tions on the growth and production of young animals through experiments incorporating suppressive drenching treatments which greatly reduce infection rates. Although economic analyses showed that limited drenching programs for young sheep yielded the highest net returns in all circumstances, drenching at monthly or even 2-weekly intervals was reported to be profitable at prevailing costs and prices (Anderson *et al* 1976; Johnstone *et al* 1976b; Morris *et al* 1977). This may have led to some increase in drenching frequency. Certainly in New Zealand mean drenching frequency of lambs increased from 4.3 for the North Island and 3.8 for the South Island in 1971/72 to 6.8 and 5.8 respectively in 1979/80 (Brunsdon *et al* 1983).

However, in the same period anthelmintic resistance has become an increasingly important problem and field occurrences are clearly associated with frequent drenching (Donald 1983). This factor should be taken into account, therefore, in any economic analysis of anthelmintic usage. By analogy with pesticide resistance (Hueth and Regev 1974), anthelmintic susceptibility in parasites is an exhaustible resource. Use of anthelmintics results in both monetary costs and "user costs" defined as "the present value of the future profit foregone by a decision to produce a unit of output today", in this case by depleting the stock of anthelmintic susceptibility. User costs have so far received little attention from producers or their advisors, but consider the following simplified scenario. In Australian sheep flocks there is now some degree of resistance to all of the currently available broad spectrum anthelmintics so that any completely new compound will possess a strong market advantage, despite a higher unit price required at least to recoup research and development costs. By contrast, if resistance had not developed to the existing compounds their cost could be expected to fall as patents expire.

If user costs in anthelmintic application were taken fully into account, they could have an important impact on economic analyses of helminth control. Even in young animals where the benefits of greatly reduced infection rates are well defined (Barger 1982), frequent drenching as a means of achieving this is likely to prove very costly, giving greater emphasis to other approaches such as grazing management. In mature animals, the effects on production of continuing exposure to helminth infection need to be better understood but present knowledge suggests that they would rarely be large enough to justify any substantial use of anthelmintics, given the problem of resistance.

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Limitations to the realisation of potential production — neonatal calf disease

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Introduction

Opinions vary as to the importance of neonatal calf disease in the limitation of potential productivity in cattle. There is very limited data on the prevalence of neonatal disease in calves and prevalence data by itself is of limited value without some measure of severity or of necessity for economic intervention or without some measure of effect on production performance. Certainly many calves experience mild enteric disorders that do not require therapy and which have no apparent long term effect on performance potential. Mortality from neonatal calf disease is more easily determined and is what is commonly used to reflect the prevalence and importance of neonatal calf disease.

A recent industry publication in the United States of America commented that 1 in 5 calves failed to survive to 4 months of age and area surveys of neonatal mortality have reported rates that vary in the range of 5 to 20% (Simenson 1982; Hancock 1983). Most surveys indicate considerable variation between herds and the existence of high risk and low risk herds. The preponderance of mortality occurs within the first 2 weeks of life. Mortality in neonatal calves is associated predominantly with the occurrence of septicemic and enteric disease. Respiratory disease is also a significant cause of mortality prior to weaning. Septicemic and respiratory disease in calves result from a complex, but poorly defined, interaction between specific infectious agents and the calf. This interaction can be profoundly influenced by environmental and other management factors. The majority of research on neonatal disease in calves has concentrated on the identification of specific etiological agents as the cause and on the interaction of these individual agents with the calf. Although this type of research is vital to the understanding of disease pathogenesis, the development of effective forms of therapy and the development of strategies for specific immunoprophylaxis, it is not necessarily the most important approach to the control of neonatal disease and strategies which influence the host, environmental or managemental determinants of neonatal disease may be equally or more cost effective. Within this context limitations to the realization of potential production imposed by the occurrence of neonatal disease in calves exist in several areas.

Etiologic Agents, Diagnosis and Specific Immunoprophylaxis

During the past 20 years there have been remarkable advances in our knowledge of the specific etiologic agents associated with neonatal disease in calves and of the mechanisms whereby they induce disease. A large number of infectious organisms have been associated with enteric disease in neonatal calves (Tzipori 1983; Acres 1985; Saif and Smith 1985; Shane and Montrose 1985). These associations have been initially made on the basis of frequency of isolation or identification of these agents in the faeces of scouring calves as compared to non-scouring calves. The enteropathogenicity of many of these bacterial, viral and protozoal agents has subsequently been confirmed by experimental challenge of conventional or gnotobiotic calves. The advances in diagnostic technologies for the identification of these various organisms in the faeces of scouring calves have been substantial. In addition to traditional cultural and identification methods many diagnostic laboratories now utilise rapid technologies such as fluorescent antibody, ELISA or direct electron microscopy to facilitate specific agent identification and these methodologies allow information on agent association with outbreaks of diarrhoea to be rapidly available to the practitioner. However with some exception knowledge on the epidemiology of these infections has not kept pace with methods for their identification and other than immunoprophylaxis specific control procedures directed against individual causal agents are limited.

Knowledge of these agents and of the mechanisms whereby they produce enteric disease has lead to the development, or the potential for the development, of methods of specific immunoprophylaxis for certain neonatal diseases and is exemplified by the advances made in neonatal disease associated with *Escherichia coli* (Acres 1985). From the loosely defined term of colibacillosis used 20 years ago it is now recognised *E. coli* have the potential to produce both septicemic and enteric disease in calves. These diseases have a separate pathogenesis and the types of *E. coli* associated with each and their virulence attributes are quite different. *E. coli* associated with enteric disease have certain structural attributes, the most important of which are pili or fimbriae which enable them to attach to epithelial cells and thereby colonise the small intestine. There are currently 5 fimbrial antigenic types that have been associated with colonisation, the most important of which appears to be K99. In addition, these enterotoxigenic *E. coli* possess the ability to produce enterotoxin, which is the biochemical mediator of fluid secretion and results in the production of diarrhoea. In the case of enterotoxigenic *E. coli* associated with diarrhoea in neonatal calves, this enterotoxin is of the STa class. The knowledge of these attributes of virulence has lead to the development of methods of specific immunoprophylaxis against diarrhoea associated with enterotoxigenic *E. coli* by the development of both vaccines and a monoclonal antibody preparation active against the K99 attachment antigen. Both have been shown effective in the prevention of *E. coli* diarrhoea. There is a potential for further developments in this area. STa has been sequenced and can probably be modified or complexed so that it is antigenic. The development of STa-directed vaccines or antibody preparations would be effective against all *E. coli* currently recognised as being associated with diarrhoea in calves and may be required should the use of current vaccines result in the emergence of enterotoxigenic *E. coli* of different pilus types. There is some evidence that the use of pilus directed vaccines in swine has led to the emergence of enteropathogenic *E. coli* of pilus types not included in the vaccine. Research on the action of STa should also ultimately result in the marketing of specific pharmacologic antigonists.

Substantial advances have also recently been made in understanding of viral and protozoal associated diarrhoeas in calves (Tzipori 1983; Saif and Smith 1985). At least 8 viruses have been associated with diarrhoea in calves. All of these infect either the villus or the crypt epithelial cells within the intestine to result in villous atrophy and the subsequent occurrence of a malabsorption-type diarrhoea. Limitations to the development of specific immunoprophylaxis against these agents currently include the inability to cultivate some in tissue culture and the development of methods of immunisation that will ensure high levels of enteric acting antibody throughout the neonatal period. Specific immunoprophylaxis for rotavirus and coronavirus is currently available, however, its antigenicity and efficacy has been questioned. The subject of virus-associated enteritis in calves and its immunophylaxis has been recently reviewed (Saif and Smith 1985). In recent years, crytosporidium has been implicated as a primary or complicating cause of diarrhoea in calves in etiological surveys from many countries (Tzipori 1985). The replication of cryptosporidium in the intestine is associated with villous atrophy, inflammation of the lamina propria, and diarrhoea of varying severity. There are currently no recognized anti-microbial products for the treatment of cryptosporidiosis and the organism is resistant to common disinfectants. In view of this, the development of specific immunoprophylaxis against cryptosporidiosis could be most pertinent. Current technologies should allow the identification of the surface antigen of cryptosporidium sporozoites associated with infection and the development of relevant immunological preventive measures.

The recent advances in specific immunoprophylaxis against neonatal calf disease have been driven by the strong research interest and research funding in the areas of disease agent identification and agent-host interaction. Current research funding thrusts suggest that advances in this area will be continued.

However, although specific immunoprophylaxis has value in the control of neonatal disease, it also has its limitations. The commercial development of vaccines is dependent upon predicted commercial success based on the prevalence of an agent and its perceived importance. Even assuming the availability of vaccines against all of the common enteropathogenic agents, it is unlikely that their use would be economically viable. There are further objections to control based on a single causal agent approach. It is common to associate several enteropathogenic agents with a single outbreak of diarrhoea in calves and commonly 2 or more enteropathogenic agents may be isolated from the intestines of an individual scouring calf. Similarly, a multiplicity of agents are involved in outbreaks of calf respiratory disease. Many enteropathogenic agents and agents associated with respiratory disease are ubiquitous in the environment of the calf and can be isolated also from healthy calves. Under these circumstances, the occurrence of disease as apposed to infection appears more likely due to management factors that result in heavy infection pressure or in some way predispose the calf rather than to chance exposure of the calf to a single pathogenic agent.

Management and Environmental Determinants

Other than failure of passive transfer of colostral immunoglobulins to the calf the managemental and environmental determinants of neonatal enteric and respiratory disease are poorly defined and as yet not quantified. Ventilation and microclimate are recognised as critical to the respiratory health of calves yet ventilatory designs of calf houses are based more on heat exchange and moisture removal than on aerosal and pathogen clearance. The success and acceptance of individual cold calf housing-the calf hutch-for calf rearing and calf health over the traditional communal calf house exemplifies the importance of environmental aspects in calf health. However in relationship to their potential importance in the control of neonatal calf disease there has been relatively little study of these determinats. Studies have identified important determinants such as group housing, types of housing and methods of feeding that can be acted upon to reduce the risk of mortality but other identified determinants such as season, size of herd and who feeds the calves need to be further quantified to identify the critical interactions before they are of practical value in evolving corrective or preventive strategies. There is however a real problem in accurately quantifying these determinants. For example stocking density in calving paddocks can have a profound influence on the occurrence of calf enteric disease in cow calf operations and Radostits and Acres (1980) have made an approach to define acceptable stocking densities in these situations. Ideally we should have knowledge of the relative risk for enteric disease associated with different stocking densities. However the descriptions of the calving paddocks situations in Radostits and Acres paper show how difficult it is to accurately define something as apparently simple as stocking density when one is working with on-farm situations. The establishment of the managemental and environmental determinants of neonatal disease in calves (or any disease in animal groups) will require an intensity of input and the development of methodologies equivalent to those inputs and methodological developments that are current in the laboratory identification of agents of neonatal disease and in the definition agent host interactions. Co-operating commercial farms will be the major setting for this type of research. Unfortunately in most institutions there is no structure or funding for research of this nature. Recent reviews of factors affecting the susceptibility of the neonatal calf to enteric disease emphasizes our lack of practical knowledge in this area (Ray 1980; Hancock 1983; Simenson and Norheim 1983). There is a severe limitation placed on our ability to improve the potential production in cattle herds by this lack of information.

Failure of Passive Transfer of Colostral Immunoglobulins

Partial or complete failure of passive tranfer of colostral immunoglobulins is a prime determinant for the occurrence of septicemic disease in neonatal calves and a major determinant for the occurrence of enteric disease and case fatality associated with it. Failure of passive transfer is also a major determinant for the occurrence and case fatality of respiratory disease in older calves and in groups of calves shows a correlation with the number of treatments and the severity of lung lesions at slaughter. These relationships and factors that can influence the occurrence of failure of passive transfer have recently been reviewed (Gay 1984; Dukamel and Osburn 1984). There are a number of minor determinants for failure of passive transfer but the 2 major determinants are the immunoglobulin mass that is fed and the age at feeding. The mass of immunoglobulin ingested is a product of the volume of colostrum ingested and its immunoglobulin concentration. In practical feeding situations the volume of colostrum fed can be manipulated, however, immunoglobulin concentration has probably the greatest significance to the occurrence of failure of passive transfer and calf health. There is considerable variation in the immunoglobulin concentration of first milking colostrums in dairy breeds and a substantial proportion of first milking colostrums have critically low values.

Several surveys have shown that the prevalence of failure of passive transfer in naturally sucking dairy calves can approach 40%. This failure results from a combination of poor calf vigour and poor sucking drive coupled with a late ingestion of inadequate volumes of low immunoglobulin concentration colostrum. This prevalence of failure is substantial, and in view of its influence of calf health, research needs to be directed into factors that affect calf vigor at birth and factors that result in poor colostrum quality. Factors such as prolonged parturition and fetal anoxia have already been identified as influences on subsequent calf vigour. The concentration of immunoglobulin in colostrum tends to repeat from lactation to lactation within the same cow but the factors that determine this are as yet unknown.

The artificial feeding of colostrum can, in theory, ensure an early intake of adequate volumes of colostrum. However, in practice, this is also commonly associated with high rates of failure. In systems where the calf is fed colostrum from its own dam the cow must be milked and substantial volumes (2.5 to 4 litres) of this colostrum must be fed during the first 12 h of life to ensure adequate passive transfer. The time constraints imposed by other mandatory farm activities on the availability of labor for milking the cow and feeding the calf at a time dictated by the cow's calving obviously limits the success of most methods of artifical feeding in commercial enterprises.

Nevertheless, with current knowledge, practical feeding systems can be devised that will result in a minimal prevalence of failure of passive transfer. These may require the use of stored colostrum, the measurement of specific gravity to eliminate colostrums with low immunoglobulin concentration and the use of an esophageal feeder to ensure a large volume intake with minimal time spent on feeding.

Failure of passive transfer is a major determinant of calf health and its continued high prevalence limits potential productivity in cattle herds. However, the practical application of existing knowledge could marketly improve limitations to productivity imposed by this determinant.

Economic Considerations

Neonatal calf disease can impair the potential productivity of herds through the costs of treatment and prevention, the costs of mortality, the loss of genetic potential, the avoidance of the potential for genetic improvement from superior but more costly semen because of fear of subsequent loss, the reduction or loss of potential elective culling and through a subsequent reduction in the lifetime potential production of recovered animals. Unfortunately, there is virtually no hard data on the economic effects of neonatal calf disease. The constraints that exist for the determination of the environment and managemental risk factors for neonatal disease also exist for the determination of economic factors associated with the complex and its control. For this reason most analyses deal purely with the effects of mortality and treatment costs. However an assessment of the economic effects requires some measure of prevalence and severity in order to determine non-mortality effects. Prevalence data is difficult to collect in on-farm situations unless non-farmer recording is used and the use of clinical scores for severity is notoriously inaccurate. One practical approach to this problem has been the use of records of treatment frequency and treatment costs as a measure of prevalence and severity of diarrhoea in on-farm situations (Andrews and Read 1983). It is reasoned that mild diarrhoea as assessed by the owner will not be treated or will be treated with inexpensive preparations such as kaolin or pectin. More severe diarrhoea or general response to it is likely to result in treatment with a more expensive antibiotic. Similarly non-response or a more protracted course will result in more frequent treatment with increasingly more expensive drugs. Although this approach may not be an exact measure of the severity of disease or of its prevalence it represents an attempt to measure these factors by a method which is applicable and practical. Similar methodologies have been used to analyse respiratory disease (Miller *et al* 1980). Such practical methodolgies need to be developed and tested as an alternative to traditional but still inexact measures. A model had been developed for the economic analysis of the effects of respiratory disease in calves (Willadsen *et al* 1977) and programs written to assist with the determination of costs and benefits associated with vaccination or other preventive measures against enteric disease. Although most considerations of neonatal disease deal with the direct costs of treatments, mortality, and the effects of mortality on replacement heifer policy there is some indication that neonatal calf disease can affect lifetime survivorship and lifetime production in affected calves that are treated and that recover. Anecdotal reports suggest that there is an effect of calfhood diseases, such as pneumonia, on subsequent time to first calving and on milk production. If such is true it adds a further dimension to the economic analysis of the effects of neonatal calf disease. The limited reports in the literature are somewhat contradictory on particularly neonatal disease associations with subsequent lifetime production but they do indicate that such an association does exist in individual situations where neonatal disease has been significant (Simenson 1983; Britney *et al* 1985). The lack of hard economic data on the effects of neonatal calf disease and on the benefits of various disease control strategies is a serious limitation to improvements in productivity.

Practical Field Application of Existing Knowledge

Although there are many areas where knowledge of neonatal calf disease needs to be improved so that its prevalence can be reduced in an economically beneficial manner, there are also other areas where the practical field application of existing knowledge could result in marked improvements in productivity. Mention has been made above of the high prevalence of failure of passive transfer in dairy herds and the fact that this could be reduced by the application of current knowledge in a practical manner. A further example for this exists with veal calf rearing establishments. Veal calf establishments commonly experience a high morbidity and mortality from respiratory disease. It can be shown in many of these establishments that the entry immunoglobulin status of the calf is a prime determinant of subsequent morbidity and mortality. There are practical and cost-effective testing procedures that can identify calves at purchase with higher resistance to disease. The principles and methodologies underlying these selection procedures have been known for many years, however, very few veal calf establishements use them.

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Applications of epidemiology to problems in food animal medicine

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The Need for Epidemiology

In a paper in Preventive Veterinary Medicine titled "The Current Epidemilogical Revolution in Veterinary Medicine", Schwabe (1982) describes the following crises that have led to new developments in the application of epidemiology to problems in food animal medicine:

- "Problem herds" encountered after a lengthy campaign against brucellosis, tuberculosis and some other chronic livestock diseases had *substantially* reduced their frequencies in some countries without eliminating them.
- Unprecedented demands upon livestock disease control authorities to document in *economic* terms the cost of specific diseases and the likely cost and benefits to be realised from pursuit of alternatives to their control.
- Absence of suitable research or control approaches not only to well-known types of costly, insidious disease complexes (such as bovine mastitis), but also to new "production diseases" of unknown or presumably complex etiologies which are being recognised increasingly in industrialised countries.
- Inability of private veterinary practitioners and livestock producers in industrialised countries to fully evolve economically and scientifically viable approaches to health maintenance in *intensive* livestock production.

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These 4 crises have one important element in common; they are all situations requiring identification, quantification and examination of multiple directly or indirectly causal and often interacting disease determinants. The tactical approaches listed by Schwabe (1982) for solving the crises are surveillance, intensive follow-up and epidemiological and economic analysis. These elements are the principal components of the epidemiological approach to population diagnosis.

In the following sections we will illustrate current levels of epidemiological literacy as applied in some specific programs dealing with food animal disease problems in Denmark. Subsequently, we will describe and discuss some basic requirements for further developments of the epidemiological approach.

Levels of Applied Epidemiological Literacy

Within epidemiological field activities in food animal medicine techniques may be applied with varying degrees of sophistication to match the nature of the problem and the complexity of the available data. In the following sections, 3 current examples of Danish investigations and control programs will be given to illustrate the increasing need for epidemiological literacy when moving from accomplishing existing tasks, through increasing the effectiveness of doing these tasks, to the devising of new applications.

Accomplishing Existing Tasks

That alone is no small job when it comes to contributions towards solving the 4 crises described previously. However,