To treat or not to treat: 
a proper use of hormones and antibiotics

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Abstract

Hormones and antibiotics are important remedies in animal reproduction. Compared to other areas of application, hormones are probably more used than antibiotics. The quantities of hormones applied in cattle reproduction are largely dependent on whether these drugs are extensively used for pharmaceutical control of breeding or not. Diseased animals should be treated both from an animal welfare point of view and to restore their production capacity. The treatment should be based on an accurate diagnosis. Some of the treatment methods used in animal reproduction do not seem to be well documented. When using antibiotics, it should be known that an infectious agent is present which will be susceptible to therapy. The use of hormones and antibiotics to solve or mask managerial problems should be avoided. Ideally, fertility and health traits should be included in a breeding programme. Therefore, all diagnoses and treatments performed should be recorded and these data made available for breeding purposes. Manipulation of the breeding cycle by pharmaceutical means should not disturb the natural reproductive performance of animals being progeny tested. Animal health and fertility should be improved by selection and good management rather than by extensive use of hormones and antibiotics. Cases of inappropriate use of pharmaceutical preparations have created a general scepticism among people concerning the use of hormones and antibiotics in modern farming. Evidence of increasing resistance to antibiotics in bacteria infecting humans has focused on the role that anti-microbial drug use in food-producing animals plays in the emergence of resistant bacteria. There is also a concern about possible residues in animal products. Further, the consumers have a growing interest in animal health and animal welfare issues, and they have ethical concerns regarding the use of hormones and antibiotics, in particular, as performance enhancers. In Europe, the number of farmers growing organically cultivated foodstuffs is increasing, and according to the regulations for organic farming, the use of hormones and antibiotics is limited. Even though the proper use of
hormones and antibiotics does not have any known negative effect on animal welfare or public health, the consumers’ concerns have to be taken into account in livestock production. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Hormones; Antibiotics; Treatments; Fertility; Cattle breeding; Ethics

1. Introduction

Veterinarians and farmers often face the question whether to treat or not to treat when trying to solve reproductive problems in a herd. When diseases occur in individual animals or in groups of animals, most people agree that an effective and safe treatment, if it exists, should be used. However, treatments may be used more or less routinely to solve managerial problems or to control breeding in groups of animals or whole herds. Consumers, veterinarians and producers in many countries are questioning this method of using hormones and antibiotics from several points of view. The purpose of this paper is not to review the literature to evaluate the effectiveness of different treatments of reproductive disorders or methods used in pharmaceutical control of breeding, but to focus on some of the concerns arising when hormones and antibiotics are used extensively. Emphasis will be made on cattle as most of the author’s experience is from cattle reproduction. However, many of the same concerns apply to other farm animals as well.

2. Primary objectives in cattle reproduction

Traditionally, the primary objective for the farmers in most countries has been to have each cow produce a calf every 12 months. In high-yielding dairy cows, however, this may be difficult to achieve and there is an ongoing discussion of what is actually the ideal calving interval in dairy production. Voluntary extending the calving to first service interval and, consequently, the calving interval may be beneficial for the fertility of high-producing cows, and they will have a longer period to recover after calving. This reduces the need for hormonal treatments due to anoestrus and reduces also the number of inseminations per inseminated cow (Larsson and Berglund, 1999). However, in areas where most of the milk is produced on pastures, concentrated spring calving is a prerequisite. Variations in prices of milk may also be a decisive factor for the calving strategy in a herd. Therefore, the farmers’ opinion of what is the ideal calving interval may vary within a country and between countries. Without regard to whether the calving strategy is seasonal or not, the profit of a dairy farm is largely determined by the reproductive performance in the herd (Refsdal, 1999). In beef cattle, where the number of calves weaned or sold is the most important measure of production, the primary goal is to have a cow calving every 12 months.

To reach the farmer’s goals, hormones and antibiotics are important remedies for the treatment of reproductive diseases, and hormones are in particular important tools to control breeding.
3. Use of hormones

3.1. Control of the oestrous cycle

Today, there has been a trend to increase the size of the herds in most countries. Using artificial insemination (AI), oestrous detection is crucial and requires a great amount of work in large herds. To save labour, synchronisation of oestrus and ovulation is propagated especially in beef cattle and in extensive dairy cattle production where seasonal calving is an objective. In many production systems, an oestrous synchronisation programme will facilitate the use of AI.

To control the oestrous cycle, many different hormones such as progestagens, oestrogens, prostaglandins, gonadotrophin releasing hormones (GnRH) and human chorionic gonadothrophin (HCG) have been used alone or in combination. The different methods for oestrous cycle control have been reviewed (e.g. Macmillan and Burke, 1996; Roche et al., 1998). The hormonal therapies produce variable degrees of oestrous synchronisation and may be combined with oestrous detection and insemination on observed heat, or the animals are inseminated at a fixed time related to the treatment (Roche, 1979; Macmillan and Peterson, 1993; Macmillan and Burke, 1996). Even though oestrous detection still is necessary when using some of the programme, the farmer will have the benefit of knowing in which period of time oestrous symptoms can be expected and concentrate his inspection to that period. Thus, several animals usually will show heat and can be inseminated at the same time. Treatments combined with a thorough heat detection and insemination at an optimal time relative to the onset of oestrus may give acceptable results. To avoid any oestrous detection, ovulation synchronisation therapies recently have been developed to schedule insemination of cows at a certain time (e.g. Pursley et al., 1995; Pursley et al., 1997; Stevenson et al., 1999). Most of the programme for synchronisation are associated with reduced conception rates after fixed time AI compared with that of nonsynchronised animals inseminated after detected oestrus. However, using these programme can help in initiating the first AI after calving and improve the reproductive efficiency in a herd compared with relying on visual oestrous detection alone. Treatments to control the oestrous cycle of cows imply a substantial use of hormones, especially when the programme not only is intended to control the luteal phase of the animals, but also for synchronisation of the follicular development.

3.2. Treatment of reproductive disorders

Exogenous luteinizing hormone (HCG) and gonadotrophin releasing hormone (GnRH) are used to induce ovulation in cases where delayed ovulation relative to oestrus and insemination are suspected as a cause of repeat breeding. A summary of different studies using GnRH treatment in repeat breeder cows indicates a positive effect on pregnancy rates compared to untreated control animals (Stevenson et al., 1990). GnRH has also been administered during the luteal phase of cows to stimulate the corpus luteum (e.g. Sheldon and Dobson, 1993). This therapy is based on the theory that insufficient progesterone production leading to early embryonic death is a main cause of repeat
breeding. The different studies performed to evaluate the effect of this treatment on pregnancy results have shown conflicting results (Thatcher et al., 1993). Progesterone administration has also been used in repeat breeder cows to support progesterone levels during early pregnancy (Sreenan and Diskin, 1983; Macmillan and Peterson, 1993). Studies have also shown that administration of GnRH 12–14 days postpartum may reduce the incidence of ovarian cysts and reduce the interval from parturition to conception (see review by Thatcher et al., 1993). Therapy for the induction of cyclicity in the anoestrous animal has also been attempted with a variety of exogenous hormones (see review by Hopkins, 1986). The treatments have been utilised to hasten the onset of puberty or to decrease the interval from calving to conception. However, the different hormone treatments do not give consistent results due to the fact that the anoestrous problems very often are caused by management errors. Therefore, the application of hormonal therapy for the treatment of an anoestrous problem must be based on a thorough investigation of the animals. Some of the treatments may be used with success in healthy, well-nourished animals having normal-size ovaries with some follicular activity.

In cystic ovaries, hormonal treatment has gradually replaced the earlier procedure using manual rupture of the cystic structures of the ovaries. Pharmacological forms of treatment seem to be more effective, and negative side effects like ovarian haemorrhage and adhesions that may follow a manual rupture can be avoided. Exogenous luteinizing hormone and, above all, gonadotrophin releasing hormones acting on the pituitary gland to cause the release of endogenous LH would usually be the preparations of choice (e.g. Whitmore et al., 1979). Sometimes prostaglandins are also used in cases where the cystic structures are luteinized. When luteinization has occurred in response to GnRH, administration of prostaglandins can be used to cause regression and reduce the interval from GnRH treatment to oestrus. Administration of gestagens is also used to re-establish oestrous cycles in cows with cystic ovaries (see review by Youngquist, 1986).

Prostaglandins are sometimes used in cases of retained placenta and have shown to reduce the incidence of the disease in cows that have been induced to calve with corticosteroids (Gross et al., 1986). Drugs like oxytocin that increase uterine motility are also used. Prostaglandins are also commonly administered in cases of pyometra to get regression of corpus luteum followed by maturation of a new follicle and oestrus, leading to uterine contractility. Thus, the purulent material is expelled. According to Paisley et al. (1986), prostaglandin F2α and its analogues provide effective alternatives to antibiotic and antibacterial therapy for most postpartum disorders.

### 3.3 Induction of abortion / termination of pregnancy

Today, prostaglandins and corticosteroids are used to induce abortion in cattle. Administration of prostaglandins usually induces abortion during the first 4–5 months of pregnancy, and it will cause termination of pregnancy in the final month of gestation. Corticosteroids alone or in combination with prostaglandins are also used for induction of parturition (Adams and Wagner, 1970; Schultz and Copeland, 1981; Peters and Poole, 1992). In some areas where seasonal calving is the prevailing strategy, termination of pregnancy has become an important strategy (Radostits and Blood, 1985). Cows that
conceive late in the season are dried off while still milking heavily, and premature calving is induced (Welch et al., 1979). Thus, the animals can be brought back to the normal conception date. Induction of premature calving often leads to loss of the calf and retention of the placenta, but some farmers may consider the loss of the calf to be not important. However, this strategy raises some ethical concerns, and would probably not be accepted in some countries as opposed to using hormones to induce abortion by unwanted pregnancies or in cases of pathologic conditions.

3.4. Embryo transfer

In many countries, embryo transfer is used in breeding programmes to enhance the speed of genetic improvement. Embryos can easily be shipped, and the sanitary risks related to embryo transfer are considered to be low, especially with in vivo produced embryos (e.g. Guerin et al., 1997). Therefore, ET has become important in the trade of genetic material. To induce superovulation in the donor cow, gonadotrophic stimulation of the ovaries with pregnant mare serum (PMSG) or follicle stimulating hormone (FSH) is administered in the mid-luteal phase of the cycle. Regression of the corpus luteum is induced by prostaglandins. More recently, superovulation protocols including progesterone, GnRH and oestrogen are developed to increase the number of ovulations and transferable embryos (see review by D’Occhio et al., 1999). Moreover, embryo transfer programme involves the administration of hormones to synchronise the oestrous cycle of the recipients with that of the donor. Thus, embryo transfer is based on a relatively extensive use of hormones.

4. Use of antibiotics

Antibiotics are commonly used as a therapy in puerperal metritis, pyometra and endometritis, foetal membrane retention and in repeat breeding. Uterine infections often occur after obstetric aid and retained foetal membranes in the cow. However, the mere presence of micro-organisms in the uterus after parturition should not be viewed as a detriment to the reproductive function. Uterine infections have also been treated with various disinfectants to avoid loss of milk due to withdrawal times. Some antibiotics and antiseptics are irritating (e.g. Seguin et al., 1974; Carleton and Threlfall, 1984), and they have a negative effect on phagocytosis (Vandeplassche, 1984). As emphasised by Hoedemaker (1998), this is considered the main reason why local intrauterine therapy often fails to successfully eliminate bacteria (Paisley et al., 1986). In animals with systemic illness, treatments with penicillin systemically are recommended to achieve the greatest concentration throughout the genital organs (Olson et al., 1986). Routine use of antimicrobials may not be economically feasible and may result in development of resistant strains of micro-organisms. Bacteria that are resistant to antibiotics often exist in the early and intermediate postpartum period and therefore intrauterine administration is not likely to be effective (Olson et al., 1986).

In repeat breeders, routine intrauterine treatment of antimicrobial drugs the day after insemination to rid the uterus of organisms that might be detrimental to survival of the
conceptus has been commonly used in many countries. Generally, the result from intrauterine therapy is poor, not in repeat breeders only, but also in animals moderately affected by endometritis (Ott, 1986). The uterus seems to have a considerable capacity of spontaneous recovery, and a large proportion of animals probably does not require any therapy at all, especially under the aspect that some therapies are ineffective and might even cause more harm than benefit (Hoedemaker, 1998).

5. Trends and policies using hormones and antibiotics

Data to elucidate the use of hormones and antibiotics in animal reproduction are difficult to obtain. On a worldwide basis, most of the antibiotics in livestock production are probably used as growth promoters. However, the use of antibiotics as feed additive has ceased in some countries like Sweden and Norway. This is also in agreement with the policy of the World Veterinary Association (1999) having the position that antibiotics are dedicated to curing of diseases and should not be used as growth promoters. Probably, a very small part of the antibiotics used in cattle is related to reproductive problems. Considering the fact that some of the therapies are ineffective, the use of antibiotics in animal reproduction most likely could be reduced. Compared to other areas of application, hormones are probably more used than antibiotics in animal reproduction. However, the quantities of hormones applied to cattle are largely dependent on whether these drugs are extensively used for pharmaceutical control of breeding or not. In Norway, hormones are mainly used to treat reproductive diseases and not as much for pharmaceutical control of breeding. According to the Norwegian health card records, only 1561 (0.38%) cows and 444 (0.26%) heifers were treated to synchronise oestrus in 1998. Even though these numbers may be questioned due to imperfect registration, oestrous synchronisation does not seem to be in general use. Percentages of cows treated for reproductive disorders like anoestrus/silent heat, cystic ovaries, retained placentas and metritis were 2.7, 1.0, 2.6 and 0.9, respectively. Generally, the number of treatments for the same disorders has been relatively low since the registration started, and for the last 10 years the trend has been declining as to the percentages of animals treated for all reproductive diseases (Refsdal, 1998). In Sweden, having a similar registration system, there has also been a decline in percentages of animals treated for reproductive diseases during the last years (Gustafsson, 1999, personal communications). Most countries, except Norway, Sweden, Denmark and Finland, seem to lack systematic registrations of treatments in cattle. In Sweden, the Farmers’ Associations decided to cease using oestrous synchronisation as a tool for AI in 1996. The reason for this was the fear for consumer reactions based on ethical concerns related to replacement of management with hormones.

Generally, the situation in Scandinavia concerning sales of veterinary medicines is different from many other countries of the world. The use of antibiotics is restricted and medicines for animal use are distributed through the pharmacies only. The veterinarians are not allowed to sell these products to the farmers except for the following up of treatments initiated by the veterinarian.
6. Treatments should be recorded

Disease journals with registrations of all treatments should be kept on every farm to help in monitoring the herd, give data for breeding purposes, give population statistics on diseases, and to give data to estimate environmental effects on diseases. It is extremely important that all inseminations and treatments are properly recorded, which makes it possible to take fertility as well as health traits into account in a breeding programme. In Norway, all milk recorded cows, comprising approximately 97% of the total number of cows, have their own disease journal kept in the barn and it follows the animal from birth to death. The system called the ‘‘Health card system’’ started in the beginning of the 1970s. All diseases diagnosed on the cow are recorded on the health card by the veterinarians. These data are sent to the central data bank by the milk recording personnel. Having very strict regulations on drug use in animal production, most of the treatments have to be performed by veterinarians. Farmers are, for example, not allowed to administer antibiotics themselves, except when following up a treatment established by the veterinarian after a diagnosis in an individual animal has been made. Because of this, the disease recording system gives a fairly complete disease journal for each cow. Thus, the health card system is a basis for including health and fertility in the breeding programme.

7. Concerns related to cattle breeding

In general, the reproductive traits have low heritabilities, which to some extent can be explained by the great influence of environmental factors. However, a serious breeding concern is that estimates from a number of studies present unfavourable genetic correlations, on average near 0.3, between various fertility measures and production (e.g. Philipsson et al., 1994). Because of this, fertility should be taken into account in any breeding programme. Norway, Sweden, Denmark and Finland have a long tradition of including fertility in their Total Merit Index (TMI). To include fertility and health traits in a breeding programme, progeny testing on large progeny groups is needed. The progeny tests on fertility are based on insemination data, and in Norway, these data are recorded by the insemination technicians and veterinarians into an AI data base and further sent to the central animal data base. In this way, female fertility has been taken into account in our breeding programme since 1974. In addition, cows with reproductive problems like cystic ovaries and anoestrus have been excluded as bull dams, and AI bulls with bad semen quality or low non-return rates have consistently been excluded from the breeding programme.

In many countries there has been a decline in reproductive performance as milk yield per cow has increased over time (O’Farrel, 1998). In contrast, the fertility in Norwegian dairy cows has steadily improved during the last years (Refsdal, 1998) and reached 71.8% in 1998 as judged by the non-return rates 60 days post insemination. This improvement is probably caused by a variety of reasons. One of them being the breeding strategy, which gives increasing weight to fertility and health traits.
8. How can the use of hormones and antibiotics affect breeding programme?

In a breeding programme that includes progeny tests on fertility based on insemination data, an extensive use of synchronisation and fixed-time insemination probably will reduce the reliability of the data if synchronised animals are included in the progeny test. To overcome this problem, all synchronised animals may be excluded from the progeny test provided that the synchronisation treatments are registered. However, if synchronisation of oestrus/ovulation and fixed time inseminations are extensively used, a large number of animals in each progeny group then will be excluded and, consequently, the number of informative daughters will be considerably lower. Thus, the reliability of the test will be reduced because of the fact that large progeny groups are needed when including low heritability traits such as fertility in a breeding programme. When cows are treated for reproductive disorders, this may not cause problems in a breeding programme including fertility, provided that the treatments are properly recorded. Veterinary diagnoses and treatments reported on “health cards” can be a rather positive contribution to the breeding work, for the farmer when selecting animals for future replacements, for the AI organisations when buying bull calves and for surveying progeny groups for reproductive diseases. In fact, information from the health cards is used when young bulls are recruited to the performance testing stations to be selected as semen donors in Norway. The health cards of the bull dams are then checked for treatments of reproductive disorders as well as other health problems, and cows treated for fertility problems like cystic ovaries, anoestrum and other diseases may be excluded as bull dams. Including fertility and health traits in a breeding programme, any treatment masking or disturbing the natural reproductive performance of the animals should be considered. All diagnoses and treatments performed should be recorded to be available for breeding purposes.

9. Public opinion

The consumers are increasingly concerned about how food is produced and food safety. Today, newspapers, magazines and television programme almost daily focus on these questions and people are worried about potentially negative side effects by using hormones and antibiotics more or less extensively. Above all, cases of inappropriate use of pharmaceutical preparations have created a general scepticism among people concerning the use of hormones and antibiotics in modern farming. Evidence of increasing resistance to antibiotics in bacteria infecting humans has focused on the role that antimicrobial drug use in food-producing animals plays in the emergence of resistant bacteria. There is also a concern about possible residues in animal products. Further, the consumers have a growing interest in animal health and animal welfare issues, and they have ethical concerns regarding the use of hormones and antibiotics, in particular as performance enhancers. Some people are not able to distinguish between different areas of application like curing of diseases, prophylactic treatment, pharmaceutical control of breeding or growth promotion. Therefore, to give information to the consumers about the benefits and the ethical concerns of using hormones and antibiotics for different purposes is a difficult, but nevertheless an important task.
10. Hormones and antibiotics in ecological farming

In many countries, the number of farmers growing organically cultivated foodstuffs is increasing. Debio is the Norwegian control and certification body for organic agricultural production. According to Debio’s regulations, the use of synthetic produced substances and antibiotics should be limited to a minimum. Treatments with medicines of synthetic origin, routinely performed, are not permitted except treatments to control parasites. Likewise, oestrous induction, pharmaceutical control of breeding and embryo transfer are not permitted. However, when treating a disease, animal welfare is decisive for the method of treatment according to these rules. The regulations concerning the use of hormones and antibiotics in organic farming may differ from country to country, but according to the idea of reducing external inputs in production, whether chemical or organic, as much as possible, a restrictive use of hormones and antibiotics would be expected in most countries.

11. The number of treatments can be reduced

Norwegian livestock producers started a 5-year project to reduce the occurrence of the most common diseases in food animal production in 1996. The goal of the project was through aimed work to reduce the occurrence of the most common diseases in animal production by at least 25% with a corresponding reduction of the use of antibiotics by 25%. According to the health card data, there has already been a reduction in the number of disease treatments in cattle by 28% (Østerås and Spanne, 1999). The registered use of antibiotics in veterinary medicine has also been reduced by 28% in the same period (Grave and Rønning, 1999). Since mastitis is the most prevalent disease in cattle, a great part of the reduction is related to a decline in mastitis treatments. However, this campaign shows that putting efforts on preventive work and correct medication can reduce the number of treatments considerably.

12. Conclusions

Veterinarians, farmers and consumers may have different opinions about what is the proper use of hormones and antibiotics. Diseased animals should be treated both from an animal welfare point of view and to restore their production capacity. The treatment should be based on an accurate diagnosis, and when hormones and antibiotics are used, the effect of the treatment should be well documented. When using antibiotics, it should be known that an infectious agent is present which will be sensitive to therapy. Extensive use of hormones and antibiotics to solve or mask managerial problems should be avoided. Some reproductive management programme involving routine use of drugs also gives rise to ethical concerns.

The consumers have a growing interest in animal health and animal welfare issues in many countries, and they have concerns about how food is produced and food safety. Evidence of increasing resistance to antimicrobial preparations and possible occurrence
of medicine residues in animal products calls for a prudent use of drugs. Even though the proper use of hormones and antibiotics does not have any known negative effect on animal welfare or public health, the consumers’ concerns have to be taken into account in livestock production. The increasing interest in organic farming in many countries probably reflects these concerns. In a cattle breeding programme that includes fertility and health traits, it is extremely important that all diseases and treatments are recorded. Thus, reliable fertility indices on large progeny groups can be calculated. When fertility is included in a breeding programme, a restrictive use of oestrous synchronisation is also essential so as not to interfere with the natural reproductive function of the animals being progeny tested. Animal health and fertility should be improved by selection and good management rather than by extensive use of hormones and antibiotics.

References


