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EPIDEMIOLOGY AND ANIMAL WELFARE

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L'intérêt général actuel pour le bien-être animal dans certaines régions du monde n'a jusqu'à présent pas impliqué particulièrement les épidémiologistes vétérinaires, même si beaucoup d'aspects du bien-être en cours de discussion sont liés à des problèmes de santé animale, en particulier pour les maladies en relation avec la production.
Cette situation mérite d'être modifiée, dans la mesure où des exemples montrent qu'une approche épidémiologique limitée a été utilisée dans des circonstances importantes.
On peut citer comme exemple la controverse BST-mammite clinique qui permet d'illustrer plusieurs points sur lesquels une critique épidémiologique vétérinaire aurait pu améliorer l'information publiée et éviter que des erreurs passées soient acceptées.
Le point essentiel pour la discussion est les effets directs-indirects de la BST et la production de lait, qui a été publié et présenté comme une évidence pour l'absence d'effets visibles de la BST et même accepté pour résoudre la controverse par des autorités consultatives internationales. On a pu montrer, cependant, qu'à cause de l'absence d'expertise épidémiologique, les résultats publiés et les conclusions sont davantage confus et biaisés que clairs, précis et corrects. Par ailleurs, il est fait référence à de nouveaux développements sur des activités orientées vers le bien-être animal pour lesquelles l'épidémiologie vétérinaire est utilisée.
Il est heureux que les demandes éthiques aux épidémiologistes dans ces situations convergent avec les obligations éthiques des vétérinaires pour promouvoir le bien-être animal.

INTRODUCTION

Animal welfare has become a topic of great interest and concern to consumers and politicians in many countries during the last 10 - 20 years. Minimum animal welfare standards are currently one of the leading topics for discussion and legislation within the European Community, and in member states there is a growing consumer demand to have access to products which carry declarations of particular animal welfare safeguards. Through market forces the animal industries have been forced to enter into political and commercial agreements and arrangements to supply particular name brands with declared welfare qualities which are sold at higher than normal prices. This development has come about through a combination of increasing public awareness of the conditions prevailing in the industrialized animal production units, which most people find distressing and appalling when shown in the public media, and a growing political influence from animal welfare societies, who benefit from the support of the public opinion.

Scientifically there has to some extent been a parallel increase in animal welfare activities. Governments as well as private foundations have launched dedicated research programs on animal welfare, and universities have taken up the topic through dedicated chairs or expansions of animal science or veterinary faculties.

Much of the research activity created from this development has centered around animal behaviour (ethology), which had until then been a rather neglected research field. Other and more conventional research fields ought to be upgraded if a wide-ranging strengthening of animal welfare research is to be achieved. In particular veterinary epidemiology are companion areas to ethology when it comes to supporting the research, development and practice of animal welfare.

EPIDEMIOLOGY : COMPONENTS OF WELFARE CONSIDERATIONS

Preventing disease is a prominent animal welfare activity. Describing disease occurrence and its consequences are parts of qualifying and quantifying animal welfare problems in herds and in larger populations. Veterinary epidemiology is thus essential to these sides of welfare research and practice. Surprisingly little epidemiological literature dedicated to such welfare considerations has been published, and only few epidemiologists seem to be engaged in research of this character. A possible reason for this might be that in large parts of established government and university departments, as well as in animal production industries where veterinary epidemiologists work it is still considered undesirable and counter-productive to engage in research on «alternative» production topics. It is true that not always does animal welfare concerns concur with traditional production promoting thinking, although sometimes they do. Most disease problems are production limiting events and will also be welfare

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problems. Some disease problems, however, have become integral parts of intensive animal production for which there are no easy solutions since their risk factors are intimately associated with the prevailing intensive production systems. Mastitis in dairy cows, respiratory infections in pigs, leg and bone problems in broilers, enteric diseases in veal calves, etc. are all examples of such frequently occurring «production diseases». For such diseases, welfare and production considerations are not immediately compatible. Most concern ought to be given to those production diseases associated with great pain or discomfort, long duration and high rates of occurrence (Willeberg 1991). The limitation of production losses that may be obtained by treatment of cases in these instances is not a satisfactory welfare remedy- only prevention will do the full job. That is the challenge facing the epidemiologist - there are no easy solutions, but rather extended needs for strong professional ethics and scientific integrity as well as for openness and engagement in designing and analyzing welfare-related studies.

BST AND CLINICAL MASTITIS : SOME EPIDEMIOLOGICAL ISSUES

An example of the need to apply rigorous epidemiologic methodology to enable proper welfare considerations of a currently discussed production factor concerns the use of bovine somatotropin (BST) for increasing milk production in dairy cows (Willeberg 1994). The substance is being used in many countries, but it is currently banned in the EU member states until the end of the century, outstanding problems with clinical mastitis being among the official reasons for the moratorium.

A number of epidemiological issues can be raised relative to the field studies of BST which form the basis for the animal safety evaluations by the various agencies involved in the evaluation of the product as part of the authorization for marketing. The application folders submitted by the pharmaceutical companies are confidential, but a series of papers in scientific journals have been published which probably contain much the same information. From these publications the following epidemiological points might be considered:

- sample size and resulting power of the individual study to identify excess disease
- herd effects and representativeness of experimental herds
- importance of different mastitis rates between treated and untreated cows during pretreatment
- relevance and correctness of the «indirect effect through milk yield» explanation

Sample size and resulting power of the individual study to identify excess disease

In Willeberg (1993) this issue has been dealt with extensively. The point to be made is that the long list of published papers on individual studies which typically include 10 - 50 cows in each of the treatment and non-treatment groups have far from enough statistical power to detect a realistic difference in the risk of clinical mastitis between the two groups. Assuming a base-line risk of 20 cases per 100 non-treated cows for the relevant part of the lactation period and hypothesizing an increase from BST by 35% in this risk would require approx. 600 cows in each group for the difference to become statistically significant. As a result of this, the great majority of single study reports conclude, that there is no increase in clinical mastitis due to BST. It requires a minimum of statistical-epidemiological expertise on behalf of the reader to critically evaluate such a conclusion as being unfounded. Subsequent meta-analyses correct for this problem of low power, and consequently estimates of increase in risk of 17-47% due to BST have been obtained (Willeberg 1993).

Herd effects and representativeness of experimental herds

Published meta-analyses (eg. Craven 1991, White et al. 1994) contain evidence of a considerable herd effect in terms of differences of risk of clinical mastitis in non-treated cows among herds as one would expect. No adjustment for these herd effects, however, were made in the critical analyses and no information was given on the representativeness of the selected herds for the population-to-be of BST-using herds. Neither have any formal study been made to try and identify the risk factors which may be responsible for these herd differences. Even more curious is the argument that since the excess risk associated with BST is less that the variation caused by herd effects and other variables such as seasonal variations it is of no concern (Monsanto 1993, White et al. 1994). Nevertheless, some reports mention the need for larger field studies to be carried out under a range of environmental and management conditions in order to detect «any subtle health effects» (cf. Willeberg 1993). Furthermore, the CVMP advising the EU Commission said in its final report on two BST applications that it is important to verify that the overall level of risk to the health and welfare of the target animal is not increased when the product is used under practical farming conditions where standards of animal husbandry may not be as high as those in the experimental herds. The recommendation is therefore that a wide-ranging study of at least two years duration should be undertaken to determine the effects of BST on the incidence of mastitis and associated metabolic disorders under practical conditions of use (CVMP 1993).

Importance of different mastitis rates between treated and untreated cows during pretreatment

In the study by White et al. (1994) the mastitis incidence during the pretreatment period was significantly higher in the to-be-treated group than in the to-be-non-treated group. The paper suggests that this may be due to a greater predisposition to mastitis in the treatment group than in the non-treatment group, ie. the randomization procedure used in assigning the cows to either group had not been successful on this point. Nevertheless, the analyses of the

treatment effects were carried through ignoring the potential bias introduced by this unfortunate event. In an important study such as this for resolving the controversy over the BST-mastitis issue the scientifically most sound solution might have been to disregard the data entirely or to analyse separately the information from herds or individual studies without differences in pretreatment mastitis rates. This, however, was not attempted. This appears to be a case of «randomize and close-your-eyes», ie. to rely on the supposedly beneficial effect of randomization even though the data itself shows that the randomization failed on a critical point.

Relevance and correctness of the «indirect effect through milk yield» explanation

Final analytical results of meta-analyses, including those of White et al. (1994) show that there is a significant excess risk in the treated group over the non-treated group during the treatment period equivalent to approx. 40%, which becomes small and insignificant when the simultaneous increase in milk production is included as a covariate. This fact is used by White et al. (1994) to argue that the effect of BST on clinical mastitis is due to an indirect causal effect mediated through the increase in milk yield, and that this is evidence for no harmful effect of BST on the occurrence of clinical mastitis:

$$\text{BST} \xrightarrow{+} \text{milk yield} \xrightarrow{+} \text{clinical mastitis}$$

This argument has so far not been questioned by the authorities and has been quoted by some as the ultimate explanation and the main reason for accepting that the mastitis issue has been resolved (CVMP 1993). A proper epidemiological evaluation of this point comes to the exact opposite conclusion, ie. this analysis and the conclusions drawn from it has confused the issue, not resolved it. Firstly, it should be noted, that analyses including milk yield as a covariate violate the basic epidemiological rule, that an intermediate variable in a causal pathway should never be considered as a confounder and should therefore not be introduced as a covariate in multivariate analyses (see eg. Greenland & Neutra 1980, Kleinbaum et al. 1982, Weinberg 1993, Joffe & Greenland 1994).

The fact is, that epidemiology has the practical purpose of discovering relations which offer possibilities of disease prevention and for this purpose a causal association may be defined as an association between categories of events or characteristics in which an alteration in the frequency or quality of one category is followed by a change in the other (MacMahon & Pugh 1970). If one wants to make sound epidemiological estimation of the causal effects of an exposure, it is therefore wrong to try to distinguish or separate indirect from direct effects - they both count in the effect of exposure to the primary variable in question (BST). A number of everyday situations can easily be shown only to give logical and intuitively sound conclusions if the correct epidemiological principle is followed.

Furthermore, according to Robins & Greenland (1992) direct and indirect effects are not separately identifiable from studies when only exposure is randomized, and adjustment for the intermediate variable by including it as a covariate as done in White et al. (1994) may be biased in estimating direct and indirect effects. Accordingly, the net effect of BST is the only useful estimate to be used and this effect is unbiasedly estimated only by the crude risk difference, which in the study of White et al. (1994) amounts to 8.3 cases of clinical mastitis per 100 cows (equivalent to 39 % above the risk in non-treated cows).

DISCUSSION

The aim of this presentation has been to show that when epidemiologic issues are at stake, even if they are only part of the general issue - be it animal welfare, pharmacovigilance, medical technology assessment, production enhancement, etc., strict epidemiologic principles must be applied. Otherwise the risks of biased results, erroneous conclusions and other poor scientific achievements are eminent, even to the degree of leading to erroneous or biased decisions by national and international bodies.

It is comforting and may be even symptomatic, that the proper epidemiologic principle as applied above also agrees with the ethically most appealing animal welfare conclusion. The argument that all cases of clinical mastitis caused by BST, whether they be indirectly or directly attributable to the treatment, is the only proper and unbiased estimate of the risk of BST is namely synonymous to appreciating that to the individual cow it would seem of little concern whether an episode of clinical mastitis is attributable to BST as such or to the associated increase in milk yield - the welfare consequences remain the same to the cow.

If it is indeed true that the main reason for the excess risk of clinical mastitis following BST injections is the increase in milk yield caused by BST, then it must also be acknowledged that other means of increasing the milk yield to the same degree should be considered equally problematic. Genetic improvement of milk yield beyond what is already common may well be an animal welfare issue, and if so it should be carefully considered to minimize the clinical mastitis problems by including this disease as a trait in the selection process. This has in fact been done in the Danish dairy breeding program, where an estimated additional progress over 10 years in milk yield of about 100 kg milk

has been sacrificed for the sake of avoiding an increase in the mastitis rate of approx. 12% units (Christensen 1995).

Other examples of similar situations with other productivity related risk factors for animal diseases of welfare importance could be given. The increased risk of respiratory infections in pigs with increasing herd size would in most instances have given rise to similar concerns, the exceptions being that the application of multi-site production and other effective means of sectioning or partitioning a large herd into smaller units or production of Specific Pathogen Free animals hold the key to preventing the otherwise unavoidable consequences of keeping large number of individuals in a herd. It would have been a futile exercise to argue whether the increased occurrence of infectious agents in large herds is the direct cause of high risk of clinical disease among pigs in large herds or whether the herd size as such is the culprit - in fact analyses will not surprisingly show that the risk of clinical respiratory disease associated with herd size decreases when serological reactor rates to common pathogens are included as covariates (Mousing et al. 1990, Enøe et al. 1997). To conclude that herd size is not to blame, but rather the associated high rate of infectious agents, would seem like a poor excuse and a futile explanation.

Veterinary epidemiologists may not only improve the scientific evaluations of production related animal welfare questions by participating in evaluations at the risk factor level. Also taking part in designing and practising animal welfare evaluations where the animals are, ie. in the herds, is to everybody's advantage. As an example, the project on «Ethical accounting» carried out in Danish dairy and pig herds has encompassed veterinary epidemiologic expertise to secure objective and unbiased data recording and analytical evaluations (Sandøe et al. 1996). Further recent examples exist of descriptive and analytical studies of animal welfare issues related to dairy and pig health at the herd level (Alban & Agger 1996a,b, Alban 1995, Dybkjær et al. 1994). A recent discussion of health as a parameter for assessing dairy herd welfare can be found in Alban & Agger (1997).

CONCLUSION

Veterinary epidemiologists should be in the forefront to deal with animal health and disease aspects, also when the issue is animal welfare. We need to become more engaged in animal welfare studies and to make ourselves more visible relative to other professions. Otherwise, these professions will take over with the eminent risk of resulting in poor epidemiologic science and thus jeopardizing a correct evaluation of the animal health and welfare issues. This may not only be detrimental to ourselves and to society, but also to the welfare of the animals. In providing our professional services as members of the scientific community at a high ethical level and in letting our critical and constructive attitude to animal health studies be apparent we will also serve as proponents of a proper ethical attitude towards securing the welfare of animals.

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