

APPROACH TO COMPLEXITY IN VETERINARY EPIDEMIOLOGY : EXAMPLE OF CATTLE REPRODUCTION

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De l'épidémiologie vétérinaire à l'écopathologie animale, un cheminement vers l'analyse de la complexité. Un état des lieux portant sur un champ de recherche en plein renouvellement et qui représente un exemple particulièrement instructif pour une interdisciplinarité entre sciences du vivant et sciences sociales, avec tous les problèmes méthodologiques qu'elle soulève.

Résumé en français p. 34

INTRODUCTION

During the last few decades, most main infectious diseases, such as tuberculosis, brucellosis, and foot and mouth disease in cattle, have been controlled in animal production. At the same time, new types of diseases (production diseases) have become much more important (Ganière *et al.*, 1991). These diseases are insidious but their economic effects may be considerable, because they may cause a decrease in production, delays in reproduction, and a poor food conversion rate (Fourichon, 1991).

The main characteristic of these production diseases is that the concept "1 cause → 1 effect" (Koch's postulate), commonly used in veterinary science and based on the intervention of a pathogen

(Sabatier *et al.*, 1994), is too limiting. Production diseases are often related to the increasing level of production of the animals and to the intensification of livestock production. They result from various equilibrium disturbances in high producing animals and thus have a multifactorial origin (Tillon, 1980) (Figure 1).

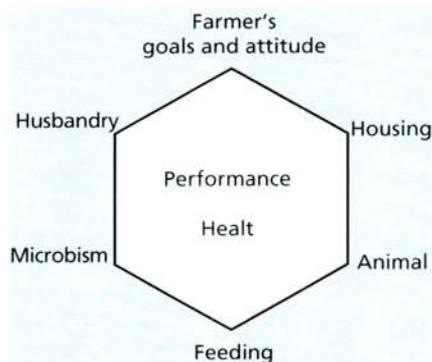


Figure 1 : The multifactorial hexagon (modified from Tillon, 1980). This hexagon is a simplified scheme for the multifactorial concept of disease causation on farms. It has an historical interest in the sense that it was developed in pig production in order to enhance the role of the husbandry and of the farmer's attitude on disease causation, at a time when only germs were taken into consideration in the explanation of disease. This new concept was developed in France during the '70s and gave birth to ecopathology, which is very close to veterinary epidemiology (see inset "The different fields of epidemiology", 3.1 and 3.3).

Figure 1 : L'hexagone multifactoriel (d'après Tillon, 1980, modifié). Cet hexagone est un organigramme simplifié illustrant la notion de pathologie multifactorielle. Il a un intérêt historique dans la mesure où il a été développé en production porcine pour mettre l'accent sur le rôle de la conduite d'élevage et du comportement de l'éleveur dans l'apparition des maladies, à une époque où seul le microbisme était pris en considération. L'approche multifactorielle a été développée en France dans les années soixante-dix et a donné naissance à l'écopathologie qui est une discipline proche de l'épidémiologie animale (voir encart "The different fields of epidemiology", 3.1 et 3.3).

ABSTRACT : Approach to complexity in veterinary epidemiology : example of cattle reproduction

One of the main goals of veterinary epidemiology is to analyse the determinants of disease, commonly called risk factors. The analysis of such systems is usually based on a pluridisciplinary approach, a planned observation of the natural state, and a judicious use of various methods to analyse the data. Most studies are carried out at the animal level, where the modelling techniques (logistic regression, Cox model) and correspondence analysis have shown complementary interest. Other studies are carried out at the farm level, considering the farm as a cybernetic system. The point of view concept plays a key role in the analysis of this complex reality.

Epidemiology as a scientific discipline addresses the question of disease occurrence at the population level. Epidemiological research has played an increasingly important role in attempts to gain insight in disease causation related to these multifactorial health problems in livestock production. The goal of this paper is to present the subject of veterinary epidemiology, the current methods, and their limits. The example of bovine reproductive efficiency illustrates that veterinary epidemiology deals with complex systems (first section). Then are presented the most commonly applied methods used to study the risk factors of disease at the animal level (second section) and at the farm level (third section). The last section discusses the types of systems observed in epidemiology, as well as the methodology of their analysis.

EPIDEMIOLOGY : DEALING WITH COMPLEX BIOLOGICAL SYSTEMS

The management of herd reproduction is one of the critical concerns for the profitability of dairy and beef-cattle operations. Furthermore, reproductive efficiency is under the control of various components so that reproductive problems represent an important subject in veterinary epidemiology.

Example : Reproductive problems in cattle

The reproduction of the cow – cycling activity, pregnancy, calving and post-calving periods – is under the control of a

complex physiological scheme. Two main organs and their effective functioning are of great importance to insure high reproductive efficiency of the female ; the ovary and its cyclic activity, and the uterus, which allows the nidation and development of the fertilized ovum. The hormonal system regulates these mechanisms. The current knowledge about infertility (that refers to reproductive disorders), acquired from physiology, clinics, and pathology, addresses two main kinds of dysfunction : hormonal disturbances that mainly affect the functioning of the ovary (postpartum *anestrus*, cycle cessation at a given stage, unusual ovulation delay after *estrus* period), and inflammatory and infectious problems that disturb uterine activity : mild cases that prevent the implantation of the fertilized ovum, or severe infections like clinical metritis.

These organic and physiological problems relate to the delicate equilibrium of the body's regulation that can be easily unsettled by various disturbances related to the environment of the animal, the word being understood in a broad sense. Studies carried out at the organismic and population level always point out the effect on fertility of various different parameters (Figure 2) like microbism, housing, feeding, weather, season, social interaction with other cows, and husbandry practices of the farmer. Some of

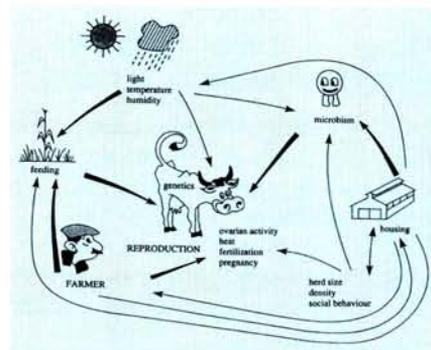


Figure 2 : Environment and reproduction (Paccard, 1981)
The reproductive efficiency of the cow is influenced by various components from the environment that are linked and interact with each other.

Figure 2 : Environnement et reproduction (Paccard, 1981)
Les résultats de reproduction de la vache sont influencés par de multiples facteurs qui sont liés et interagissent entre eux.

these parameters are also related to each other.

A deeper view of the question is given in Figure 3 (Ducrot, 1993) that illustrates a study performed in France with a pluridisciplinary group (Rosner, 1984). It shows the effect on fertility of bad calving circumstances and farmer's practice at calving, as well as the role, on calving difficulty, of various parameters related to the type of housing, the feeding and the characteristics of the cow and of the calf(ves).

The risk factors for disease

The example provided above is quite typical of the kind of results observed in epidemiological studies carried out on production diseases. The main characteristics of the type of situation describing the determi-

nants of infertility are clearly typical of a complex system, as mentioned by Landais (1991). According to Pavé's definition of complexity (1994), we find a structural complexity in such a situation. Several different determinants, commonly called *risk factors*¹, are involved in explaining and producing the disease, say the reproductive inefficiency. Each of these components has a small effect on disease causation, and none of them has a major and decisive effect ; the combined effects of many of the risk factors, and their possible potentialisation induce the reproductive inefficiency. One may consider that it may be possible to reduce the observed scheme, or in other words to combine these components, because of the presence of a common determinant. This is not plausible because components from very different domains are involved

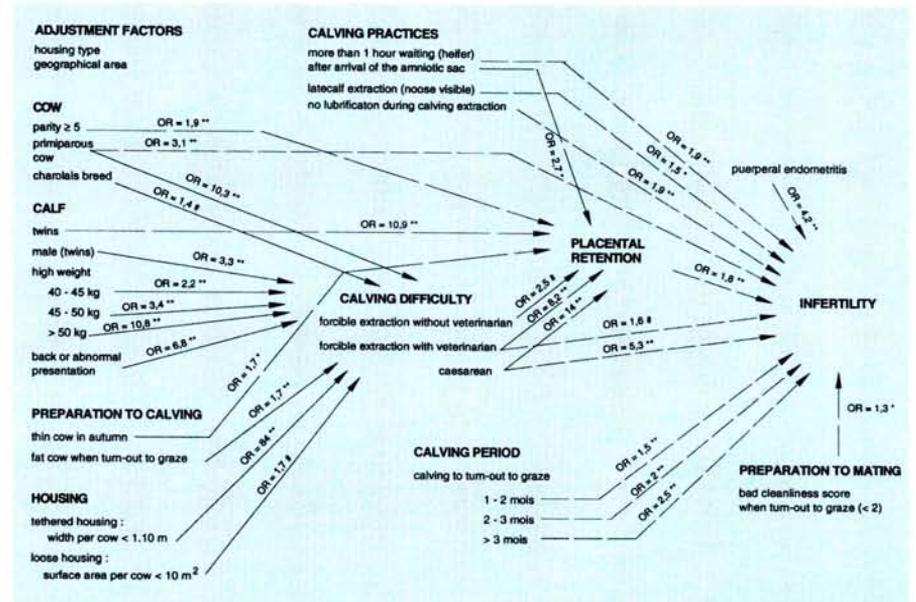


Figure 3 : Path analysis scheme for infertility (Ducrot, 1993). This figure summarizes the results of an epidemiological study performed in France and carried out on 116 beef cattle farms from the Rhône-Alpes, Centre and Bourgogne regions ; 2993 cows, mostly of the Charolais breed, were followed up over 2 years, from 1987 until 1989, by 33 surveyors (veterinarians, advisors, inseminators). The goal of this observational study was to analyse the risk factors for infertility (calving interval greater than one year), and especially those related to the calving period. The odds ratio measures the strength of the association between the risk factors and the outcome (see inset "Odds ratio") (OR = conditional odds ratio ; ** $p \leq 0.01$; * $p \leq 0.05$; # $p \leq 0.20$).

Figure 3 : Modèle de path analysis relatif à l'infécondité (Ducrot, 1993). Cette figure résume les résultats d'une étude épidémiologique réalisée en France et portant sur 116 élevages de vaches allaitantes des régions Rhône-Alpes, Centre et Bourgogne ; 2993 vaches, pour la plupart de race charolaise, ont été suivies durant 2 ans, de 1987 à 1989, par 33 enquêteurs (vétérinaires, techniciens, inséminateurs). L'objectif de cette étude d'observation était d'analyser les facteurs de risque d'infécondité (intervalle entre mises bas supérieur à 1 an), et plus particulièrement ceux relatifs à la période de la mise bas. L'association entre les facteurs de risque et l'infécondité est mesurée grâce au odds ratio (voir encart "Odds ratio") (OR = odds ratio ajusté ; ** $p \leq 0.01$; * $p \leq 0.05$; # $p \leq 0.20$).

(individual animal, farmer, weather, environment, etc.) and are not related to each other strongly.

In addition to that, different effects may follow one another temporally. For example, excessive birth weight of the calf puts the cow at risk for calving difficulty, and the calving difficulty itself has an effect on subsequent fertility. This situation can be visualized with path analysis schemes (Curtis *et al.*, 1985) (Figure 3). Furthermore, some of the factors of interest may be strongly interrelated and different relationships with infertility are produced by confounding effects.

Complexity is also observed at the different organization levels involved in the system (Pavé, 1994). The system, described at the animal level, must also be considered from the herd point of view. The cow belongs to the herd, which is an upper level of the system hierarchy. This system is dynamic, *i.e.* time is an important component affecting the states of the animals and the entire herd. In addition, the farmer, who is also a part of the system (Landais, 1987), reacts to the changes in the system. If, for instance, disease incidence is increasing, the farmer will often react by changing some management routines. If a study was concerned with investigating the effects of such routines on disease incidence, a severe bias would be introduced if this reaction were not recorded and accounted for in the analysis.

Finally, different scientific and technical fields are involved in the system (physiology, pathology and clinics, theriogenology, husbandry, ecology, sociology), which is typical of a methodological complexity (Pavé, 1994). A possible answer to the need of various knowledge fields and competences in epidemiology is a multidisciplinary approach. It has been formalized and developed in the field of veterinary epidemiology (Rosner, 1984 ; Calavas *et al.*, 1995).

Epidemiology : understand to prevent

The underlying long term purpose of epidemiology is to improve the health of the animals and "the economic health" of the

farm (Jolivet, 1991). The goal of epidemiological studies, and more especially analytical studies, is to understand the complex relationships between system components and disease. Even if epidemiological studies do not provide strong explicative elements for each given factor, the predictive aspects they permit may then be used in herd health management programs. The general idea of epidemiology is to study and observe numerous animals, and to compare them in order to determine which risk factors distinguish those that become sick from those that remain healthy.

The question is then to find the way and choose the methods that allow the analysis of such a complex system. In other words, which methods or approaches can provide the opportunity of studying the relationships between the disease and various factors that are linked or interact with each other, as well as accounting for the time component and the organisation of the factors both at the animal and farm levels ?

ANALYSIS AT THE ANIMAL LEVEL

Observing what is happening in nature

Different methods have been applied to study the relationships between various risk factors and disease at the animal level. Based on theoretical biological knowledge and experts observations (practical experience), some authors have developed normative mathematical models to try to reconcile the prediction of their model with the current knowledge and reality (Moutou *et al.*, 1994 ; Sabatier *et al.*, 1994). Nevertheless, very few studies have been carried out in this field, perhaps because the knowledge required in order to perform such models is currently too sketchy for most production diseases. It is why most studies are based on a *planned observation of the natural state*, the experimental willingness of the researcher lying on the planning of the observation (Legay, 1993). These empirical studies consist of data collection

1. Martin *et al.* (1987) define determinants as those factors that when altered produce a change in the frequency or characteristics of disease ; and risk factors as putative causes of disease. Both terms are commonly used interchangeably in the sense that we rarely have the assurance that a factor has a real effect on disease.

from the field according to a sampling plan, and analysis of the hypothesized relationships with various statistical methods.

Currently, most of the epidemiological studies carried out on farm animals are conducted *at the animal level*. Most knowledge developed for human epidemiology has been integrated and adapted for veterinary epidemiology (study design, data collection, and analysis); this has sometimes required adaptation to animal characteristics and to the farm context of animal production. The development that follows is focused on the analysis part of epidemiological studies².

As in other fields (Daudin, 1987), two main approaches have been used and applied independently to analyse the data collected from the farms: correspondence analysis and related multivariable techniques on the one hand, and linear modelling with one response variable on the other hand. They appear to have complementary goals and results.

Correspondence analysis and clustering

Borrowed from ecologists and sociologists, correspondence analysis was developed and used in France for epidemiological purposes (Faye, 1986, Madec *et al.*, 1988) in the '70s. The main purpose of this multivariate descriptive method is to give an understandable and practical view of the complex relationships between factors; it basically aids in discovering structure in the data, and consequently helps to identify groups of animals with a high risk of disease and to set up plausible hypotheses about the possible effect of relevant risk factors on disease.

In that sense, it appears to be an appropriate method in the initial stages of a study of poorly understood disease complexes. Furthermore, an advantage of correspondence analysis is the absence of any assumption about the distribution of variables. However, the weakness of this approach is that it does not consider the

previously addressed interaction and confounding questions; it does not allow one to measure and distinguish the individual effect of each factor on disease.

The kind of results obtained from correspondence analysis can be illustrated with the beef-cow infertility study mentioned previously (Ducrot, 1993) (see above). Correspondence analysis indicated (Figure 4) different interrelationships between the breed of the cow, the body condition score, feeding, the sex and birth weight of the calf, and the risk of calving difficulty. The clustering of the cows according to these different risk factors resulted in different groups of cows that also differed strongly at the level of calving difficulty (Ducrot, 1993).

Linear modelling

A solution to the weaknesses of correspondence analysis and other related tech-

niques is given by modelling. It was introduced to epidemiology by human epidemiologists and then adapted to veterinary epidemiology, primarily in Anglo-Saxon countries.

Logistic model

One of the most widely used models is the logistic one, which belongs to the generalized linear model family (Armitage *et al.*, 1987). Developed by Cornfield in 1961, it is usually applied to data with a binary (categorical) outcome and gives an estimate of the outcome probability for a set of predictors (Jenicek *et al.*, 1987). It is the multivariable analysis of choice to adjust for confounding and to study interaction effects.

It can be illustrated with the beef-cow infertility study. The various parts of the path analysis scheme (Figure 3) were analysed with the multivariable logistic model,

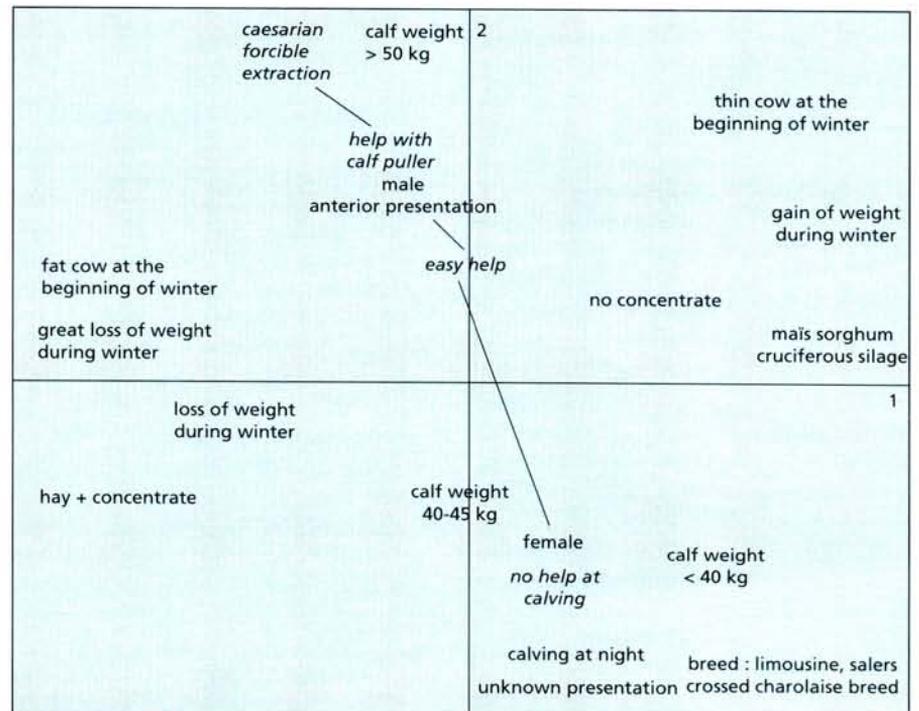


Figure 4: Calving difficulty and variables related to the breed of the cow, calving condition, and feeding (Ducrot, 1993). Plot of correspondence analysis, dimensions 1 and 2 (17% of the overall inertia) (acting variables, illustrative variable).

Figure 4: Difficulté de mise bas et facteurs relatifs à la race de la vache, aux conditions de mise bas, et à l'alimentation (Ducrot, 1993). Plan factoriel 1-2 de l'analyse des correspondances multiples (17% de l'inertie totale) (variables actives, variable illustrative).

the relationship measure being the odds ratio (Kleinbaum *et al.*, 1982)(see inset). In the analysis of risk factors for calving difficulty, the adjustment provided by the regression allowed for the elimination of those factors that were in fact linked to calving difficulty through a confounder, for example, the type of feeding.

Cox model

Even though it is widely used, logistic regression is not always the method of choice for analysing epidemiological studies. This is particularly the case when the outcome is a time interval, for example the delay between calving and first artificial insemination (days to first breeding), or the delay between calving and next conception (days open), or the interval between calvings.

Survival analysis allows the inclusion of data which lack an observed endpoint for an interval-type outcome variable. The length of this interval in veterinary field studies (from calving to the next event) may not be known for all cows, because the cows are culled, sold, die, or do not experience the event of interest before the end of the study. The probability distribution function of the event time (survival) may take many forms. A frequently employed distribution for event time is the Weibull distribution. However, parametric models have limited applicability because one often has no idea of the form of the underlying distribution. In such a case, a semiparametric technique called proportional hazards modelling can often be used. Consequently, a Cox proportional hazards model has become the method of choice for field data. The application of survival analysis techniques to the days open question was explained by Harman *et al.* (1995a), demonstrated in companion papers (Harman *et al.*, 1995b ; Harman *et al.*, 1995c), and discussed (Eicker *et al.*, 1995).

Caution

At the present time, statistical modelling appears to be a very powerful

method in veterinary epidemiology as well as it is in modelling used by animal breeders in order to study the genetic value of animals tested on farms. However, it must be applied with caution for different reasons :

- Modelling requires a rather good knowledge of the nature of the disease of interest in order to correctly specify the model and the functional form of the relations. If not, the expected gain from this method is lost and the estimated parameters are inconsistent and may be biased (Gujarati, 1988).

- Apart from the chosen mathematical model, which may not agree with the usually unknown biological model, there is a limit to the analysis of epidemiological data, which is related to the number of parameters that can be introduced in the analysis. Too many parameters make the model difficult to run and to interpret, and increase the risk of misspecification, multicollinearity, and other problems. Furthermore, it induces multiple testing problems and, to correct them, a great decrease in the statistical power of the study. Apart from increasing the sample size or studying separately different subpopulations of interest, the common advice is to restrict the number of parameters included in the models, but the major disadvantage of that practice is to distort the reality.

- Another question of current interest is that animals are grouped in herds, buildings, and so on. Cows from the same herds share the same husbandry practices which are different from those of other herds (Gröhn *et al.*, 1995). From a statistical point of view, this means that cows are not independent from each other, which violates one of the fundamental assumptions required for modelling (Dagnélie, 1975). Different methods are used to adjust for cluster effects in epidemiologic studies (McDermott *et al.*, 1994a), but the proper way to address the question is to include a clustering effect in the model, either fixed or random, which concerns the residual group effect (McDermott *et al.*, 1994b).

2. Authors made the choice to focus their attention on the data analysis, in order to present and discuss the various different ways used to analyse the complex systems. However, it is worth stressing the role of the study design (Kleinbaum *et al.*, 1982, Martinet *et al.*, 1987), of the data collection on farms (Faye *et al.*, 1991, Calavas *et al.*, 1994, Faye *et al.*, 1994), and of the data management that ensure data quality (Pérochon *et al.*, 1994, Sulpice *et al.*, 1994) ; these are, hence, of high importance in the quality of the data analysis.

Complementary aspects between both approaches

Correspondence analysis and modelling have complementary strengths that were discussed in different fields, for example in human epidemiology (Leclerc *et al.*, 1985, Leclerc *et al.*, 1988) and sociology (Baccini *et al.*, 1987); used together, they help to explain the reality more accurately (Ducrot, 1993). Modelling gives detailed and precise (providing that the model is correctly specified) information about the relationships between factors and disease, and correspondence analysis draws an overall and intelligible picture of the complex relationships between factors. These methods can be associated in different ways (Cazes, 1987); correspondence analysis is sometimes used prior to modelling to simplify the studied mathematical model; but it can also be used after the modelling process and can help to interpret the results from modelling (Dohoo *et al.*, 1995).

ANALYSIS AT THE FARM LEVEL

The choice of the farm level

Even if some statistical solutions can be found to solve the clustering question of animals in herds in studies carried out at the animal level, many authors believe that in epidemiology the unit of interest often is not the animal but the herd. Faye (1995) states that the pertinent unit for epidemiological studies is the farm in which the herd is under the constraints of the local environment as well as under the effects of the farmer's choices.

Analysis performed at the farm level was already the case in the first ecopathological³ studies carried out in France on truit (Tuffery, 1977) and pigs (Madec *et al.*, 1984). Actually, the new and main idea developed during the '70s was that disease was caused not only by some specific germ, but was also the result of the various components of a farm, including in addition to the animal itself, feeding, housing, husbandry, microorganisms, and the intervention of

the farmer (Tillon, 1980) (Figure 1). Animals were no longer considered as individuals in such an approach; they were pooled and their only contribution to the study was to create figures, for example percentage of diseased animals in a herd.

The systemic view of disease manifestation

More recently, epidemiologists have taken an interest in considering the farm as a cybernetic system (Figure 5). This approach has already been developed to study farm management (Landais, 1987), also considering that the farmer is part of the studied system. Input factors are classified as controllable and uncontrollable factors, output factors are products (e.g., milk and meat), and "regulation" is performed by the farmer through a farm management strategy. In the systemic view of the farm, cows play an individual role in the system, depending on their characteristics and potentiality.

This systemic approach can integrate disease as a part of the system, and is in agreement with different field observations. For example, Danish field studies with the individual animal as the unit of interest show that the risk factors for disease

often manifest themselves differently from herd to herd (Enevoldsen, 1993); in other words, there is interaction between risk factors and the environment, which indicates the importance of studying the "contents" or the nature of the interaction effects related to husbandry and managerial control. This makes some scientists believe that epidemiological research must integrate both the cow and the herd levels of the system hierarchy. Furthermore, if the farm is being regarded as a cybernetic system, it is crucial to take the time component into account because of the feedback between the states of the animals (and the herd) and the farmer's adjustments. This is why the epidemiologic model must be dynamic.

Ecopathological approach

Even if not defined explicitly, the ecopathological studies performed in France since the '70s have been based on a systemic view of disease manifestation. Recently, Faye (1995) analysed ecopathological studies in the light of a systemic approach. On the way of analysing the complexity of the relationships between the health of the herd and the farm system, he defined six different goals that have been pursued already. They

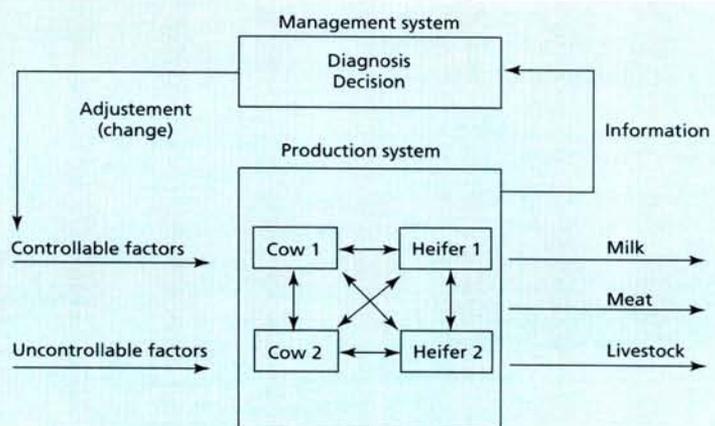


Figure 5: The herd as a cybernetic system (modified from Sorensen, 1995). Input factors are regarded as controllable and uncontrollable factors, output factors are products (e.g., milk and meat), and "regulation" is performed by the farmer through a farm management strategy (e.g., strategies for reproduction and culling).

Figure 5: L'élevage vu comme un système cybernétique (d'après Sorensen, 1995, modifié). Les entrées du système comportent des paramètres contrôlables et d'autres qui ne le sont pas, les sorties sont les produits de l'élevage (lait, viande), et la régulation du système est réalisée par l'éleveur au moyen d'une stratégie de conduite d'élevage (stratégie relative à la reproduction, à la réforme des vaches...).

refer to the following points : definition of an hygiene indicator (synthetic information required to manage the farm system) ; description of the space-time variation of the main diseases ; analysis of the relationships between diseases at the farm level ; study of the risk factors for economically important diseases and analysis of risky farm systems ; approach of the specific role of the farmer's personality through his management ; integration of the time component in the analysis of individual animal and herd data.

Naturalistic inquiry

Other authors have recently pursued a different way in order to consider a systemic approach of disease at the farm level. Instead of pooling all cows of all herds together and estimating the direction and magnitude of associations for the population as a whole, their aim was to try to understand and analyse thoroughly the individual herds, to obtain a farm-specific "diagnosis", and, if the data permit, to draw some more generalizable conclusions (Enevoldsen, 1993). Meek (1993) suggested that a "naturalistic inquiry" (case study technique or qualitative research methodology) is well suited to the study of management related issues. Enevoldsen *et al.* (1994) applied a case study technique to gain insight into such interactions. The approach followed this line of questioning in relation to various health problems :

- Is the problem real and not due to random variation in key-figures ?
 - Is prevention practically possible with regard to farm facilities and farmers' attitudes ?
 - Is prevention imperative due to animal welfare considerations ?, and
 - Is prevention profitable in economic terms ?
- This approach allowed biologically, practically, and economically important problems to be revealed. The "design" of such a study was a combination of traditional quantitative (statistical) and qualitative research methods.

Simulation models

However, the dynamic nature of the production process in an open dynamic population like a livestock herd, and the combination of the herd and the animal level in the system hierarchy, is difficult to comprehend. For that reason, several normative herd models have been developed during recent years (Sorensen *et al.*, 1992). Based on a dynamic, stochastic, and mechanistic herd simulation model (SIMHERD), a framework for conducting a whole herd analysis has been developed (Enevoldsen *et al.*, 1995). The framework allows an iterative "fitting" of the relations among the states of the individual animals in an actual herd, consumption of input factors (e.g., feed and inseminations), production of output factors, and a thoroughly described management strategy. These models can then be used in order to study diseases at the farm level and this has just begun. For example, Sorensen *et al.* (1994) applied this approach to evaluate the biological, technical, and economic effects of a bovine virus diarrhea infection in a dairy herd.

SYNTHESIS : ANALYSING THE COMPLEXITY

Type of systems in epidemiology

Faced with the complexity of disease causation, it seems hardly possible to give useful advice based on epidemiological results. In the example about reproduction, the analysis pointed out that many factors are involved, they have various interrelationships, their effects are tiny, and they deal with all components of husbandry (housing, feeding, herd, cow, farmer's practice, environment, and so on). Furthermore, some of the observed relationships are not statistically significant and we have no idea of their precise role in the studied system. It is hence difficult to make recommendations to the farmers and their advisors, and somebody could consider that it is a failure.

An alternative is to think, on the contrary, that these kinds of results are

3. Ecopathology is a french branch of veterinary epidemiology.

quite interesting. They show that *such systems exist and the researcher has to find a way to deal with them*. Even if there are no dominant risk factors for reproductive inefficiency, it is a real fact that some cows have good reproductive results while others have reproductive problems. These problems are definitely the result of various risk factor associations and interactions, each of the risk factors having a small effect on disease.

This kind of situation is quite common in epidemiology. Cancer epidemiology can take credit for suggesting that disease is determined by numerous parameters from the environment and the genetic susceptibility of the subject (Estève, 1993). In the field of sociology, Moles (1990) defines the "imprecise sciences", *that we prefer to call sciences of complex systems*, as sciences dealing with poor correlations, uncertain deductions, and poor impact of reasoning sequences. For him, "a poor correlation is nevertheless different from no correlation at all ; it is really a scientific subject, and a subject of great interest because this subject is the fabric of the real life".

Technical answers

It is necessary to give an answer to this accurate and complex situation. As Legay (1993) says, « facing a complex reality, it is necessary to create a research design with a similar level... The needs for method have become as important as those for physics instrumentation ». The classic answer to this type of situation is a very demanding study design, especially for the sample size. Another possible answer is to break up the question into sub-components, some basic factors being fixed (for example parity or breed).

At the analysis stage of such studies, non-significant relationships are difficult to interpret. The usual discussion would suggest that such factors do not belong to the system of interest. However, most studies do

not have sufficient power to show a significant relationship when the link is poor. Furthermore, « the conjectures and the refutation procedures related to a complex subject are in fact more complicated than those related to a simple subject » (Legay *et al.*, 1993).

This is why *interpretation plays an important role* in these studies. It can be argued and based on the knowledge from the lower level of the system organisation. For example, the effect of feeding on reproductive inefficiency of the cow can be clarified with our current knowledge about physiology.

Since the '70s, the technical answers given to the analysis of complex systems in veterinary epidemiology have been changing in order to fit the reality better and better. First, epidemiological analyses were performed considering a static situation, and they were based on the analysis of various relationships between the factors and the disease, either at the farm or animal level independently. Different models were developed successively in order to take into account confounding and interaction effects, time interval outcomes, clustering effect, and more recently time correlated data. Then the time component of the system was considered, firstly with the help of path analysis schemes, then with the development of dynamic models. More recently the cybernetic concern appeared, and the desire to consider at the same time both the animal and the farm level of the system. This cybernetic view of disease causation, including biological components as well as the role of the farmer (Godard *et al.*, 1992b), is recent and represents one of the future directions of veterinary epidemiology.

The point of view concept

In every case, it is hardly possible to study the whole system at once. The Cartesian approach does not give good results for complex systems (Le Moigne, 1990).

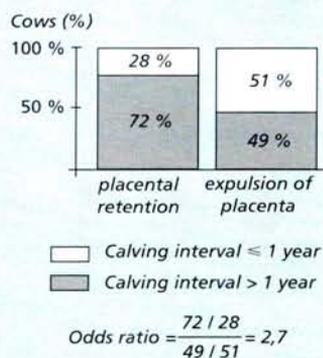
Accepting the complex reality requires a global approach to it (Legay, 1993) and a new epistemological position. Because the whole question is out of reach, *the symmetrical approach, in relation to the Cartesian one, is considered the point of view concept* (see inset). Liu (1992) emphasizes the complementary interest of different representations of the reality. In other words, the analysis of a system can be performed from different points of view. Pavé (1994) develops the same idea in biology and ecology, the point of view depending on the researcher's interest. Discussing the sciences of complex systems in sociology, Moles (1990) tells that « after determining different shapes in this foggy landscape, we need to travel on it mentally, in order to find different points of view and different perspectives ».

In the case of veterinary epidemiology, each system, like reproductive inefficiency, can be analysed from different points of view that give complementary knowledge about the system. It can be a disciplinary point of view, with a dominant discipline ; for example a biological point of view (dysfunction mechanism), or an economic point of view (economic determinants and consequences). It can also be a pluridisciplinary point of view related to a theme ; for example, the reproductive inefficiency observed at the organismic level, or at the husbandry system level.

The point of view concept is a basic statement that is helpful in going further in the analysis of complex systems. Another important difference between the analytic approach and the point of view concept lies in the scientific impact and significance of the results, which is more modest in the analysis of complex systems (evidences are replaced by successive consistencies (Legay, 1993)). Different methods are applied to perform such studies and have been partly described in the paper. However, using Moles' words (1990), « a real methodology for "imprecise" sciences has not been established yet. This methodology will partake widely of the "science under way" process ».

ODDS RATIO

In epidemiological studies, the frequency of disease occurrence among individuals who have a certain characteristic (usually referred to as "exposed") is generally compared with the corresponding frequency among those who do not have that characteristic ("unexposed"). This comparison constitutes the fundamental way of studying the association between exposure and disease occurrence (or other outcome). For example, we may be interested in whether retained placenta is a risk factor for a long calving interval. One way to determine this is to compare the cows with a history of retained placenta to those that do not have such a history and see whether the two groups have different frequencies of long (>1 year) and short (<1 year) calving intervals (see figure).



In the example, 72 % of the cows that had a history of retained placenta also had a long calving interval while 28 % had a short calving interval. The odds of having a long calving interval among exposed (cows with a history of retained placenta) is 2.6 (72/28). The same calculation show that the odds for the unexposed group (those without retained placenta) is 0.96 (49/51). In the example, the odds ratio between exposed and unexposed is 2.7 (= 2.6/0.96). This tells us that cows with retained placenta are 2.7 times more likely to have a long calving interval than those without retained placenta. The odds ratio is significant when its confidence interval at a given alpha level (usually set at 5 %), does not include "one".

CONCLUSION AND PERSPECTIVES

Epidemiology is no longer the "science of large epidemics". Veterinary

epidemiology now deals with the complex relationships between the animal, its production, and the environment in a broad sense ; this is the ground and specificity of what was called "ecopathology" in France. It takes into account not only the animal itself, but also the farm and its organisation and management.

This complexity, the acceptance or rejection of which is the researcher's decision, requires new methods to investigate the reality and to interpret the results (Legay, 1973). The point of view concept does not break the complexity in order to analyse it. It requires modesty in the confidence and scientific impact of the results, as well as watchfulness in the methodology to achieve the goals of research.

As one goes deeper into the process of understanding the multifactorial causes of diseases, the need for more sophisticated analytic methods becomes greater. The statistical methods currently available hardly allow the epidemiologist to study simultaneously all the variables he (she) ought to consider. However, all these methods have complementary aspects and the reality, or more truly, our simplified picture of the reality, can be built from numerous partial drawings using different approaches and methods. Complementary representations are established by adding various different points of view (Liu, 1992). Furthermore, interpretation, based on prior knowledge and more or less subjective beliefs, plays a very important role in this field, although often implicitly.

Although epidemiological studies on production diseases have been carried out since the '70s, this is still a brand new discipline. Reviewing the situation of veterinary epidemiology, the present paper points out the fact that different developments are going on currently, both on epistemological and technical questions. Their interest will be analysed with the passing of time. Furthermore, new developments in the methodology of veterinary epidemiology will have to take into account :

■ the need for methods to model multivariate responses efficiently. Bayesian Nets may be a very attractive method to model multivariate responses (Vaarst *et al.*, 1994). Gibbs sampling is another attractive option to estimate a large number of parameters in large complex data sets (Smith *et al.*, 1993).

■ the goal of identifying and applying mathematical models which are closer to the biological mechanisms. In other words, the goal is to expand the choice of the mathematical formalism in order to better solve the problem (Pavé, 1994). Such models as those applied in the field of infectious epidemiology should be screened and analysed (Capasso, 1993).

■ the necessary expansion of the point of view concept and its use in the field of veterinary epidemiology. ■

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THE REPRODUCTIVE CYCLE OF THE COW

The cow has cyclic sexual activity throughout the year. Each sexual cycle is on average 21 days long and is marked by a short estrus -or heat- period, when ovulation occurs. Fertilization is followed by a 9 month period of pregnancy. After calving, a one-to-two month anestrus period is usually observed before sexual cyclic activity resumes.

This sexual physiology allows an annual rhythm for bovine reproduction. The control of the calving period is an important economic issue because every delay costs money or decreases gain.

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THE DIFFERENT FIELDS OF EPIDEMIOLOGY

Epidemiology is a very old science, yet it did not flourish until after the "germ theory" of disease causation became established in the 1800s. From that time until approximately 1960, epidemiology was closely allied with microbiology in the battle against disease (Martin *et al.*, 1987). Since 1960, epidemiology has become a more holistic discipline, studying the distribution and determinants of disease prevalence (MacMahon, 1970) ; three main fields can be distinguished (Rumeau-Rouquette *et al.*, 1993) : descriptive epidemiology (disease distribution over time and space), analytical epidemiology (determinants of disease), and operational epidemiology (disease prevention programs).

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COMPLEX SYSTEMS AND POINTS OF VIEW

We do not agree with the restrictive and finally reductionist definition of complexity that relates to the chaotic phenomena.

According to a more general process in agreement with the set theory, we define a *complex system* as a system whose nature changes as soon as one of its components is removed. On the contrary, the Cartesian approach required that the system did not lose anything if broken up. This permitted the splitting up of the system into simple components and allowed resorting to evidence for each of the analysed components.

Adopting a *point of view* in the study of a complex system is the necessary complement to the previous definition. The goal is then to keep the definition and the structure of the system intact while shedding light on it in a certain way and analysing the corresponding features. The evidence criterion is lost, the pluridisciplinary approach is maintained, and the understanding of the reality is better fulfilled.

The *confrontation* of results obtained after adopting different successive points of view and the possible report of their consistency lead to a better knowledge of the system.

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RÉSUMÉ : Approche de la complexité en épidémiologie animale ; exemple de la reproduction des bovins

Un des objectifs majeurs de l'épidémiologie animale est d'étudier les causes des maladies, notamment celles des maladies d'élevage d'origine multifactorielle. L'exemple de la reproduction en élevage bovin, développé dans l'article, illustre le fait que l'épidémiologie animale relève de l'analyse de systèmes complexes. Les troubles de la reproduction chez la vache proviennent en effet de déséquilibres au niveau de la régulation physiologique de l'organisme, qui sont sous la dépendance de multiples facteurs appelés facteurs de risque. L'effet de chaque facteur est limité et peut varier en fonction d'autres facteurs ; ces facteurs concernent les diverses composantes de l'environnement pris au sens large du terme (microbisme, conduite d'élevage, alimentation, conditions climatiques, ...).

L'analyse de tels systèmes repose habituellement sur une observation planifiée de la réalité à travers des enquêtes à large échelle conduites en élevage, et sur l'utilisation pertinente de méthodes biométriques diverses pour analyser les données, certaines équipes développant ces travaux dans le cadre d'une approche pluridisciplinaire.

Dans la plupart des études, l'analyse est conduite à l'échelle de l'animal, études dans lesquelles l'analyse factorielle et les méthodes de modélisation ont montré leur complémentarité. Ont été développés successivement le modèle logistique, adapté aux situations, fréquentes en épidémiologie, où la maladie à expliquer est

qualifiée en présence/absence, et qui prend en compte les facteurs confondants, le modèle de Cox pour analyser des intervalles de temps, l'intégration au modèle d'un paramètre aléatoire pour prendre en compte des effets de groupe (élevage), et actuellement l'analyse des données corrélées dans le temps.

Cependant, un certain nombre de recherches sont menées à l'échelle de l'élevage, considérant ce dernier, en tant que système piloté, comme niveau d'organisation particulièrement important dans l'explication de la maladie. L'écopathologie, branche de l'épidémiologie animale développée en France depuis les années soixante-dix, relève de cette approche, de même que le développement récent d'études de type qualitatif à l'échelle de la ferme et de modèles de simulation dynamique et stochastique intégrant tout à la fois chacun des animaux du troupeau, avec ses caractéristiques et son devenir, et l'élevage, avec son organisation et sa gestion.

Accepter la complexité dans le déterminisme des maladies nécessite d'envisager une approche globale pour l'étudier. La notion de point de vue, qui consiste à donner des éclairages différents du système étudié sans le réduire, joue un rôle important dans une telle situation méthodologique, en remplacement de l'approche cartésienne de décomposition des objets complexes. Néanmoins, elle requiert, au moins à court terme, plus de modestie quant à l'impact scientifique des résultats obtenus.