.284$) in histological findings between placebo and vaccinated lambs (Table 5.7).

Table 5.7: Histopathology results from samples of lambs from four commercial sheep flocks in New Zealand grouped by placebo or vaccinated lambs ($p = 0.284$).

Type of pneumonia	Placebo lambs	Vaccinated lambs
Group 1: Early CNP, mild CNP	4	13
Group 2: Bronchopneumonia, collapsed lung parenchyma, moderate CNP with bronchopneumonia, moderate to severe CNP	24	31
Group 3: Recovering CNP	2	5
Total	30	49

There were no statistically significant differences ($p = 0.649$) in histological classifications of disease between lungs with negative or positive *P. haemolytica* or *P. trehalosi* isolation from pneumonic lung lesions (Table 5.8).

Table 5.8: Histopathological classifications of disease from samples of lambs from four commercial sheep flocks in New Zealand grouped by isolations of *P. haemolytica* or *P. trehalosi* from pneumonic lung lesions ($p = 0.649$).

Type of pneumonia	<i>P. haemolytica</i>	<i>P. haemolytica</i>
	or <i>P. trehalosi</i> negative	or <i>P. trehalosi</i> positive
Group 1: Early CNP, mild CNP	8	9
Group 2: Bronchopneumonia, collapsed lung parenchyma, moderate CNP and/or bronchopneumonia, moderate to severe CNP	20	30
Group 3: Recovering CNP	4	3
Total	32	40

5.4 Discussion

This is the first extensive field study of *Pasteurella* vaccine efficacy for sheep pneumonia under New Zealand farming conditions. The vaccine, Ovipast Plus®, has been on the New Zealand market for several years.

An unusually dry summer during the study period forced some trial farmers to sell lambs considerably earlier to “livestock” sale yards at lighter weights than would be expected under typical growing seasons. The increase in lamb supply at this time also limited the available killing space at the processing plant where lungs were assessed for pneumonia, forcing some trial farmers to sell lambs to processing plants elsewhere. Data from such lambs were not available for analysis of vaccination effects on lung lesions or ADG. This primarily affected the data from three flocks (1, 2 and 4). This was outside the control of the researchers and was regarded as a disadvantage in the conduct of such a trial in commercial sheep flocks. Duplicate tag numbers, misread tag numbers and lost ear tags also contributed to the loss of data available for analysis to some extent. In flocks 3 ($n =$

750) and 6 ($n = 300$) ewe lambs were included in the trial, but as they were kept as replacements, only ADG data from these lambs was able to be contributed to the analysis. However, the available data were sufficient, with adequate statistical power and confidence in providing evidence for the null-hypothesis of 'no positive vaccine effect'.

The significant relationship between pneumonia category and the overall ADG of lambs observed in this study confirms earlier findings (Jones et al., 1982; Alley, 1987a; Goodwin et al., 2004) and demonstrates that pneumonia affects growth performance to a considerable extent. Thus lambs from these flocks were an appropriate study population. Also, the high prevalence of pneumonia recorded in this study indicates that the risk of disease was high, resulting in a good test of the vaccine's efficacy. The effect of pneumonia category on ADG may have been biased by lamb selection methods in the current study, as farmers select lambs by body condition and weight. These criteria effectively select against smaller, slower-growing lambs, whose weight gains may have been adversely affected by pneumonia. In an earlier study, we observed only a small effect of pneumonia category on ADG in lambs selected by condition and weight, but a strong effect in lambs selected for slaughter at random (Goodwin et al., 2004). The true effect of pneumonia on ADG in this study was probably even stronger than that suggested by the data.

The interaction between vaccination and flock was statistically significant for ADG in the first 11 weeks post vaccination 1, but not between weeks 11 and 23 post vaccination 1, or between vaccination 1 and slaughter, providing little evidence for an effect of the vaccine in some flocks due to differences in micro-flora species present. In flock 4, in the period between weeks 11 and 23 post vaccination 1, Ovipast plus[®] had a protective effect on ADG. This may indicate that at this time the vaccine protected against pathogen challenge of *P. haemolytica* and *P. trehalosi* strains in this flock, while no effect was evident in the other trial flocks. The efficacy of the vaccine at this time however, was relatively low at 27%. It could be hypothesised that this was a small subgroup of heavily challenged lambs where a vaccine effect was evident. This was not the case, as the prevalence of moderate to severe pneumonia was 7.0% for flock 4, which was below the average of 8.4% for all flocks. It is likely that a type 1 error has occurred where we have rejected the null hypothesis of no effect of vaccination on moderate to severe pneumonia, when in fact it is true. We believe this to be the case as the protective effect of vaccine occurred in lambs (n

= 392) in only one growth period (W2–W3) and in only one out of seven commercial flocks.

The vaccine producer claims Ovipast Plus® reduces mortality without available published evidence of its efficacy in the field. Mortality was not measured in the current study due to the cost and logistics of conducting post mortems within several hours of death, in consideration of the geographical spread of farms and number of lambs involved in the trial.

There was no statistically significant effect of Ovipast Plus® on sub-clinical effects of lamb pneumonia, measured as average daily weight gain and severity of pneumonic lung lesions. Vaccinated lambs grew significantly slower in the first 11 weeks post initial vaccination compared to placebo lambs. ADG was also measured between 11 and 23 weeks post vaccination, and there were no statistically significant effects of vaccination on ADG in this period. In addition to this, no significant effect of vaccine on overall ADG of lambs from the first vaccination to slaughter was observed, when month of slaughter and flock of origin were taken into account. As there was no vaccination effect on the amount of moderate to severe pneumonic lesions, the absence of an effect on ADG is not surprising.

The overall pneumonia prevalence of lambs ($n = 5,050$) in this study was high (55.4%) corresponding to earlier reported prevalence of sub-clinical lamb pneumonia from 21 to 93% (Kirton et al., 1976; Thurley et al., 1977; McGowan et al., 1978; Davies, 1985b; Black, 1997; Goodwin et al., 2004). These flocks would not be likely to represent the general population of flocks but rather those with high pneumonia prevalence. The prevalence of pneumonia (categories 1 to 4) in vaccinated lambs (57.0%) was significantly higher than that of placebo lambs (53.8%). The proportion of vaccinated lambs with moderate to severe pneumonia (categories 3 to 4) was 1.6% higher than placebo lambs but this was not statistically significant. The increased prevalence of vaccinated lambs is perhaps related to increased stress due to immune response leading to increased pneumonia as reflected in a decreased ADG in the first 11 weeks post vaccination 1.

The *Pasteurella* serotypes contained in Ovipast Plus® would seem to be appropriate for New Zealand conditions, as these serotypes have been shown to occur at a high frequency (Black, 1997). *P. haemolytica* and *P. trehalosi* were isolated from pneumonic lung tissue from vaccinated lambs but because these were not typed in this study, it is unknown whether the same serotypes (*P. haemolytica* A1, A2, A6, A7, A9 and *P. trehalosi* T3, T4, T10 and T15) were isolated that were contained in the vaccine. Likewise, *P. haemolytica* and *P. trehalosi* were not isolated from some pneumonic lung samples. It could be speculated that in these cases, other pathogens caused the pneumonia present, as we only tested for the presence of *P. haemolytica* (serotype group A) and *P. trehalosi* (T serotypes). Serotypes occurring in the field may be different to that contained in the vaccine. Other possible explanations are that by the time of culture any *P. haemolytica* and *P. trehalosi* present had died, thus the culture result was false negative or that the *Pasteurella* infection was no longer active whereas the pathology was still present.

Vaccination apparently did not decrease affect the proportion of *P. haemolytica* or *P. trehalosi* isolations from lung lesions, or the histopathology of lung lesions. Samples of lungs, however, were not performed at random. Surprisingly, we did not find statistically significant differences between the histological classification of disease and *P. haemolytica* and *P. trehalosi* isolation in lung lesions. This suggests that the histological and bacteriological outcomes were independent response parameters of vaccine efficacy. Our conclusion that the vaccine was inefficacious was therefore substantiated by four response parameters (ADG, lesion prevalence, bacteriology and histopathology) of which only ADG and lesion prevalence were correlated. The study of Gilmour et al. (1991) showed Ovipast Plus® to have a high level of protection against experimental challenge with PI₃ virus and *P. haemolytica* serotype A2. Our study of Ovipast Plus® indicates that under field conditions protection is not evident.

Two other field studies of *Pasteurella* vaccine efficacy against lamb pneumonia in New Zealand were conducted on shipments of lambs to Saudi Arabia (Black and Duganzich, 1995; Black et al., 1997). These studies showed no effect of vaccine on lamb mortality or pneumonic lesions either. The environment on-board a ship is vastly different than that in commercial sheep flocks in New Zealand, however, these studies support our findings, indicating *Pasteurella* vaccines may not be efficacious under various conditions.

5.5 Conclusions

In conclusion, our study has shown that vaccination of lambs with Ovipast Plus® did not prevent or reduce pneumonic lung lesions or ADG. It appears that vaccination against *Pasteurella* spp. to reduce lamb pneumonia is currently not a feasible option to control pneumonia in New Zealand sheep flocks. Future research into control methods for sheep pneumonia should focus on other factors contributing to the disease, such as host immunological and physiological factors, environmental factors and farm management, until an effective vaccine is produced.

Economic effect of chronic non-progressive pneumonia and pleurisy in New Zealand lambs

6.1 Introduction

In New Zealand, the term chronic non-progressive pneumonia (CNP) is used to describe a sub-acute or chronic pneumonia which is enzootic in lambs of slaughter age (Alley and Clarke, 1979). Acute pneumonia (AP) occurs sporadically and often results in mortality, but recovery with on-going CNP also occurs. CNP is widespread among lambs in New Zealand and causes considerable reduction in growth rate (Alley, 1987b, a; Goodwin et al., 2004) and a predisposition to pleurisy, both resulting in substantial economic loss for New Zealand sheep farmers. At the processing plant lamb carcasses with pleural lesions have to be trimmed to allow market access. The rib cage often has to be removed or entire carcasses condemned, resulting in a reduced payout to farmers and increased workload for the identification and trimming of pleural lesions. Literature reports on mortality rates due to clinical pneumonia are only available from a few case flocks (Smith, 1975; Anonymous, 1976; Sorenson, 1976; Anonymous, 1978; Davies, 1986; Orr and Black, 1996; Orr et al., 1998; Clark et al., 2001) ranging between 2 and 14%. No population reference data have been provided that could be used for the calculation of the cost of mortality due to pneumonia. Studies of CNP have reported prevalence of gross pneumonic lesions at slaughter of 21 to 93% (Kirton et al., 1976; Thurley et al., 1977; McGowan et al., 1978; Davies, 1985b; Black, 1997; Goodwin et al., 2004). While CNP is perceived to be widespread and frequent, causing considerable production loss through reduced growth rate, acute pneumonia associated with lamb mortality is sporadic and would not contribute significant loss to New Zealand sheep farmers as a whole. However, recovery from acute pneumonia may result in persisting CNP but this rate of recovery is unknown.

The prevalence of lamb pleurisy in the 1974/1975 season was estimated by Dysart (1976) at 3.2%, based on 816,700 carcasses. The average pleurisy incidence in lambs in the North

Island was more than twice that of the South Island. Hathaway and McKenzie (1987) estimated that by September more than 27% of lamb carcasses would be affected by pleurisy in the North Island compared to about 9% in the South Island. An assumption was made by Dysart (1976) that 65% of lambs with pleural lesions end up in 'cutter grades' (some or all of rib cage removed). The associated reduction in value would be approximately 30% per carcass (S. Brown, personal communications, 23 June, 2005). More current data (2002/2003) of pleurisy prevalence from ASURE New Zealand Limited (P.O.Box 1141, Christchurch) indicated similar average prevalence for lambs in the South Island and the North Island at 8.4% and 8.9%, respectively.

A dated report estimated the direct loss to the New Zealand farmer from lambs with pleurisy at \$1.8 million per annum (Dysart, 1976). No such estimates have ever been derived for the cost of pneumonia to New Zealand farmers or the meat industry.

The aim of the current study was to estimate the cost of lamb pneumonia and pleurisy to the New Zealand sheep industry based on field studies and current data, and to inform future cost-benefit calculations of control programmes to reduce the incidence of pneumonia.

6.2 Materials and Methods

1. Parameters and Data Sources

Input data to estimate the annual cost of lamb pneumonia and pleurisy to New Zealand farmers was derived from the following sources:

1. The effect of pneumonia on average daily gains (ADG) of lambs in the month prior to slaughter (Goodwin et al., 2004).
2. The prevalence of moderate to severe (MS) pneumonia ($\geq 10\%$ lung surface area affected) and pleurisy at slaughter (ASURE New Zealand Limited (P.O.Box 1141, Christchurch), Goodwin-Ray et al., 2006b).
3. National slaughter statistics including average carcass value, carcass weight, the annual number of lambs slaughtered and proportion of all lambs that were slaughtered between January and June (MWNZ, 2005).

4. National demographic statistics of the number of sheep farms in New Zealand (AgriQuality, 2004).

The majority of pneumonia diagnosed at slaughter was presumed to be CNP although some residual lung lesions from recovered AP may also have been present.

2. Calculations

2.1. Loss of carcass value due to pneumonia

Reduced ADG in the month preceding slaughter due to pneumonia was the only cost related to pneumonia included in the calculation, as limited data was available on mortality due to acute pneumonia. The data used was from a longitudinal study (Goodwin et al., 2004), conducted in 1999 to 2000, on 14 commercial sheep flocks, five from Southland, five from King Country (refer Figure 2.2, Upper Wanganui/Taupo) and four from Northland. Pneumonia was known to be a problem in lambs in all flocks selected. In each flock 200 lambs were randomly selected at weaning and weighed at 4-weekly intervals. The extent of pneumonic lesions was scored visually at slaughter in 40 randomly selected lambs per month per flock. Lamb liveweight was measured prior to slaughter. The effect of pneumonia on growth rates of lambs in the month preceding slaughter was used to calculate the cost of reduced weight gain (i.e. days affected x reduced growth relative to unaffected lambs (grams/day)). Pneumonia at slaughter was classified according to the percentage of lung surface area affected in the following categories: Category 0, no pneumonia; Category 1, 0.1–4.9%; Category 2, 5–9.9%; Category 3, 10–19.9%; and Category 4, $\geq 20\%$ lung surface area affected.

Similar data were available from a clinical trial evaluating the effect of vaccination against lamb pneumonia (Goodwin-Ray and Heuer, 2006). This was a field trial using a randomised split-flock design involving 9,174 lambs from seven commercial flocks of lambs with a history of pneumonia, enrolled and vaccinated with Ovipast Plus® (a *Pasteurella haemolytica* and *P. trehalosi* vaccine) or placebo by systematic random allocation.

The reduction in the ADG of lambs for pneumonia categories 2 to 4 was included in calculations of overall loss. It was assumed that ADG due to pneumonia started in mid December. Therefore, reduced ADG was assumed to last 30, 60, 90, 120, 150 or 180 days

if lambs were slaughtered in January, February, March, April, May or June, respectively. ADG was converted from live weight to carcass weight on the basis of a regression equation for calculating dressing out percentage ((carcass weight x 100) / live weight), by Kirton et al. (1984), based on 2,207 lambs). This resulted in an average loss per lamb in the flock due to pneumonia, which was weighted due to the extent of pneumonia and the month of slaughter, based on 21 flocks (11,974 lambs) (Goodwin et al., 2004; Goodwin-Ray and Heuer, 2006). For the purpose of this study, the average loss per lamb from these study flocks was regressed on the prevalence of MS pneumonia ($\geq 10\%$ lung surface area). The regression coefficients indicated the loss per lamb and were used to associate MS pneumonia prevalence (per percentage point in the flock), to the average loss per lamb in a larger and more representative sample (Goodwin-Ray et al., 2006c).

In the 21 study flocks, average monthly loss (AML) due to pneumonia was calculated as:

$$AML_{kj} = \sum_{2,2,1}^{i,j,k} A_i B_{ij} C_k D_k \quad \text{(Equation 1)}$$

Where:

i = pneumonia category (2-4)

j = flock (1-21)

k = month (2-6)

A_i = Proportion of lambs in pneumonia categories of $i = 2,3,4$ from 21 flocks (Goodwin et al., 2004; Goodwin-Ray and Heuer, 2006).

B_{ij} = ADG from 14 flocks (Goodwin et al., 2004) according to pneumonia categories of $i = 2,3,4$.

C_k = Number of days affected ($k = 1$: Jan, 30 days; $k = 2$: Feb, 60 days; $k = 3$: Mar, 90 days; $k = 4$: April, 120 days; $k = 5$: May, 150 days; $k = 6$: June, 180 days).

D_k = Price per kilogram of carcass weight (MWNZ, 2005).

The result is shown in Figure 6.1. Monthly average lamb price (per kg carcass weight) at net present value was assumed to follow a normal distribution. The monthly means and standard deviations of lamb price (per kilogram of carcass weight) at net present value for January to June were \$4.09 (\$0.43), \$4.05 (\$0.40), \$4.02 (\$0.40), \$3.99 (\$0.23), \$4.11 (\$0.21) and \$4.20 (\$0.08) respectively. There were no data available to calculate AML for May and June so the AML calculated for April was extrapolated to both of these months (Figure 6.1 (d)).

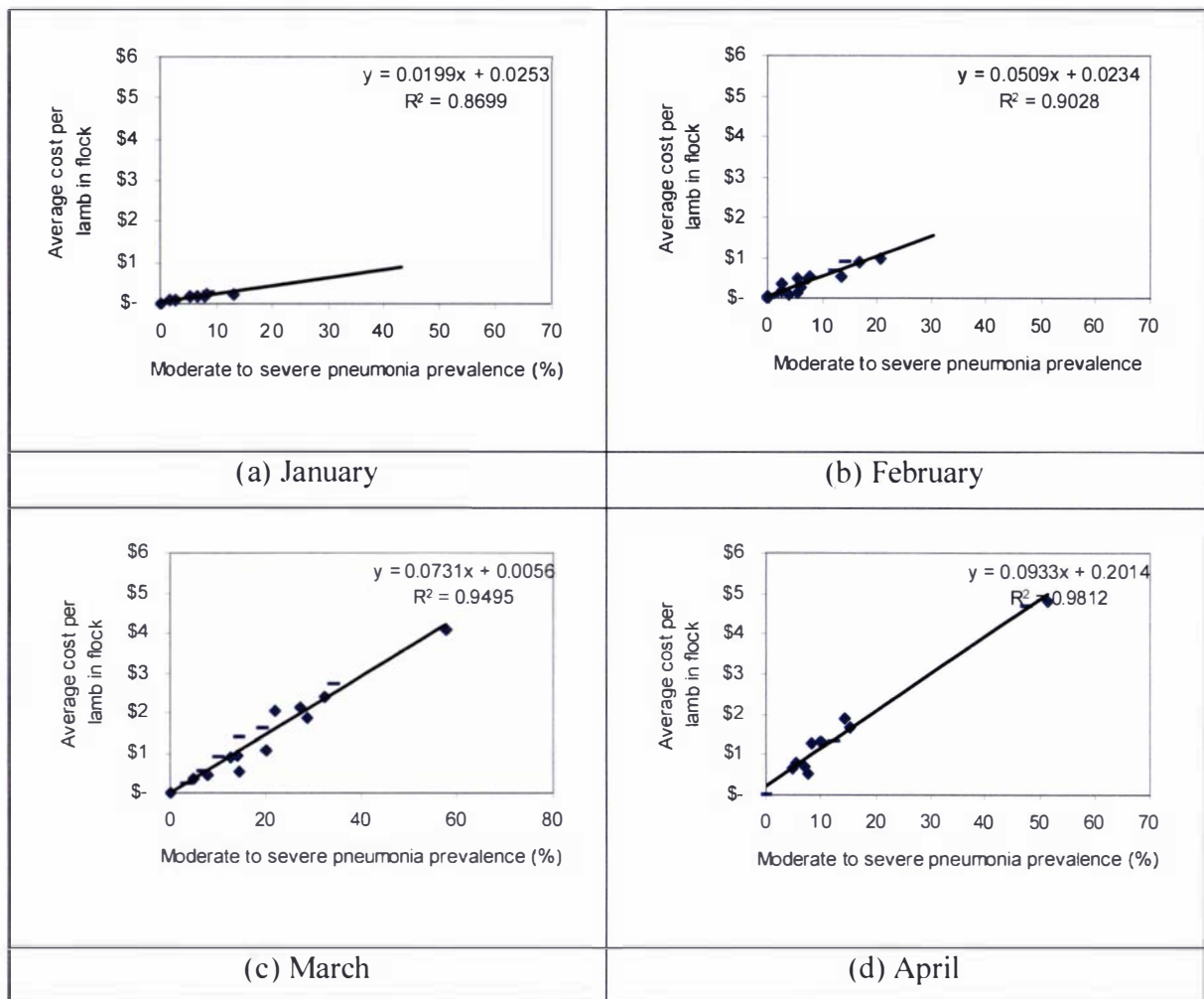


Figure 6.1: Stochastic model to estimate the direct annual cost of pneumonia and pleurisy to New Zealand farmers. Scatter plots, regression equations and multiple coefficients of determination (R^2) of average cost of pneumonia per lamb (AML) for 14 (♦) flocks (Goodwin et al., 2004) and 7 flocks (–) (Goodwin-Ray and Heuer, 2006), according to moderate to severe pneumonia (\geq Category 3) prevalence (% of lambs) for (a) January, (b) February, (c) March and (d) April.

2.2 Moderate to severe pneumonia prevalence

In 2002/03, lungs of all slaughter lambs from 1,719 flocks with 50 or more lambs were scored by meat inspectors for MS pneumonic lesions ($\geq 10\%$ lung surface area) at three processing plants (Gisborne, Manawatu, Christchurch) over a 9 month period (December 2000 to September 2001) (Goodwin-Ray et al., 2006c). The scores of meat inspectors were compared to parallel scores of the first author and estimates of sensitivity and specificity calculated using the first author's scores as the gold standard. The apparent MS pneumonia prevalence (apparent prevalence, AP) at flock level was adjusted for lack of

sensitivity (Se) and specificity (Sp) to obtain an estimate of true prevalence (TP) by the formula $TP = (AP + Sp - 1) / (Se + Sp - 1)$ (Rogan and Gladen, 1978; Dohoo et al., 2003). Additional parameters used to calculate economic loss included: total annual number of lambs slaughtered (MWNZ, 2005), proportion of all lambs that were slaughtered from January to June, and the number of sheep farms in New Zealand (AgriQuality, 2004). Lamb prices from 2002-2005 were converted to net present value via an inflation calculator (Reserve Bank of New Zealand, 2005).

2.3 National cost of lamb pneumonia

The annual direct cost to New Zealand farmers of growth rate loss due to pneumonia, without accounting for acute pneumonia deaths that may occur, was based on the following equation:

$$TotalCost = \sum_{k=1}^6 \sum_{i=1\%}^{100\%} E_i \times G_k \times AMC\%_k \times FS_k \quad (\text{Equation 2})$$

Where:

E = Proportion of flocks ($n = 1719$) at each ' i ' = 1% increment of moderate to severe prevalence ($i = 0-100\%$) (Goodwin-Ray et al., 2006c).

G = number of sheep flocks sending lambs to slaughter in month ' k ' = January (1) to June (6) in New Zealand (AgriQuality, 2004).

AMC % = slope coefficient of the average monthly cost per 1% increase in moderate to severe pneumonia prevalence of 21 study flocks in month ' k ' = 1 to 6.

FS = average flock size in month ' k ' in New Zealand (AgriQuality, 2004) divided by G_k

2.4 Loss due to pleurisy

Data of pleurisy prevalence were also collected from these 1,719 flocks, including numbers of lambs with minor pleurisy (not devalued), major pleurisy (devalued) and carcasses condemned due to pleurisy (zero return). The annual direct cost to New Zealand farmers of pleurisy, accounting for losses through devalued and condemned lamb carcasses was based on the following equation:

$$TotalCost = \sum_{k=1}^6 H_k I J + \sum_{k=1}^6 L_k M_k \quad (\text{Equation 3})$$

Where:

H = number of lambs slaughtered (Goodwin-Ray et al., 2006a) for each ' k ' = 1,2,3,4,5,6 that are condemned for pleurisy (Goodwin-Ray et al., 2006c).

I = average annual price per kg of carcass weight based on 1989-2004 (MWNZ, 2005).

J = average annual lamb carcass weight based on 1995-2004 (MWNZ, 2005).

L = price per kg of carcass weight for pleurisy downgraded carcasses for each ' k ' = 1,2,3,4,5,6 based on a reduction in value of 30% per carcass (S. Brown, personal communications) and ' I '

M = kg of lamb carcass weight affected by pleurisy downgrades ' k ' = 1,2,3,4,5,6 based on the number of downgraded carcasses due to pleurisy and ' l '

2.5 Stochastic Modelling

A spreadsheet-based simulation approach using the Excel spreadsheet add-on software @RISK (Palisade Corporation, USA) was used. Several equation inputs were based on assumed probability distributions (Table 6.1). The model included only the months of January to June. The outcome from the model provided probability distributions of the cost of pleurisy, cost of pneumonia and combined cost of both diseases. The stochastic model was run in @RISK (Palisade Corporation, USA) for 1000 iterations. A sensitivity analysis was also run in @RISK (Palisade Corporation, USA) to determine which input distributions had the biggest impact on the model output. Correlation coefficients were calculated between the output values and each set of sampled input values. The most significant input variables were those with the highest correlation coefficients.

Table 6.1: Most likely value, standard deviation (SD), minimum, maximum and assumed distribution of stochastic model variables.

Variable	Variable value		Assumed distribution	
		Most likely (SD)		Minimum, Maximum
ADG per pneumonia category (kg CW/day)	Category 2	0.007 (0.004)	0.000, 0.016	Normal
	Category 3	0.010 (0.005)	0.002, 0.017	Normal
	Category 4	0.026 (0.013)	0.016, 0.035	Normal
Price per kg CW (\$)	January	4.68 (0.43)	3.74, 4.37	Normal
	February	4.65 (0.40)	3.78, 4.35	Normal
	March	4.62 (0.40)	3.78, 4.32	Normal
	April	4.31 (0.23)	3.75, 4.03	Normal
	May	4.11 (0.21)	3.92, 4.34	Normal
	June	4.20 (0.08)	4.11, 4.27	Normal
	National No. lambs slaughtered annually		25.7 mill (1.3 mill)	23.3 mill, 28.0 mill
Slope coefficient of AML per 1% increase in MS pneumonia prevalence	January	0.031 (0.015)	0.013, 0.070	Normal
	February	0.057 (0.026)	0.025, 0.128	Normal
	March	0.074 (0.015)	0.038, 0.100	Normal
	April	0.117 (0.025)	0.069, 0.155	Normal
	May	0.117 (0.025)	0.069, 0.155	Normal
	June	0.117 (0.025)	0.069, 0.155	Normal
	Proportion of lambs sold	January	0.137 (0.017)	0.118, 0.159
February		0.127 (0.011)	0.115, 0.142	Normal
March		0.153 (0.016)	0.134, 0.171	Normal
April		0.135 (0.011)	0.119, 0.147	Normal
May		0.095 (0.010)	0.080, 0.100	Normal
June		0.056 (0.008)	0.050, 0.060	Normal
Pleurisy prevalence		January	0.012 (0.014)	0.0, 9.1
	February	0.024 (0.026)	0.0, 20.0	Log Normal
	March	0.042 (0.042)	0.0, 33.3	Log Normal
	April	0.086 (0.073)	0.0, 100.0	Log Normal
	May	7.11 (7.58)	0.0, 100	Log Normal
	June	11.11 (8.51)	0.0, 46.0	Log Normal
	Proportion of carcasses downgraded due to pleurisy	January	0.6 (0.2)	0.0, 1.0
February		0.6 (0.4)	0.0, 1.0	Normal
March		0.6 (0.3)	0.0, 1.0	Normal
April		0.6 (0.3)	0.0, 1.0	Normal
May		0.3 (0.3)	0.0, 1.0	Normal
June		0.3 (0.3)	0.0, 1.0	Normal
Average carcass weight of lambs (kg CW)			16.29 (0.71)	15.19, 17.26
Value of pleurisy downgraded carcass as a proportion of a healthy carcass		0.7 (na)	0.5, 1.0	Triangular
Proportion of carcasses condemned for pleurisy	January	0.001 (na)	0.000, 0.091	Pert
	February	0.004 (na)	0.000, 0.333	Pert
	March	0.004 (na)	0.000, 0.333	Pert
	April	0.002 (na)	0.000, 0.200	Pert
	May	0.009 (na)	0.000, 1.000	Pert
	June	0.003 (na)	0.000, 0.030	Pert

ADG – average daily weight gain (kg/day)

AML – average monthly loss due to pneumonia

CW – carcass weight

mill – million

MS – moderate to severe

na – not available

6.3 Results

The effect of pneumonia on lamb growth rate based on earlier data (Goodwin et al., 2004) is reproduced in Figure 6.2. The difference in the average daily weight gain of lambs in pneumonia categories 2 to 4 compared to Category 0 was used in the model. Lambs in categories 2, 3 and 4 grew at 9, 18 and 72g/day slower than lambs in category 0 which grew at 136g/day.

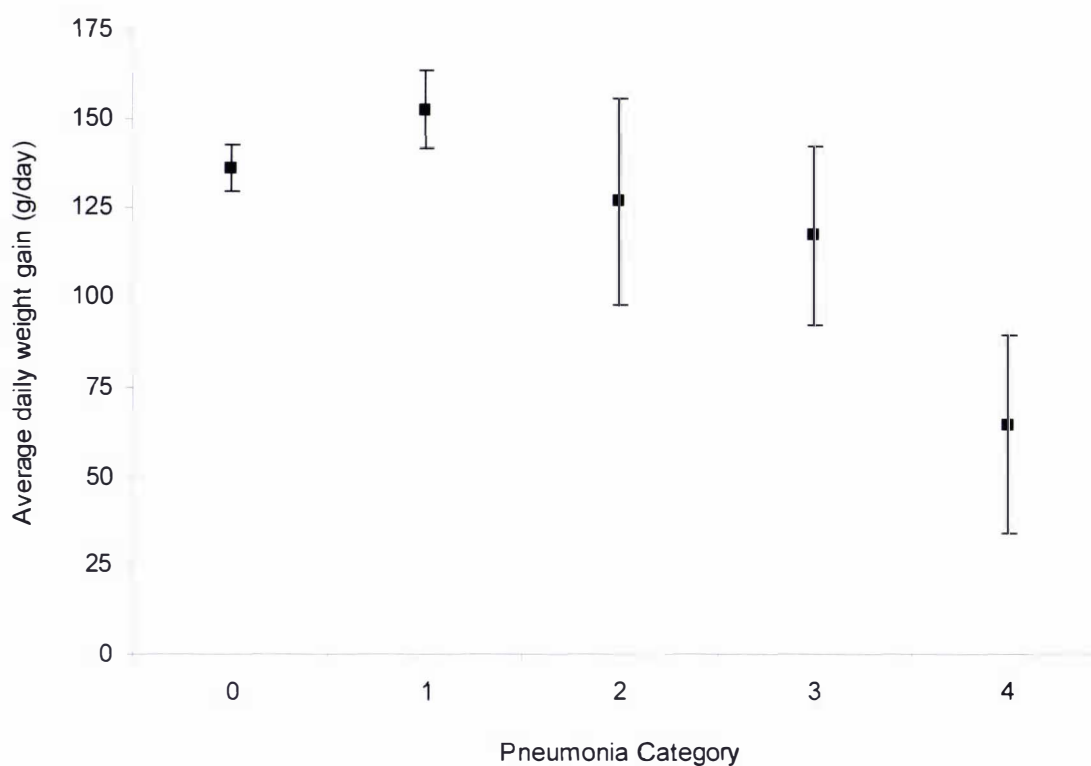


Figure 6.2: Least square means (■) (and 95% CI) of average daily weight gains (g/day) of randomly selected lambs in the month prior to slaughter in categories of: 0, no pneumonia; 1, $\leq 5\%$ lung surface area affected; 2, 5-9.9%; 3, 10-19.9%; and 4, $\geq 20\%$ lung surface area affected.

Figure 6.3 shows a distribution of true moderate to severe (MS) pneumonia prevalence based on 1,719 flocks from Canterbury, Manawatu and Gisborne processing plants. It was assumed to reflect the national lamb flocks' MS pneumonia prevalence distribution. The linear increase in average cost per lamb to the flock's overall MS pneumonia prevalence from Figure 6.1 was used for a cost estimate per 1% increment of MS pneumonia prevalence from 0–100% (equation 1, Materials and Methods). The average (median) of

true MS pneumonia prevalence for January to June was 2.7 (0), 7.3 (0), 14.1 (6.9), 13.5 (7.3), 7.1 (5.0) and 11.1%(9.8) respectively.

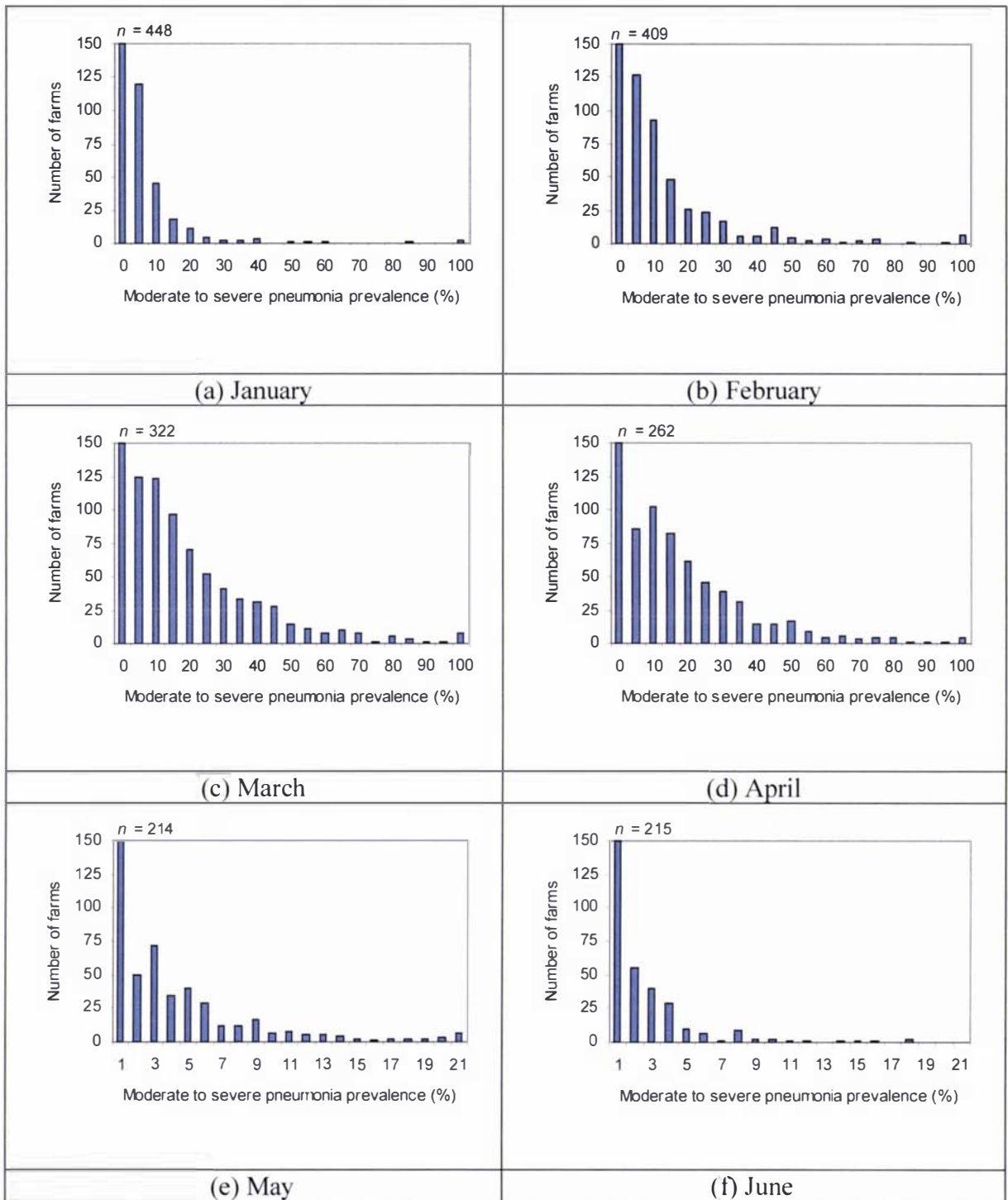


Figure 6.3: Stochastic model to estimate the direct annual cost of pneumonia and pleurisy to New Zealand farmers. Distributions of true moderate to severe pneumonia ($\geq 10\%$ lung affected) prevalence (adjusted according to sensitivity and specificity (Table 6.2) based on 1,719 flocks for January (a), February (b), March (c), April (d), May (e) and June (f) (frequency of flocks with 0 prevalence indicated at top of bar (n = number of flocks in category 0)).

The sensitivity of meat inspector diagnosis of MS pneumonia was low at all processing plants, indicating a low rate of positive diagnosis of pneumonic lungs (Table 6.2). The specificity was high, indicating a high rate of negative diagnosis of lungs without pneumonia. Therefore the occurrence of MS pneumonia was likely under-estimated due to a significant proportion of lungs with pneumonic lesions being diagnosed as negative.

Table 6.2: Sensitivity and specificity (with 95% confidence intervals), of inspector diagnosis of moderate to severe pneumonia for Canterbury, Manawatu and Gisborne processing plants.

Region	Sensitivity (95%CI)	Specificity (95% CI)
Canterbury	0.172 (0.136, 0.214)	0.979 (0.976, 0.982)
Manawatu	0.173 (0.142, 0.210)	0.923 (0.913, 0.932)
Gisborne	0.155 (0.093, 0.247)	0.991 (0.985, 0.994)

The mean pleurisy prevalence increased from January to June in all regions (Table 6.3). Lambs from Canterbury had the lowest mean prevalence from January to May and Gisborne lambs had the lowest in June. Lambs processed at the Fielding plant had consistently the highest mean prevalence of the three regions for four of the six months.

Table 6.3: Mean pleurisy prevalence (95% CI) from January-June 2001 for Canterbury, Manawatu and Gisborne processing plants.

Month	Processing Plant		
	Canterbury	Manawatu	Gisborne
January	1.10 (1.00, 1.20)	1.35 (1.20, 1.50)	–
February	1.78 (1.61, 1.95)	2.66 (2.34, 2.98)	3.33 (2.82, 3.84)
March	3.09 (2.88, 3.30)	6.06 (5.54, 6.58)	4.06 (3.37, 4.75)
April	9.33 (8.43, 10.23)	10.16 (9.45, 10.87)	4.10 (3.26, 4.94)
May	4.96 (4.39, 5.53)	12.16 (11.11, 13.21)	5.86 (4.30, 7.42)
June	13.58 (12.45, 14.71)	12.85 (11.50, 14.20)	5.66 (4.64, 6.68)

The model output distribution of the estimated annual cost of pneumonia to New Zealand farmers is shown in Figure 6.4. The average estimated cost was NZ \$28,110,990 (US \$17,991,034) with a stochastic standard deviation of \$8,618,695 and 95% stochastic interval of \$14,968,320–\$41,944,310.

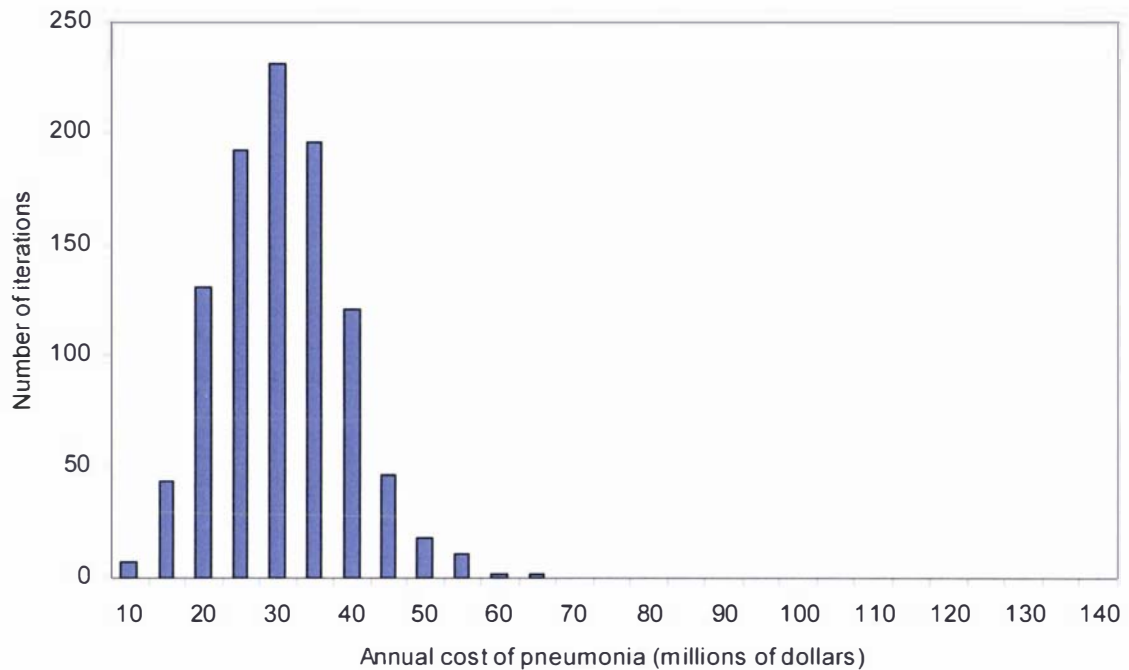


Figure 6.4: Stochastic model to estimate the direct annual cost of pneumonia and pleurisy to New Zealand farmers. Distribution of the estimated annual cost of pneumonia to New Zealand farmers.

The regression coefficients indicating the loss per lamb associated with MS pneumonia prevalence in April, March and February had consecutively the largest impact on model output (total cost of pneumonia), as defined by correlation coefficients (Table 6.4).

Table 6.4: Correlation coefficients between model output (total cost of pneumonia) and sets of sampled input variables ($n = 5$), ranked according to significance.

Input variables	Rank of significance	Correlation coefficient
June regression coefficient of AML*	1	0.472
April regression coefficient of AML*	2	0.290
March regression coefficient of AML*	3	0.230
May regression coefficient of AML*	4	0.189
Average number of lambs slaughtered per flock	8	0.137

*AML - average monthly loss due to pneumonia (\$ loss/1% increment of moderate to severe pneumonia prevalence)

The model output distribution of the estimated annual cost of pleurisy to New Zealand farmers, determined by carcasses downgraded and condemned for pleurisy at slaughter is shown in Figure 6.5. The average estimated cost was NZ \$25,093,750 (US \$16,060,000) with a stochastic standard deviation of \$12,104,740 and 95% stochastic interval of \$10,240,980–\$48,093,080.

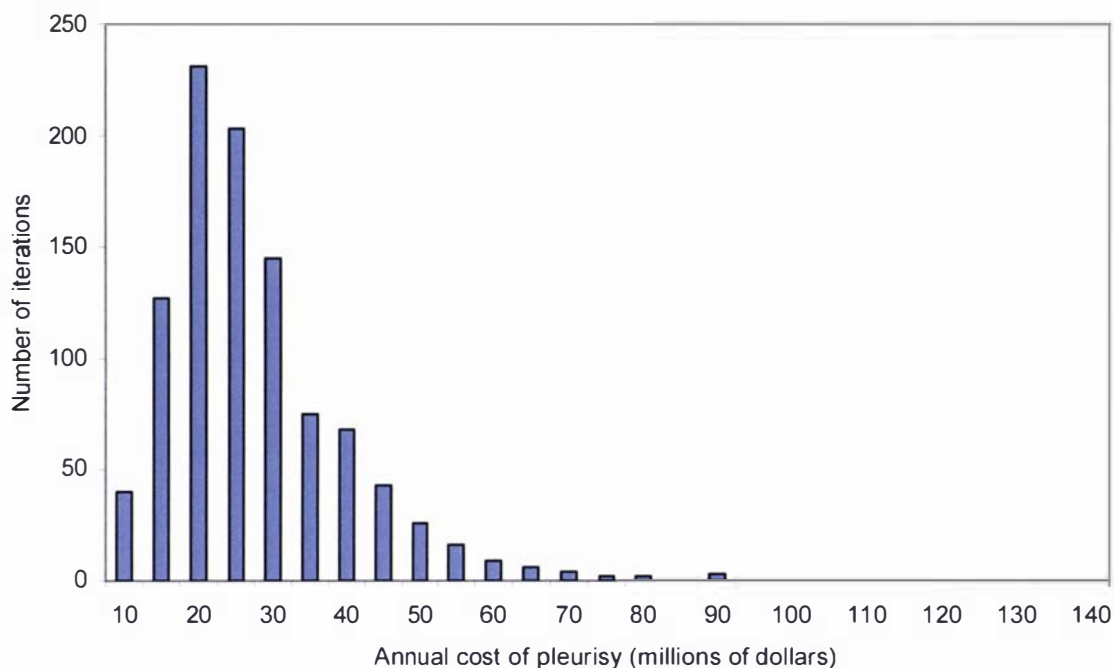


Figure 6.5: Stochastic model to estimate the direct annual cost of pneumonia and pleurisy to New Zealand farmers. Distribution of the estimated annual cost of downgraded or condemned carcasses due to pleurisy to New Zealand farmers.

The prevalence of pleurisy in April, March and May had the largest impact on model output (total cost of pleurisy), as defined by correlation coefficients (Table 6.5). The value of a pleurisy downgraded carcass compared to a healthy carcass and the proportion of carcasses downgraded for pleurisy in April also had large impacts on the outcome of the model.

Table 6.5: Correlation coefficients between model output (total cost of pleurisy and sets of sampled input variables ($n = 5$), ranked according to significance.

Input variables	Rank of significance	Correlation coefficient
April pleurisy prevalence	1	0.538
March pleurisy prevalence	2	0.406
May pleurisy prevalence	3	0.395
Value of pleurisy downgraded carcass compared to a healthy carcass	4	0.243
Proportion of carcasses downgraded for pleurisy in April	8	0.243

The model output distribution of the estimated annual cost of pneumonia and pleurisy to New Zealand farmers is shown in Figure 6.6. The average estimated cost was NZ \$53,204,730 (US \$34,051,027) with a stochastic standard deviation of \$14,372,310 and a 95% stochastic interval of \$32,446,150–\$78,931,780. The minimum cost attributed to pneumonia and pleurisy from this model was \$19,656,450 million.

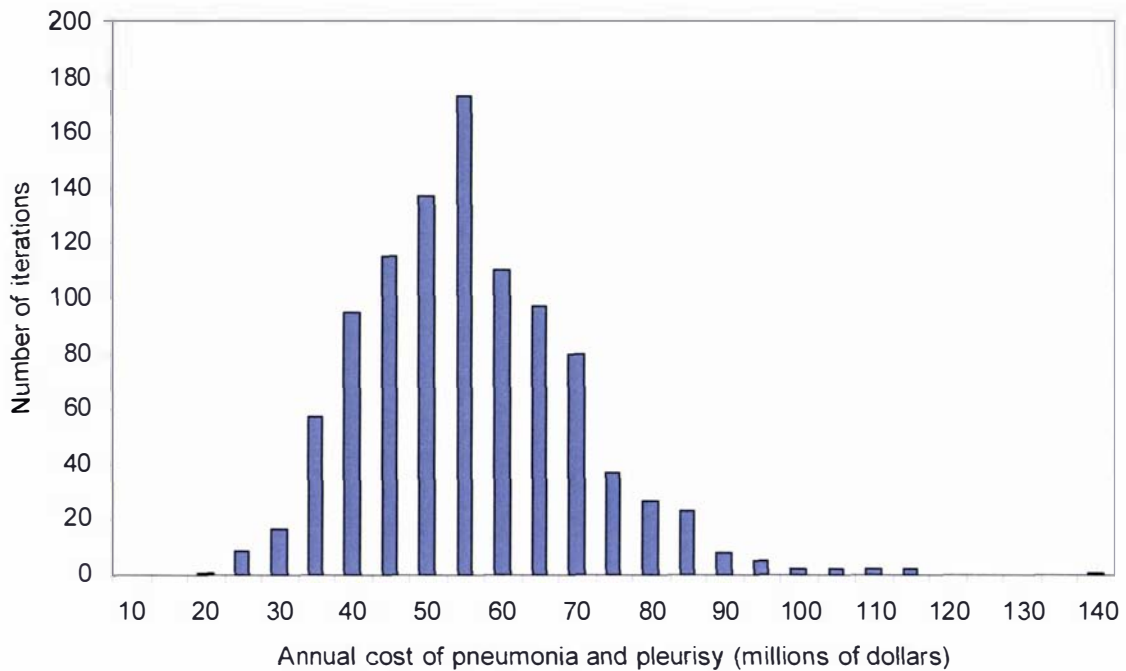


Figure 6.6: Stochastic model to estimate the direct annual cost of pneumonia and pleurisy to New Zealand farmers. Distribution of the estimated annual cost of pleurisy and pneumonia to New Zealand farmers.

The prevalence of pleurisy between March and May had the largest impact on model output (total cost of pneumonia and pleurisy), as defined by correlation coefficients (Table 6.6).

Table 6.6: Correlation coefficients between model output (total cost of pneumonia and pleurisy) and sets of sampled input variables ($n = 10$), ranked according to significance.

Input variables	Rank of significance	Correlation coefficient
April pleurisy prevalence	1	0.453
March pleurisy prevalence	2	0.342
May pleurisy prevalence	3	0.334
June regression coefficient of AML*	4	0.264
Value of pleurisy downgraded carcass compared to a healthy carcass	5	0.204
April proportion of carcasses with pleurisy downgraded	6	0.204
April regression coefficient of AML*	7	0.176
February pleurisy prevalence	8	0.156
June pleurisy prevalence	9	0.143
May proportion of carcasses with pleurisy downgraded	10	0.141

6.4 Discussion

This study provides the first estimate of the annual cost of pneumonia and pleurisy to New Zealand farmers. The average estimated annual cost from the stochastic model was NZ \$53,204,730 (US \$34,051,027), with just over half of this cost due to pneumonia, and the remainder to pleurisy. The variables with the greatest impact on the overall loss were the pleurisy prevalence in March, April and May. Although the pleurisy prevalence peaked in June, the impact on the model was not significant as fewer lambs were sold in this month.

The mortality rate due to acute pneumonia has not been accounted for in the current model. Consequently, the estimated cost of pneumonia may be conservative. It is difficult to estimate the extent of underestimation, as the only scientific literature of mortality rate is

from case flocks (flocks with mortality attributable to acute pneumonia). In such flocks mortality only occurs sporadically, which would be difficult to extrapolate to the wider population of flocks. Case flocks with confirmed pneumonia diagnoses from animal health laboratories (Smith, 1975; Anonymous, 1976; Sorenson, 1976; Anonymous, 1978; Davies, 1986; Orr and Black, 1996; Orr et al., 1998; Clark et al., 2001), had mortalities (2 to 4%) occurring in lambs or hoggets in the January to June period. However, because the reported mortality rate is relatively low and only occurs sporadically over the whole population, it would not be expected to contribute significantly to the overall cost of pneumonia.

This stochastic model was made up of a wide range of data and assumptions. The validity of this data and these assumptions should be reviewed to authenticate the model. Firstly, the relationship of pneumonia and ADG (Goodwin et al., 2004) was the only recent data available for naturally occurring pneumonia in New Zealand lambs. This was a cohort study where lambs were selected at random and at equal intervals over the lamb growth period from three regions, so the data was not biased by farmer selection of lambs for slaughter. The data of the prevalence of moderate to severe (MS) pneumonia at slaughter involved a large number of commercial flocks ($n = 1,719$) from three regions over nine months (Goodwin-Ray et al., 2006c). Pneumonia is not routinely recorded and ASURE New Zealand meat inspectors collected this data outside of their contractual agreements without reimbursement. The sensitivity of meat inspector diagnosis was low leading to an underestimate of lamb pneumonia at slaughter, but this was the most comprehensive data available to us. The pleurisy prevalence data used in our model was routinely collected at slaughter by ASURE meat inspectors, although the quality of this data is unknown as it was not validated. However, the proportion of lamb carcasses requiring trimming due to pleurisy would be expected to be accurate. One of the main limitations of the pneumonia and pleurisy prevalence data used, is that collection was conducted over only one season and variations between seasons are likely to occur which was not able to be corrected for in our model. The national slaughter statistics were produced by Meat and Wool New Zealand (MWNZ, 2005), a single levying body funded by livestock producer levies and can be assumed to be accurate. AgriBase (AgriQuality, 2004) was used to determine the number of sheep farms in New Zealand in order to calculate the number of lambs produced per farm. It is anticipated that this data is also accurate.

Another approach to the estimation of the cost of pneumonia would be to value additional days that lambs with pneumonia would have to spend on-farm in order to reach desired target slaughter weight. The problem with this methodology is that it is difficult to estimate the cost of additional days lambs spend on-farm in terms of grass, labour and resources for pneumonia prevention or treatment along with the opportunity cost. Opportunity cost measures the cost of any economic choice in terms of the next best alternative foregone. For example, the opportunity cost of grass in the late summer to autumn period could be that foregone by grazing additional stock, or making winter supplements, or that of increased quantity and quality of pasture available to ewes before mating for increased ovulation rates.

Partial budgeting techniques are often adopted to quantify economic losses due to disease where the revenue (e.g. production) and expense items (e.g. animal health treatments), as affected by the disease, are estimated and the net effects summarised. However, for partial budgets, inputs and outputs have to be easy to put prices on. For pneumonia, effective vaccines are not available in New Zealand (Goodwin-Ray and Heuer, 2006), and not typically used. Antibiotics may be administered if acute pneumonia is a problem, but as this type of pneumonia tends to occur sporadically they are also not widely used. Consequently, calculation of the expenses for the control of pneumonia is difficult and does not suit a partial budgeting approach. The additional revenue resulting from pneumonia control would consist of increased growth rates, reduced mortality if acute pneumonia was a problem and reduced incidence of carcass downgrades at processing plants attributable to pleurisy.

In modelling the cost of pleurisy for the period January and June, the costs incurred earlier (July to December) were ignored. However, between October and December it is expected that these costs would not be large, as pleurisy at slaughter would have been lower in new season lambs and a reduced proportion of lambs (0.2) would have been slaughtered in comparison to that between January and June (0.7). From July to September, a reduced proportion of lambs are sold (0.1) and the population of lambs at this time cannot be well defined. Lambs slaughtered in this period may originate from lamb traders or out-of-season lambing flocks. As we did not account for pleurisy levels between July and December in our model a bias would have been introduced resulting in conservative estimates due to the cost of pleurisy, although the majority (70%) of the lambs killed

annually were accounted for. Another reason for underestimating the loss in this study was the lack of sensitivity in scoring lungs for pneumonia by meat inspectors of ASURE NZ Ltd. The sensitivity of MS pneumonia diagnosis was low (0.15 to 0.17). Thus the true prevalence, adjusted according to meat inspector sensitivity and specificity, may not have been an accurate estimate. However, it was the best estimate of pneumonia prevalence available with sufficient representation of the wider population.

Estimates of the economic impact of disease inform the feasibility of intervention measures such as vaccination or management practices to reduce the disease. In the case of lamb pneumonia, there are no effective vaccines currently licensed in New Zealand. The cost of pneumonia to New Zealand farmers may also be used as a gauge of how economically important the disease is nationally, and how much future research focus and money should be invested in developing effective control measures. As limited success has been gained with vaccines for lamb pneumonia, research should focus on control strategies through management. Significant areas of risk or protection found in the study of Goodwin-Ray et al. (2006a) should be further tested in intervention trials to assess their impact. More specifically, important risk factors were: shearing lambs at weaning, having ewe breeds other than fine wool breeds in Canterbury and increased flock size. Contact with other flocks through the purchase of lambs post weaning was indirectly associated with an increased risk of pneumonia. Protective factors included set stock grazing lambs post weaning and Vitamin B12 treatment of lambs at tailing and at weaning. In addition to this, other areas of risk or protection, for which previously there has only been anecdotal evidence could also be tested in this way, such as avoiding hand to nose contact of whole mobs when drenching (Alley, 1991), avoiding yarding and mustering under hot and dusty conditions (Davies, 1985b; Alley, 1991; Bruere et al., 2002), minimising stress for lambs and hoggets, minimising driving distance, use of sprinkler systems in yards to reduce dust in the yards, controlling dogs when they're not working around sheep that are yarded (Bruere et al., 2002) and maintaining a high general health standard (Davies, 1985b; Bruere et al., 2002). The general aim of these studies would be to develop control strategies for pneumonia focused on management or farm factors such as breed.

6.5 Conclusions

In conclusion, the average cost of pneumonia and pleurisy to the New Zealand sheep industry due to reduced lamb growth and decreased carcass value is likely to be between NZ \$32.4 and \$78.9 million (US \$20.7 and \$50.5 million). This is a conservative estimate indicating that pneumonia and pleurisy have substantial economic impact on sheep farming in New Zealand. Considering that 23,833,000 lambs were sold in 2003/2004, this cost would equate to \$1.36 to \$3.31 per lamb or \$1,361 to \$3,312 per 1000 lambs. If individual farms with a low, medium and high prevalence of pneumonia are considered the cost per lamb is likely to be around \$2.87, \$6.29 and \$7.32 respectively.

7.1 Introduction

Pneumonia in New Zealand lambs has long been recognised as a widespread problem leading to production loss through reduced growth rate and a predisposition to pleurisy resulting in economic loss to the sheep industry. The disease is complex in nature resulting from the interaction between microbial agents, immunological and physiological features of the host, and environmental factors. A wide range of micro-organisms are capable of causing pneumonia, therefore vaccination has not been an efficient tool to reduce the pneumonia prevalence in slaughter lambs. Consequently, New Zealand lamb producers demanded solutions for better, cost-effective control options. This thesis therefore addressed questions of the distribution of lamb pneumonia in New Zealand, economic loss attributable to the disease, possible causes and efficacy of prevention.

The thesis presents investigations of pneumonia prevalence in lambs in Canterbury, Manawatu and Gisborne, along with spatial patterns occurring in each region. The data are considered to be representative of the wider population, as it involves all lambs supplied to single processing plants within each study region over a ten month period. An economic estimate of the cost of lamb pneumonia and pleurisy to New Zealand sheep farmers is presented highlighting the financial consequence of the disease and need for further research. Exploring the web of causation of this multifactorial disease, a case-control study of lamb pneumonia in New Zealand presents several significant 'on-farm' protective and risk factors for the disease. An extensive clinical field trial investigating the efficacy of a vaccine currently available to New Zealand farmers was conducted, allowing farmers to make informed decisions about vaccine use based on the results.

7.2 Prevalence of pneumonia

Chapter 2 is the first data of pneumonia prevalence representing several regions with large samples of flocks ($n > 500$ flocks per region). The multi-level model suggested that pneumonia in slaughter lambs was higher in Canterbury than in Manawatu or Gisborne. It was previously assumed that pneumonia was a widespread problem on New Zealand sheep farms, often, based on limited samples of sheep farms (Kirton et al., 1976; Thurley et al., 1977; McGowan et al., 1978; Black, 1997; Goodwin et al., 2004). The results of the current study supported this assumption with sensitivity-adjusted pneumonia prevalence in slaughter lambs in Canterbury, Manawatu and Gisborne lambs of 29%, 22% and 24% respectively. Considering that this data provided a good representation of the population of farms in each of these regions, the mean pneumonia prevalence was high. The peak of pneumonia prevalence was two months earlier in the Gisborne region. Some characteristic of the environment or farm management system could be responsible for this peak (such as; steeper terrain, higher temperatures, different lambing/weaning dates), although limited detail of study farms prevented us from confirming this. It is also possible that this peak was a coincidental observation; multiple seasons of pneumonia prevalence data would be required to obtain a more accurate answer. The sensitivity of meat inspector diagnosis was low meaning a significant amount of lesions at slaughter were not detected. If slaughter lines had an apparent prevalence of zero it is likely lesions that were present were not observed and true prevalence was underestimated. Meat inspector diagnosis of pneumonic lesions at slaughter may be an inaccurate diagnostic tool and would not be an effective means of surveillance unless the sensitivity of diagnosis was improved dramatically. This could be achieved by increased training and providing incentives for a high standard of diagnosis along with several validation periods to monitor performance throughout each slaughter season.

Results of a multilevel model which accounted for clustering at the mob and flock level showed pneumonia scores of lambs at slaughter were more variable between mobs within a flock than between flocks. Therefore, pneumonia scores of lambs as recorded by meat inspectors are considered to be poor indicators for the pneumonia level of the flock due to their lack of repeatability. While we are relatively confident our prevalence estimates are robust at the regional level, the sensitivity of diagnosis was probably much more variable

at mob level and was therefore a possible explanation for increased variation in pneumonia prevalence at mob level compared to farm level.

7.3 Spatial patterns of pneumonia

Areas in each region were isolated where a high pneumonia incidence risk was present (Chapter 3, Figure 3.5) indicating spatial patterns of flock pneumonia prevalence may be evident. A cluster analysis reaffirmed this for Canterbury but not for other study regions. Binned omnidirectional variograms computed from standardised residuals of the multilevel model for each region (Figure 3.6) confirmed that no significant spatial autocorrelation was evident between case flocks in any region after adjusting for the fixed (processing plant, month) and random (clustering at mob and flock level) effects of the multilevel model. One limitation of this analysis was that only centroid coordinates were available for the geographical location of farms, which do not take account of farm size. However, at the spatial resolution used it appeared flock-level factors were of more importance than geographical location in determining pneumonia prevalence. This finding shows promise for the development of control methods for pneumonia. While geographical location of a farm is outside the control of farm managers short of re-locating, other farm-level factors may potentially be manipulated to reduce disease levels. In the multilevel model we showed significant regional differences in pneumonia prevalence. These regional differences could be explained by any factors that vary between regions. However, it is difficult to show causality in observational studies and in particular with regard to pneumonia where disease is only measured at slaughter. It is likely that adverse weather conditions may predispose lambs to pneumonia but would be difficult to provide evidence for this.

7.4 Risk Factors for Lamb Pneumonia

Previous to the case-control study presented in Chapter 3, only anecdotal evidence existed about 'on-farm' risk factors for lamb pneumonia in New Zealand. Significant risk factors for case farms were: (1) shearing lambs on the day of weaning, (2) breeding ewe replacements on-farm (3) number of lambs sold (an indicator of flock size) and (4) increased percentage of lambs sold between March and May. Significant protective factors

included: (1) set stocking lambs after weaning, (2) injecting lambs with Vitamin B12 at the time of tailing, (3) injecting lambs with Vitamin B12 at weaning.

In Canterbury, flocks with Romney ewes and other ewes had an increased risk of pneumonia risk than those with fine wool type ewes (Merinos, Corriedales or Halfbreds). The protective effect of Merino based breeding ewes in Canterbury may be a true breed effect as has previously been suggested anecdotally, or related to the way they are managed on farms. However, in our analysis the sheep grazing area of the farm and number of breeding ewes were incorporated into the models as potential confounding variables which may take account of the more extensive farms on which these breed types are run. Due to the fact that we controlled for factors related to these farm types and previous anecdotal evidence our results suggest a true breed effect is evident. Only a small subgroup of study flocks had mostly Merino based breeding ewes in Canterbury representing 7% of study flocks with completed questionnaires. Also the confidence intervals were wide due to this small number of flocks with fine wool type ewes consisting of only two case flocks. However, the effect appeared to be large after controlling for confounding factors and other protective and risk factors, suggesting that a breed effect cannot be ruled out.

Shearing of lambs at weaning was the strongest risk factor for pneumonia in lambs with a high odds ratio of 7.6. This may be caused by stress factors (weaning, fasting, crowding together, heat and handling) that reduce the capability of immune function along with the increased duration lambs are in close confinement increasing the risk of transmission of pathogenic micro-organisms. Flocks breeding their own ewe replacements had an increased percentage of lambs sold later in the season increasing the risk for pneumonia. It is likely these lambs would be ewe replacement lambs culled due to inferior quality, possibly due to poor growth from pneumonia. The path model suggested that the effect of breeding ewe replacements was in-part due to increased average lambing and weaning dates, increased likelihood of shearing lambs at weaning and an increased percentage of lambs sold late in the season.

Flocks with an increased proportion of lambs sold later in the season were more likely to be case flocks. As farmers send lambs for slaughter when they reach a sufficiently high slaughter weight, this appears to be an effect of pneumonia rather than a cause.

Administration of Vitamin B12 to lambs at tailing and weaning were protective factors. It cannot be determined from our results whether there is a real effect of Vitamin B12 or whether this is spurious result, and whether other unmeasured factors, such as the 'good manager effect', caused both, vitamin supplementation and a lower pneumonia incidence. In flocks where lambs were set stocked after weaning the pneumonia risk was reduced. It was thought that set stocking reduces the contact that lambs have with each other reducing risk of transmission of potential pathogens. Flock size as represented by the total number of lambs sold was a significant risk factor for case flocks in our study with a relatively large effect (OR 2.04 per SD (1896)). An increased risk with increased flock size has also often been found in epidemiological studies (French et al., 1994; Wittleberg et al., 1994; Healy et al., 2004). Dercksen et al. (1996) related this observation to either direct effects of the number of animals on disease introduction, spread and maintenance of infections within the flocks, or different management in large and small herds.

Because of the retrospective nature of the study some possibly important details could not be obtained from respondents, such as, frequency and duration lambs spent in yards throughout the season.

7.5 Path model

Path analysis illustrated several significant associations with significant risk and protective factors for pneumonia from the composite analysis.

The purchase of sheep was not a significant factor in the composite analysis, although the purchase of lambs was significant in the path analysis. If lambs were purchased from weaning onwards, the average slaughter age of lambs increased, which was in turn associated with the percentage of lambs sold late in the season increasing the risk of being a case flock. The increased pneumonia risk may be due to a longer exposure time to pneumonia pathogens in these flocks. The path model also showed that flocks purchasing lambs were less likely to graze lambs using a set stocking regime which was a protective factor for pneumonia. Therefore, the path model revealed that lamb purchase was indirectly associated with an increased risk of pneumonia at slaughter while being non-significant in the initial composite model.

Lambs from flocks which bred their own replacements spent longer in the yards at weaning probably related to them being shorn. This direct relationship however was not significant in the path model but explained partly by an indirect route through such flocks having later average lambing and weaning dates, making them more likely to shear lambs at weaning. Univariate statistics supported this indirect route as 9% of flocks that did not breed replacements shorn lambs at weaning compared to 20% of flocks that did. Typically, flocks breeding their own ewe replacements would shear only those lambs of the ewe replacement breed and other lambs (usually earlier maturing 'terminal sire' breeds), would not be shorn accounting for this relationship. The path model suggested that the effect of breeding ewe replacements was in-part due to increased average lambing and weaning dates, increased likelihood of shearing lambs at weaning and an increased percentage of lambs sold late in the season (March to May).

The injection of lambs with Vitamin B12 at weaning was more likely at higher stocking rates. Perhaps farm managers of properties with a more intensive farming system are more likely to supplement lambs with Vitamin B12 in an effort to increase lamb production regardless of whether there is a soil deficiency for Cobalt or not.

7.6 Vaccination against pneumonia

Currently, the vaccine Ovipast Plus® is commercially available to New Zealand farmers for sheep pneumonia caused by strains of *P. haemolytica* and *P. trehalosi*. Results of our clinical trial show Ovipast Plus® to be ineffective in reducing pneumonic lung lesions. There was also no effect of vaccine on, the average daily weight gain of lambs under New Zealand farming conditions, the isolation of *Pasteurella* from pneumonic lung samples, or histological classification of pneumonia. This finding has been published in farming literature providing New Zealand farm managers with independent information about vaccine efficacy that has previously not been available. Ovipast Plus® has been registered in New Zealand since 1992, without conclusive evidence of its efficacy under commercial farming conditions. It has been claimed, that vaccination with Ovipast Plus® reduces on-farm mortalities due to acute pneumonia. This claim has been used to promote and advertise the product to the farming public and veterinarians. It was shown that the

vaccine was not efficacious in reducing lung lesions on seven New Zealand commercial farms, although conclusive comments cannot be made about mortality as accurate mortality data could not be obtained. The reduction in lamb growth rate due to pneumonia is considered to be of more economical importance than mortality due to acute pneumonia which tends to only occur sporadically on very few farms.

The pathogens *Pasteurella haemolytica* serotypes A1, A2, A6, A7, A9 and *P. trehalosi* serotypes T3, T4, T10 and T15 were contained in the vaccine. While these pathogens and serotypes are important, there are other pathogens equally capable of producing pneumonia including *P. multocida*, *M. ovipneumoniae* and *M. arginini*. This was highlighted in our study, as *P. haemolytica* and *P. trehalosi* were not isolated from some pneumonic lung samples and there was no statistically significant difference between the histopathological classification of disease and *P. haemolytica* and *P. trehalosi* isolation in lung lesions. *Pasteurella* may not have been isolated from some pneumonic lesions in our study because (1) pathogens other than *Pasteurella* caused the pneumonia present, (2) the infection with *Pasteurella* was no longer active but the pathology remained, (3) by the time of culture any *Pasteurella* present had died and the test was false negative or (4) the vaccine was ineffective against pneumonia caused by *Pasteurella*. Ovipast Plus® was studied by Gilmour et al. (1991) where a high level of protection against experimental challenge with *P. haemolytica* A2 and PI3 virus was shown. This was substantiated by a mean group disease score consisting of clinical findings, lung lesions, isolation of *P. haemolytica* and pleurisy scores. A high level of protection has been shown to Ovipast Plus® under experimental conditions but there was no protection evident under field conditions from our study.

Our vaccination trial showed a significant negative effect of the extent of pneumonia on ADG of lambs between the first vaccination and slaughter. This indicates an increased energy demand for immune response, reducing that available for growth, in the absence of a positive vaccine effect.

In this trial lambs were selected for slaughter by live-weight and condition. This selection method selects against smaller, slower growing lambs whose ADG was likely to have been affected by pneumonia and thus did not represent a cross section of the flock at different stages of disease. Random selection of lambs for slaughter would have given a better

representation of the effect of pneumonia on ADG and not just that of lambs in good body condition at target slaughter weight. In an earlier study (Goodwin et al., 2004), the ADG of lambs selected based on live weight and condition was not affected by pneumonia although a large effect was shown in randomly slaughtered lambs. The true effect of pneumonia on ADG in the current study is likely to have been even stronger than that suggested by the data.

7.7 Economic effects of pneumonia and pleurisy

The stochastic model presented in Chapter 6 provides the first estimation of the annual cost of pneumonia and pleurisy to New Zealand farmers. This annual cost is approximately \$53.2 million (95% stochastic interval \$32.4 – \$78.9 million). Pneumonia comprises just over half of this figure. This would equate to between \$1.36 and \$3.31 per lamb, or \$1,361 to \$3,312 per 1000 lambs, considering the number of lambs slaughtered in 2003/2004. The cost of pneumonia and pleurisy due to reduced lamb growth rate and downgrading of lamb carcasses to New Zealand farmers estimated in this study is substantial and likely to be conservative. Therefore, further research is warranted in looking at how to control or reduce pneumonia and pleurisy in lambs. For example, assuming vaccination cost of \$2.16/lamb, an annual estimated cost of \$2.23/lamb associated with pneumonia and pleurisy, either the vaccine would have to be 100% efficacious vaccine, or a cheaper vaccine would be required in order to gain an economic benefit from vaccination use. In terms of individual farms with a low, medium and high prevalence of pneumonia the cost per lamb is high at around \$2.87, \$6.29 and \$7.32 respectively. The economic model presented in this thesis is likely to be the most comprehensive available. If routine inspection and recording of pneumonic lesions in lungs would be conducted at processing plants (to a higher standard than that which we experienced) on a continuous basis, the model could be updated regularly to monitor the benefits of interventions to control this disease in New Zealand.

7.8 Gaps in findings

The case-control study showed several significant on-farm factors that were protective or risk factors for flock pneumonia, but evidence for other anecdotally proposed risk factors were not found to be significant or could not be tested in this type of study. For example,

the risk of pneumonia associated with dust, open-mouth panting, heat stress and grouping lambs together in hot conditions. It was outside the scope of this questionnaire-based study to acquire objective quantitative measures on some of these factors. Also, because the questionnaire was retrospective accurate details of events could not be reliably obtained.

Similarly, we could not test the effect of vaccination on pneumonia induced mortality. The main reason for this was the added cost for conducting post-mortem examinations within the required time due to the geographical separation of the trial farms. Whilst the focus of our studies has been on sub-clinical pneumonia, it would have been beneficial to be able to compare the effect of vaccination on mortality rate to validate the pharmaceutical company's claims. Representative estimates of mortality due to acute pneumonia and the associated costs are not currently available. To provide representative estimates of mortality due to acute pneumonia a longitudinal study of randomly selected farms would need to be conducted. We have included some cost of acute pneumonia in our estimate, as lambs recovering from the acute stage of pneumonia may become chronically affected but we're unsure of these exact costs.

The question arises as to whether vaccine control of lamb pneumonia is possible. Due to the variation in pathogens in the field as compared to experimental conditions it would seem apparent that only a multivalent vaccine would be suitable to effectively control the disease. While *P. haemolytica* appears to be the most common bacteria isolated from pneumonia cases it is an opportunistic pathogen incapable of producing disease in the absence of viral infection (Davies et al., 1980a; Davies, 1985a; Brogden et al., 1998). Perhaps some thought should be given to vaccines against PI3 virus, which is not commonly isolated from pneumonic lesions but there is serological evidence for its presence in flocks when pneumonia prevalence is high (Davies et al., 1982). Likewise, *Mycoplasma* vaccines have not been trialled against pneumonia in sheep although are commonly isolated from pneumonic lungs. *Mycoplasma* vaccines are widely used and effective against pneumonia in pigs. Disease control is the main area for concern and while effective vaccines are still not available we have provided some focus for control efforts and further study in terms of significant areas of risk from our case-control study. It is likely that an integrated approach of management strategy and vaccine administration will provide the optimum disease control for the future.

7.9 Recommendation for further studies

The aims of further studies of sheep pneumonia in New Zealand should focus on the development of control strategies until effective vaccines are available. As a result of the case-control study there is a more refined focus of areas to study further. These areas, along with other proposed areas of risk or protection anecdotally evident in the past, or unable to be measured reliably in the case-control study are the direction in which further research should proceed.

Due to the wide range of pathogenic microorganisms for pneumonia, only a multivalent vaccine has potential to control or reduce the disease. A detailed up-to-date description of the prevalence and spatial distribution of pathogens for pneumonia and their genetic diversity in New Zealand is not available. This type of survey would provide the essential background information before successful vaccines could be developed.

As a follow-up to the case-control study future studies could include intervention trials to assess the effects of some of the significant risk and protective factors found. Flocks that shear lambs at weaning had the highest odds of being case flocks and this would be the obvious starting point, comprising an intervention trial between flocks that shear lambs at weaning and those that do not. The risk of shearing at weaning is either, related to the stress imposed on the lamb at this time affecting the capability of the immune system which increases susceptibility to infection and disease or an increased risk of the transmission of pathogenic organisms due to the prolonged period of close confinement. An interaction between these two factors is also likely. Several stresses of importance at this time include; the stress of weaning, the stress of no food or water for a prolonged period, the stress of the actual practice of shearing or the environmental stress imposed on the lamb (increased atmospheric ammonia, increased temperature and humidity). Further intervention studies aimed at separating out which of these factors or combination of factors provides the most risk would be warranted. In addition to this, an investigation into the environmental variables of the yards and shearing shed such as temperature, humidity, air movement and ammonia levels would be worthy of investigation.

The effect of set-stock grazing is another factor that could be tested in an intervention trial. If there is a protective effect of grazing method this could be a simple measure farmers could adopt to reduce the detrimental effects of pneumonia.

A comparison of lambs from Merino based breeding ewes and those from crossbred ewes grazed on similar country under the same farming system would assess whether there was a breed effect. If there was a true breed effect further trials could be conducted to determine which genes are responsible for the protective pneumonia trait in Merinos. The superior heat tolerance by Merino based breeds over British breeds may be the means by which they are less susceptible to pneumonia. The relationship of Merino based breeds, heat tolerance or heat stress and pneumonia is also worthy of further investigation. Indications of how often lambs become heat stressed in New Zealand conditions would be the starting point to these investigations.

The biggest quandary in studying pneumonia is in the absence of a diagnostic test in the live animal. Realistically, this limits future research to the flock level, where a sample of lambs can be slaughtered at regular intervals to determine the flock disease status.

7.10 Conclusions

This thesis has shown lamb pneumonia to be a widespread disease. The average flock pneumonia prevalence was 29%, 22 and 24% in lambs from Canterbury, Manawatu and Gisborne. In these regions, 70% of flocks had at least one lamb with pneumonic lesions diagnosed at slaughter. Previous studies have reported estimates of pneumonia prevalence from flocks with a known history of pneumonia but our study provides the first estimate of pneumonia prevalence in the general population over a significant period of time. The currently available vaccine had no effect on lamb ADG and was not effective in reducing pneumonia as determined in seven commercial lamb flocks. It is concluded that a wider array of pathogens likely to cause pneumonia would have to be included in order to present a more promising candidate vaccine. Farm-level factors were shown to have an effect on pneumonia prevalence. Therefore, as long as effective vaccines are not available, these factors should be the focus for further research and development of control strategies. Pneumonia and pleurisy currently costs New Zealand sheep farmers approximately \$50

million per annum through reduced lamb growth and downgraded carcasses at slaughter. This vast cost to the industry provides incentive for further research into how the disease can be reduced on farms.

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Appendix

The EpiCentre of  Massey University



Enzootic Pneumonia in New Zealand Lambs

Please return this questionnaire as soon as possible - Your information is important to the industry!

Enzootic pneumonia is a common disease of New Zealand lambs and is associated with production losses through

- Decreased lamb growth rate
- Pleurisy at slaughter
- Lamb mortality in acute cases

The costs to the industry are estimated to be considerable.

Why have we sent you this questionnaire?

Your flock was selected according to meat inspection findings at slaughter: either because of *very few* or *very frequent* pneumonia lesions in lambs at slaughter. Meat New Zealand has funded this project to investigate the differences between these two groups, so that:

- High frequency flocks can identify possible causes for pneumonia on farm
- Low frequency flocks are aware what management factors are related to pneumonia

You will receive a summary of the results once the data compilation and analysis is complete.

Confidentiality: We guarantee that all information will be treated by us as strictly confidential. No information will be used in any way that could reasonably be expected to identify any individual farm, or farmer.

Filling in the Questionnaire is easy!

Several farmers have assisted in developing this questionnaire to make it applicable to New Zealand sheep flocks and easy to understand. Although it contains a number of pages, it may take you only 20-30 minutes to complete.

Accurate information is ideal, but please enter your best estimate if exact figures are not known.

Please fill in all questions rather than leave them blank. Approximate dates and rounded numbers are better than leaving questions blank. Else, please enter a zero or 'not known'.

Feel free to ring me if any questions arise, or if you like assistance with the questionnaire. Also, feel free to write extra comments or explanations.

Contact: Kathryn Goodwin, EpiCentre, Private Bag 11222, IVABS, Massey University, Palmerston North. Telephone: (06) 350-5855 (Fax: (06) 350-5716), E-mail: K.A.Goodwin@massey.ac.nz

Farm details

1.1 Name of owner of the farm and date form completed

	/ /2001
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1.2 Postal address

1.3 Location address

Please do not give a PO Box number or Rural Delivery number - these should go in Postal address above.

Rapid No (if you have one)	
Road name	
Locality	
Nearest town/city	

1.4 Contact phone, fax and email

Phone		Mobile phone	
Facsimile		Email address	

1.5 What is the total and effective land area of the farm (hectares)?

Total area		Effective area	
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1.6 What is the **approximate** land area (hectares) of the farm used for sheep-farming?

1.7 **Approximately** how many paddocks (other than holding paddocks) are used for grazing sheep?

1.8 Main farming activity: What is the **main** activity carried out by this farming enterprise? (please tick one)

Main Farming Activity	<input checked="" type="checkbox"/>
Sheep (Finishing)	<input type="checkbox"/>
Sheep (Breeding/finishing)	<input type="checkbox"/>
Beef	<input type="checkbox"/>
Deer	<input type="checkbox"/>
Dairy grazing	<input type="checkbox"/>
Cropping	<input type="checkbox"/>
Other (specify)	<input type="text"/>

1.9 Breakdown of the main farm enterprises in terms of the percentage of land area used per enterprise:

	Sheep	Cattle	Deer	Cash crops	Total	Other (specify the enterprise)
Approximate land area %						
Example	40%	40%	0	20%	100%	

2.1 People working on the farm

Please give your estimates of the average number of persons employed for the sheep enterprise. Include the farmer and casual workers. Part persons are OK, e.g. 3½.

3.1 Sheep breeds

Please give the number of sheep wintered on the farm in 2000.

	Rams (2-tooth & over)	Ewes (Mixed age)		Ewes (2 tooth)		Ewe Hoggets		Ram and wether hoggets	Wether (2-tooth and over)
		Put to ram 2000	Dry - NOT put to ram 2000	Put to ram 2000	Dry - NOT put to ram 2000	Put to ram in 2000	Dry - NOT put to ram 2000		
Romney									
Coopworth									
Perendale									
Corriedale									
Halfbred									
Merino									
Borderdale									
Drysdale									
Border Leicester									
Cheviot									
South Suffolk									
Suffolk									
Texel									
East Friesian									
Finish Landrace									
Composite (3 or more breeds - specify breeds below)									
Specify composite breeds									
Other breeds and crosses (please specify)	Note: For crosses, show the breed of the SIRE first. e.g. Texel (Sire) & Romney								
Total sheep as at June 1 2000									

Farm topography

4.1 How would you classify the part of your farm you run sheep on in terms of topography/terrain?

Terrain type (tick those that apply)	✓
Flat	<input type="checkbox"/>
Flat to rolling	<input type="checkbox"/>
Moderate to steep hill country	<input type="checkbox"/>
Mixture of flat and hill country	<input type="checkbox"/>

Ewe mating

5.1 How many ewes, 2-tooths and hoggets were mated in 2000? What date did the main mating start and finish during the 2000 season? What was the average mating weight if recorded?

Ewe age class	Number	Dates rams went out	Date rams withdrawn	Ave.mating weight
Hoggets		/ /2000	/ /2000	
2-Tooths		/ /2000	/ /2000	
Mixed age ewes		/ /2000	/ /2000	

Management of pregnant ewes between the start of mating and lambing

6.1 Were the ewes pregnancy scanned in 2000?

no	<input type="checkbox"/>	Go to 6.2	yes	<input type="checkbox"/>	Go to 6.1.1
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6.1.1 Please give details of scanning below and average weight if recorded

Ewe age class	Number single bearing ewes	Number multiple bearing ewes	Overall scanning %	Average weight at scanning
Hogget				
2-Tooth				
Mixed age				

6.2 Please indicate the feed source for ewes between the start of mating and lambing, the type or brand and months when fed? (tick the feed source(s) applying to each ewe class in the specific columns, you may tick more than one box)

Feed type	Ewe age class (3)			Indicate type or brand (e.g. maize silage)	Months when fed
	Hogget	2-Tooth	Mixed age		
Pasture (indicate type)					
Hay					
Haylage					
Silage					
Grain					
Brassica crop					
Greenfeed crop					
Sheep nuts					
Other					

6.3 On what date(s) did you shear your ewes in 2000?

Ewe age class	Date shorn		Date shorn	
Hogget	/	/2000	/	/2000
2-Tooth	/	/2000	/	/2000
Mixed age	/	/2000	/	/2000

6.4 Did you vaccinate your ewes prior to lambing with any of the following vaccines (please tick)?

	5 in 1	Androvax	Eweguard	Campylobacter	Salmonella	Toxoplasma
Ewe hoggets						
2 teeth						
Mixed age ewes						

Lambing

7.1 What was the main system of grazing management you used for your ewe and lambs over the lambing period? (please tick)

Grazing management system	✓
Shifts every 2-5 days	
Shifts every 6-10 days	
Shifts at intervals of longer than 10 days but not set-stocking	
Set-stocking	

7.2 How much shade/shelter (trees, scrub, gorse etc) did your ewes and lambs have over lambing?, (please tick)

	✓
Nil	
Low	
Moderate	
High	

7.3 What was the **approximate** stocking density over the lambing period? (up to tailing)

Single bearing ewes		Ewes/ha OR		Ewes/acre
Multiple bearing ewes		Ewes/ha OR		Ewes/acre
ALL ewes if not scanned		Ewes/ha OR		Ewes/acre

Tailing

8.1 When did tailing start and finish in 2000?

Ewe age class	Start date of tailing	End date of tailing
Hoggets	/ /2000	/ /2000
2-Tooths	/ /2000	/ /2000
Mixed age ewes	/ /2000	/ /2000

8.2 Which method was used for tailing the lambs? (please tick)

Tails	✓	Purses	✓
Rubber rings		Rubber rings	
Hot iron		Crypt	
Knife		Burdizzo	
Other (please specify)		None (left entire)	
		Other (please specify)	

8.3 If not all male lambs were castrated, please specify what percentage fit into these categories

Ram	%	Wether	%	Cryptorchid	%
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8.4 Please tick what animal health treatments, if any lambs were given at tailing?

Scabby-mouth vaccination		Fly treatment		Worm drench		Vitamin B12	
Clostridial vaccine		Other (specify)					

Management of ewes and lambs between tailing and weaning

9.1 What was the **approximate** stocking density of ewes between tailing and weaning?

Single bearing ewes		Ewes/ha OR		Ewes/acre
Multiple bearing ewes		Ewes/ha OR		Ewes/acre
ALL ewes		Ewes/ha OR		Ewes/acre

9.2 What water sources did the ewes and lambs have access to between tailing and weaning? (please tick all those that apply)

Water Source	<input checked="" type="checkbox"/>
Running water (stream, creek or river)	<input type="checkbox"/>
Surface water (rain water run off) in a dam	<input type="checkbox"/>
Dam water reticulated into troughs	<input type="checkbox"/>
Underground water (artesian, spring) into troughs	<input type="checkbox"/>
Bore reticulated into troughs	<input type="checkbox"/>
Spring water reticulated into troughs	<input type="checkbox"/>
No water provided	<input type="checkbox"/>
Other (specify)	<input type="checkbox"/>

9.3 Please tick if any of the following animal health treatments were given to lambs between tailing and weaning

Worm	<input type="checkbox"/>	B12 Vaccination	<input type="checkbox"/>	Other (specify)	<input type="checkbox"/>	<input type="checkbox"/>
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Management of lambs from weaning onwards

10.1 What was the weaning date(s) in 2000/01? And how many lambs were weaned

Mob weaned	Date of weaning	Number of lambs weaned	Average weight

10.2 What was the number of lambs weaned for the flock and each component (if recorded)?

whole flock	<input type="checkbox"/>	hoggets	<input type="checkbox"/>	2-tooths	<input type="checkbox"/>	MA ewes	<input type="checkbox"/>
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OR What was the lambing percentage (lambs weaned/ewes at start of lambing)

whole flock	<input type="checkbox"/>	hoggets	<input type="checkbox"/>	2-tooths	<input type="checkbox"/>	MA ewes	<input type="checkbox"/>
-------------	--------------------------	---------	--------------------------	----------	--------------------------	---------	--------------------------

10.3 What treatments did the lambs receive at weaning? (please tick all those that apply)

Treatment	✓	Details
Crutching		
Shearing		
Drench		
Dip		
Vaccine (specify)		
Fly treatment		
Other (specify)		

10.4 If the lambs were dipped please tick the method below

Wand		Pour-on		Shower		Spray		Race	
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10.5 For **approximately** how long were the lambs in the yards and/or shed on the day of weaning?

	Approximate duration (hours)
Yards	
Shed	

10.6 Did you buy in lambs in 2000? If yes please give the number of sources the lambs were bought from

no		Go to 10.7	yes		Number of sources lambs bought from		Go to 10.6.1
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10.6.1 How many lambs did you buy during the season? (NA if not applicable)

	Number of lambs bought per month
October	
November	
December	
January	
February	
March	
April	
May	
June	

10.7 How many lambs did you sell this season (2000/20001) in each of the following months?

	Number of lambs sold per month		
	To Progressive Gisborne Ltd. or Feilding Lamb Packers Ltd.	To other works	Store or paddock sale
October			
November			
December			
January			
February			
March			
April			
May			
June			
July			
TOTAL (to date survey filled out)			
Lambs still on hand			

10.8 Please tick the **approximate** frequency of worm drenching for lambs in the 2000/2001 season?

4 weekly	<input type="checkbox"/>	5 weekly	<input type="checkbox"/>	6 weekly	<input type="checkbox"/>
Other (specify)	<input type="checkbox"/>				

10.9 Did you take preventative measures for fly strike in lambs after weaning? (please tick)

no	<input type="checkbox"/>	Go to 10.10	yes	<input type="checkbox"/>	Go to 10.9.1
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10.9.1 If yes please indicate the method of application and month used?

Method of fly strike prevention	Month used
Spray	
Shower	
Pour-on	
Wand	
Race	
Spot-treatments of affected lambs	

10.10 Were the lambs crutched and/or shorn in the 2000/20001 season? (please tick) If so please provide mobs and dates (NA if not crutched or shorn)

Mob of lambs (e.g. ram lambs)	Date	Shorn	Crutched
		✓	✓
	/ /20		
	/ /20		
	/ /20		
	/ /20		

10.11 Please indicate the feed source(s) and month(s) fed for lambs from weaning onwards? (tick the feed source(s) that apply, please indicate the type or brand and month(s) when fed)

Feed type	✓	Indicate type or brand (e.g. greenfeed oats crop)	Months when fed
Perennial ryegrass/ clover pasture			
Annual ryegrass/clover pasture			
Crop			
Other (specify)			

10.12 What systems of grazing management did you use for your lambs from weaning onwards? (please tick) Please indicate what month(s) the grazing management method was used

Grazing management	✓	Months when used
Daily shifts		
Break feeding		
Shifts every 2-5 days		
Shifts every 6-10 days		
Shifts at intervals of longer than 10 days but not set-stocking		
Set-stocking		

10.13 What was the most frequent means of mustering lambs? (please tick one)

Means of mustering	<input checked="" type="checkbox"/>
Motorbike	<input type="checkbox"/>
Truck	<input type="checkbox"/>
Tractor	<input type="checkbox"/>
Horse	<input type="checkbox"/>
Foot	<input type="checkbox"/>
Other (specify)	<input type="checkbox"/>

10.14 Do you use dogs for working lambs? (please tick those that apply)

Use of dogs for	<input checked="" type="checkbox"/>
Mustering/shifting	<input type="checkbox"/>
In yards/shed	<input type="checkbox"/>

10.15 What water sources did the lambs have access to after weaning? (please tick those that apply)

Water Source	<input checked="" type="checkbox"/>
Running water (stream, creek or river)	<input type="checkbox"/>
Surface water (rain water run off) in a dam	<input type="checkbox"/>
Dam water reticulated into troughs	<input type="checkbox"/>
Underground water (artesian, spring) into troughs	<input type="checkbox"/>
Bore reticulated into troughs	<input type="checkbox"/>
Spring water reticulated into troughs	<input type="checkbox"/>
No water provided	<input type="checkbox"/>
Other (specify)	<input type="checkbox"/>

10.16 How much shade/shelter (trees, scrub, gorse etc) do your lambs have over summer? (please tick)

	<input checked="" type="checkbox"/>
Nil	<input type="checkbox"/>
Low	<input type="checkbox"/>
Moderate	<input type="checkbox"/>
High	<input type="checkbox"/>

10.17 Are your sheepyards covered? (please tick) If yes please indicate the proportion of that area covered

	✓	Proportion of area covered
No		
Yes (working area only)		%
Yes (working area and holding yards/paddocks)		%

10.18 Did you have a **problem** (e.g. greater than 5% of flock) with any of the following in lambs in the 2000/2001 season?, if so please give details and tick the severity of that event

Event	Month	Severity (✓)			Approximate % of flock affected
		Mild	Medium	Severe	
Abnormal death					
Ill-thrift					
Scouring					
Nasal discharge					
Coughing					
Fly strike					
Facial eczema					
Scabby mouth					
Lameness					
Staggers					
Pneumonia					

Ewe replacement policy

11.1 Do you breed your own ewe replacements? (please tick)

yes		Go to 12.1	no		Go to 11.2
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11.2 What is the age of your ewe replacements when you buy them? (please tick one or more boxes)

Lambs/hoggets		2-tooths		MA ewes	
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11.3 Do you know how many different source farms replacements were bought for 2000? (please tick)

Yes (please indicate number)			No	
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Ram buying-in practices

12.1 How many different studs have you sourced most of your rams from over the past 5 years?

Replacement Sires	
Terminal Sires	

Background animal health details

13.1 Did pneumonia cause any problems in your older sheep in the 2000-2001 season? (please tick)

Yes	<input type="checkbox"/>	No	<input type="checkbox"/>
Don't know			<input type="checkbox"/>

13.2 If yes, please list the class(es) of sheep affected (e.g. MA ewes), the number of deaths in each class and the time of the year

Class of sheep affected	Number of deaths	Time of the year

Thank you for taking the time to fill in this questionnaire. We would appreciate any comments about the disease that you feel may be useful to us. We value your opinion and would like to hear from you.