

Aus dem Institut für Tierzucht Mariensee

**Lorne Babiuk
Ruth Lysons
Jos P. Noordhuizen
Stefan Schwarz
Martin Wierup**

**Marian C. Horzinek
Volker Moennig
Peter Schmid
Jorgen M. Westergaard**

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Summary animal health

Lorne Babiuk, Marian C. Horzinek, Ruth Lysons, Volker Moennig, Jos. P. Noordhuizen, Peter Schmid, Stefan Schwarz, Jorgen M. Westergaard and Martin Wierup

One of the most crucial parameters in modern animal husbandry and production is animal health. Animal welfare, consumer protection and economic success are directly linked to the health status of farm animals. In addition poor animal health seriously damages the public image of animal production. Major factors influencing animal health, i.e. housing, breeding and feeding were subject of other workshops in the series "Sustainable Animal Production". This workshop dealt with treatment and prophylaxis of health problems of farm animals due to infectious diseases. For this purpose the field was subdivided in several areas:

- Major health problems of farmed animals caused by infectious agents
- Emerging and reemerging diseases
- List A diseases: Threat and control
- Antibiotic resistance
- Progress in the diagnoses of infectious diseases
- Modern vaccines
- New anti-infective drugs
- Strategies to avoiding health problems of farmed animals

Major health problems of farmed animals caused by infectious agents

Endemic infectious have a considerable negative impact on the profit of animal production and there are large variations in animal health status between the different EU member states, countries, regions and even farms. Factors contributing to this phenomenon are the prevailing differences in husbandry systems, marked differences in management quality levels, the highly intensified production, the physiologically marginal potential of food animals to cope with all kind of stresses including infectious agents and the largely monotrait focussed genetic selection programmes. Special attention should be given to food animals affected by metabolic stress. This is a relative problem, largely provoked by one-sided genetic selection on productivity mainly. As a result of this metabolic stress (e.g. after calving or around piglet weaning), endocrinological, neurological and immunological functions are impaired. This may ultimately result in increased disease susceptibility

paving the way for a number of facultatively pathogenic micro organisms causing disease. Apart from these multi-factorial infectious diseases several endemic mono-causal infectious agents, e.g. Aujeszky's disease, influenza, paratuberculosis and IBR/IPV give rise to serious economic losses. A serious public health issue is the fact that modern livestock production carries implicitly the risk of presence of carriers of zoonotic agents, e.g. salmonella and *Streptococcus suis* II, representing a potential risk for man, sometimes even without causing overt disease in animals.

Emerging and reemerging diseases

Outbreaks of so far unknown diseases, e.g. BSE, paramyxovirus infections in horses and pigs in Australia, zoonotic H5N1 influenza in Hong Kong and AIDS in man, have drawn our attention to the subject of emerging diseases. Today we know that new diseases will strike time and again, and their causative agents will be identified ever more quickly, either as being well-known agents that have undergone subtle genetic changes, or as recombinants with other viral or cellular genes. They may also turn out to be really new, hitherto undiscovered agents. Every now and then, one of the emerging agents might turn out to be a 'killer' virus wreaking havoc – either to be controlled by veterinary efforts or peter out in virulence to become a harmless commensal. It is safe to assume that high animal population densities combined with the close proximity of different species could play a favourable role in the emergence of new diseases. One classical example of a re-emerging disease is tuberculosis, once though to be well under control.

List A diseases: Threat and control

List A diseases are defined by the World Organisation for Animal Health (Office International des Epizooties, OIE, located in Paris) as transmissible diseases which:

- have the potential for very serious and rapid spread, irrespective of national borders;
- are of serious socio-economic or public health consequence,

- are of major importance in the international trade of animals and animal products.

The List A comprises at present (2000) 14 predominantly viral diseases. The reservoir of List A disease agents in wildlife and in domestic animal populations, the route and the mode of disease transmission play a major role, when evaluating disease threat and deciding on control measures to be applied. The threat or risk of a List A disease entering a susceptible domestic animal population can arise from several possible sources and it is imperative to assess the risk. Whenever possible this type of assessment should be based on a quantitative risk-analysis, which gives a transparent, objective and defensible estimate of the risk posed by a particular action. A precondition for success in the control of a List A disease outbreak includes a comprehensive and well-rehearsed contingency plan. The plan must clearly describe: the legal power held as regards disease notification, stamping-out, payment of compensation, movement controls, vaccination and use of penalties. Other aspects of the plan refer to the chain command; the establishment and operation of disease control centres; the use of diagnostic laboratories; training of staff and publicity. In the long-term measures of importance for better disease control include: increased disease surveillance; better protection measures at farm level and protection measures relating to movement of animals.

Antibiotic resistance

The ability to treat bacterial infections in animals and man with chemotherapeutic agents represents one of the most important medical achievements of the twentieth century. However, as a result of the exposure of bacteria to antimicrobial agents, a large number of genes and mutations associated with antimicrobial resistance has been developed and the introduction of an antimicrobial agent into clinical use in both humans and animals has been either accompanied or followed shortly by the occurrence of resistant bacteria underlining the extraordinary capacity of bacteria to quickly and efficiently respond to the selective pressure imposed by the use of antimicrobials. In recent years, bacteria have also shown to be able to develop resistance to completely synthetic substance and resistance to several antimicrobial agents as well as against disinfectants, heavy metals or nucleic acid binding substances, respectively. As a consequence of the widespread use of antimicrobial agents in all fields of medicine food producing animals as well as pets and humans can act as a reservoir of resistant bacteria. Of particular interest if not concern is the ability of a few

multiresistant bacteria with pathogenic potential for humans to cross from their animal hosts to humans via the food chain. Among them subspecies of *Salmonella enterica*, *Campylobacter* spp. as well as *Enterococcus* spp. are suspected as human pathogens. However, in the public perception this problem is largely overestimated. Based on the present evidence, antimicrobial use in animals mainly causes resistance problems in animals while antimicrobial use in humans mainly accounts for the resistance problems encountered in human medicine. With the exception of the afore mentioned resistant zoonotic pathogens, both disciplines are mainly responsible for their own "home-made" resistance problems. The real problems of veterinary medicine are the increase in number of resistant bacteria in animals and the banning of some anti-infective drugs. New anti-infective drugs are reserved for human medicine only.

Progress in the diagnoses of infectious diseases

A prerequisite for the control of infectious disease in animals is the availability of suitable, i.e. reliable, sensitive and inexpensive diagnostic tests. The main reasons for use of diagnostic tests in farm animals are for individual animal diagnoses, herd investigations, disease control or disease surveillance. In countries with a highly developed agriculture the requirement for farm animals is increasingly for large-scale surveillance programmes. These are usually designed with a mathematical basis to answer specific epidemiological questions. In several European countries there is currently a particular emphasis on surveillance of livestock for prevalence of specified food borne zoonoses such as salmonella, *E. coli* O157. Large-scale testing requires cheap and robust tests. The enormous progress in biomedical technology during the last two decades made the development of novel tests possible, including sensitive genetic analyses for different purposes, e.g. the selection of sheep resistant to Scrapie or the rapid identification of dangerous pathogens, respectively. Internal and external quality assurance of testing is essential and will increasingly be implemented using independent accreditation, e.g. ISO 9000 or ISO 17025.

Modern vaccines

Successful vaccination against infectious diseases has been practised for over 200 years, and it is safe to assume that vaccination is the most cost-effective method of reducing animal suffering and economic losses due to infectious diseases in animals. However, even with these successes, infectious diseases

continue to be of economic significance to society in reduced productivity and animal death. The advent of genomics, proteomics, and biotechnology, combined with our understanding of pathogenesis and immune responses to various pathogens provides us with an unprecedented opportunity to develop safer and more effective vaccines for many pathogens. In addition to using vaccines to cure infectious diseases of animals, it is also possible to immunise animals against various hormones and cellular proteins to improve growth and alter reproductive efficiency. Different types of genetically engineered vaccines are presently at different stages of development, clinical trials, or licensing. They include: 1) live vaccines, 2) live chimeric vaccines, 3) live replication-defective vaccines, 4) subunit vaccines, 5) peptide vaccines in various modifications of monovalent, multivalent, or chimeric subunit vaccines delivered as individual components or incorporated into virus-like particles for improved immunogenicity, and 6) polynucleotide vaccines. However, despite all promising developments the common knowledge that "However smart we are, microorganisms are smarter than us" might still be true in the future.

New antiinfective drugs

The driving force in the search for new drugs is the human health sector. We can therefore realistically expect that in the medium term this is where new antiinfectives for animals will come from. In the medium term, as in the past, the animal health industry will therefore rely primarily on spin-offs from the human sector.

Four principal drug discovery approaches are employed in the search for new antiinfectives, namely,

- the expansion of known drug classes to cover organisms resistant to earlier members of the class, i.e. the development of new variations of known antibiotics, e.g., cephalosporins, β -lactams or macrolides. Apart from some short term advantages the main disadvantage of this strategy is cross resistance. Thus, this approach can only be considered at best a temporary solution to the problem of resistance.
- the reevaluation of un(der)explored molecules, especially a variety of synthetic and naturally occurring peptides with antiinfective activity is a promising approach for a new class of antiinfectious agents
- the classical screening of synthetic compounds and natural compounds isolated

from fermentation broths of microorganisms, plants or other organisms

- and the identification of novel agents active against previously not-exploited or even unknown (novel) targets within the pathogen using the tools provided by genomics, proteomics, bioinformatics and high throughput screening of substances against known targets.

With prudent use it will be possible to control the spread of the resistance problem also in the long term. The therapeutic arsenal will grow in the short and medium term by traditional approaches (i-iii). In the long term, leading edge biochemical and molecular biological methods together with bioinformatics provide a good chance of controlling bacterial infections in entirely new ways.

Strategies for avoiding health problems of farmed animals

So far disease risk management is an underestimated instrument in disease combat programmes while emphasis has been on vaccination and medication. Of course sick animals should be given the best possible treatment in order to prevent suffering, death and economic losses. However, in the animal production it is too late to undertake first when clinical signs of disease have developed. Therefore, a health control scheme should be established that continuously focuses on disease prevention in order to avoid health problems. Appropriate measure can be summarised as follows:

- profound knowledge about and proper diagnosis of infectious diseases
- eradication of epizootic diseases, e.g. list A infections
- control, reduction or elimination of non-epizootic diseases on all levels of animal production, e.g., combat sources of infection, decrease of exposure, optimising hygiene, prudent use of antimicrobial treatment
- improve host resistance by e.g., breeding, optimal nutrition, optimal housing and ventilation, good management (e.g. all in all out), reduction of stress
- boost Immunity by e.g., vaccination, good maternal immunity, control of immunosuppressive diseases

The significance of the measures exemplified above can be better understood when considering that most infectious diseases caused by one specific microbe usually primarily have a multifactorial course. All factors thus decreasing the risk of an

infection becoming established will contribute to an improved health situation in individual animal and on a herd basis.

Conclusion:

The intelligent use of the wide panorama of available disease preventive measures, as exemplified above, easily contributes to a good health situation and improved economy of animal production. The implementation on both herd and national level needs close co-operation between producer, stakeholders, vets and responsible authorities and sometimes also consumers. Economic incitements are usually a driving force and ideally a disease preventing health control should be driven from the producer. At herd level basic hygienic routines should first be implemented. Disease preventing health controls is a continuously ongoing process with the object to maintain and improve animal health.