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*Lehden artikkelien otsikot löytyvät aiheittain ryhmiteltynä Lääkelaitoksen kotisivulta [www.nam.fi](http://www.nam.fi) kohdassa Julkaisut – TABU Index. Hakemistossa ovat mukana artikkelit ensimmäisestä numerosta (1.93) lähtien. Viimeisimmät numerot löytyvät kotisivuilta pdf-muodossa.*

# Summary

Hannes Wahlroos  
DIRECTOR GENERAL  
National Agency for Medicines

Editorial

## National Agency for Medicines and publicity

From time to time the personnel of the National Agency for Medicines (NAM) find themselves in the situation that health care professionals, not to speak of ordinary consumers, do not know NAM. Our institution might be confused with a pension insurance institution; e.g. the National Board of Health abolished no less than ten years ago, or even a pharmaceutical company.

The pharmaceutical profession and consumers following the media may wonder why NAM fails to take an active stand in public, although news of innovative, revolutionary medicines and their adverse reactions are featured daily in the media.

It seems that the publicity associated with NAM is often negative in nature: A medicine is taken off the market, or its advertisements are prohibited, some pharmaceutical or herbal product has serious adverse effects, a "revolutionary" pharmaceutical innovation has been refused marketing authorisation, a medical device gives rise to severe hazards, pharmacies have been denied the right to render diagnostic services, or the import of a medicine ordered through the Internet has been refused. Experiences as these make us think of our public image and NAM's objectives, and the means we can resort to in the media.

The public image of each organisation is based on its own actions and objectives, the interest it is shown in the media, how the media attention is focussed, and on the nature of the organisation's business as such. In the case of NAM, the decisive factor is the basic nature of our business and the publicity supporting it. Legislation concerning the right-of-access principle and government guidelines on public relations set the framework for our activities and the expression of our views in the media.

The National Agency for Medicines' function is to maintain and promote the safety of medicines, medical devices and blood products. To succeed in this work, it is necessary that the information we release is reliable, and that it is experienced as such by the public. We have not wanted to jeopardise our credibility and trustworthiness by issuing a steady stream of statements or press releases, or by any kind of automatic expression of our opinion. Appearing or being visible in public is

by no means an end in itself or a priority for NAM. We need strong and valid arguments supporting our basic function before we actively seek publicity on an issue. All the same, NAM endeavours to co-operate with the media on a sound basis, for instance by responding without delay to any request for information by the media, as far as legislation on confidentiality allows.

It has been shown in practice that NAM has no difficulty in making any matters public at its discretion. Nor have we had any problems with regard to representatives of the media contacting us. In the first four months of this year, NAM was featured in the printed and electronic media about 150 times according to a follow-up of the media. Despite that, NAM appears not to be all that well known among the public.

The business of the National Agency for Medicines consists in practice of administering marketing authorisation procedures concerning pharmaceutical products, of other control and guidance measures, and of disseminating information to health care professionals. The consumer can not be all that aware of this. Even the health care professionals, with the exception of the younger generations, are seldom well aware of the controller's role of the authority. The facts that the control works, and that the efficacy, safety and quality of medicines and medical devices can be relied on in Finland is all that matters for them.

If NAM were to feel that it needs a far more visible public image for carrying out its business, it would have to boost its liaison with media considerably. That would involve having to accept the rules of publicity in the media, as well. The fact that NAM would not then be in a position to choose which issues it will raise in the media, would not be the least of the drawbacks.

In the information society, however, the media are significant disseminators of information on the use of medicines to the public, being thus able to influence public opinion. For that reason NAM has to concern itself with making use of the background information and expert resources at its disposal when participating in the public debate.

Translation Liisa Fellman-Paul

# Summary

Jaana Husu-Kallio

DIRECTOR GENERAL

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## The aims of drug control in veterinary medicine

*In veterinary drug control, the Veterinary and Food Department of the Ministry of Agriculture and Forestry has three main aims. The most important one is to ensure that foodstuffs of animal origin are clean and clear of drug residues and other foreign substances harmful to human health. The second aim of supervision is to maintain a well-managed use of drugs and to ensure compliance with the regulations. The Department also has a long term aim which is to prevent the increase in resistance of bacteria to antibiotics.*

The use of drugs in veterinary medicine is regulated by the Medicines' Act, the Veterinary Medicines' Act, and the Act on Veterinary Practitioners. The purpose of the Medicines' Act is to maintain and promote the safe use of drugs and ensure their appropriate manufacture and availability in Finland. The National Agency for Medicines has the supervisory role of enforcement of regulations issued on the basis of the Medicines' Act. The purpose of the Veterinary Medicines' Act is to prevent and reduce the harmful effects of veterinary medicine on humans, animals and the environment. The chief supervisory role of enforcement of the Act belongs to the Ministry of Agriculture and Forestry. Following the instructions of the Ministry, the Provincial State Offices have the advisory and supervisory role of enforcement of regulations issued on the basis of the Act in each province. The Provincial State Office may appoint veterinary practitioners to assist it in its supervisory duties. According to the Act on Veterinary Practitioners, a veterinary practitioner is entitled to prescribe drugs from a pharmacy for veterinary purposes. The Veterinary and Food Department of the Ministry of Agriculture and Forestry issues more detailed regulations on the prescrip-

tion of drugs and supervises their enforcement.

International trading in foodstuffs has increased the importance of residue control in food of animal origin. Cultural differences between countries and continents are also reflected in the ways of breeding of animals. In particular, there have been heated discussions recently about hormones and other growth-promoting substances used in beef or milk production. The use of growth-promoting substances in animal breeding has been prohibited by the EC which also requires that imported foodstuffs are free of such substances. By the same token, a condition of the EC requirements is that the hygiene of a Member State's own domestic production can be guaranteed through an active and methodical control of foreign substances. The EC norms applied on the control of foreign substances form the internal EC standard in foodstuffs trading between the Member States and impose requirements also on other countries exporting foodstuffs to the EC.

The control of foreign substances is also of great importance to the Finnish strategy of food quality. Finland cannot compete in the world food markets with its production volume, but Finnish food produc-

tion excels in the quality and purity of its products. In Finland, the control of foreign substances in food production is based on the EC legislation, with responsibility for its national application resting with the Veterinary and Food Department of the Ministry of Agriculture and Forestry as far as live animals are concerned, and with the National Veterinary and Food Research Institute for food-stuffs of animal origin. Drug residues and other impurities, such as environmental contaminants, are controlled at breeding units of live animals and at abattoirs, in dairies, egg-packaging units and fish-processing units where foodstuffs of animal origin are concerned. Residues of prohibited growth-promoting substances are traced and studied in samples taken from live animals. Samples taken from foodstuffs are also checked for residues of legally used veterinary drugs and other foreign substances. Spot checks for foreign substances are also carried out nationwide according to an annual plan and in suspected cases when necessary.

To promote human health by safeguarding the production of food of animal origin, scientific assessment must be carried out on the safety of all drug substances used in the treatment of animals bred for

human consumption and those found as residues in food-stuffs of animal origin. Food producing animals include beef cattle, pigs, sheep, goats, reindeer, poultry, horses and other hoofed animals as well as wild species bred for food purposes - including mammals, birds, reptiles, amphibians and snails, farmed fish and other aquatic animals, and bees used for the production of honey. On the basis of scientific assessment, a drug substance can, if necessary, be prescribed with a withdrawal period, which is the minimum period calculated from the last administration of the drug during which the meat of a butchered animal or milk, honey or eggs of animals may not be supplied for use in food production. Drug residues may also, on assessment, be found to cause a health risk of such significance to the consumer that their minimum legal concentration in food cannot be prescribed. The use of such drugs in food producing animals is prohibited.

The increase of bacteria resistant to antibiotics is considered a major threat to human health. The main reason for increased resistance is the increased use of antibiotics both in human and in veterinary medicine as well as in additives in animal feed. The use of antibiotic additives in animal feed ceased in Finland in the autumn of 1999. The Ministry of Agriculture and Forestry has consequently contributed to the improvement of conditions of animal husbandry, feeding and hygiene to prevent animals from becoming ill and requiring treatment with antibiotics. The same antibiotics are of-

ten used in both veterinary medicine and human medicine, which is increasing the trend of resistance to these drugs in particular. The mass medication of animals in the form of broad-spectrum antibiotics that are mixed in the feed is considered a particular problem. Resistant bacteria are known to be transmitted both from one human to another, and from animals to humans in direct contact with animals, via food of animal origin or through the environment. Resistance transmitted via foodstuffs is not restricted by borders between countries, and co-operation on an international level is therefore crucial in its prevention and control. In national efforts to prevent resistance, the Ministry of Agriculture and Forestry has taken an active role to guide and supervise the well-managed use of antimicrobial drugs that would actually curb the increase of resistance within veterinary medicine.

The control of veterinary drugs is also facing new challenges from the changing circumstances in agriculture. In the future, only larger units are considered to be economically viable to continue animal breeding. In animal husbandry and medical treatment a change from the conventional treatment of individual animals will be made to preventive animal health care for the entire herd or production unit. The Veterinary and Food Department of the Ministry of Agriculture and Forestry is making an important contribution to the development of animal health care. Farms that have signed an animal health care agreement will have a veterinary practitioner specif-

ically designated to them, and supervision of the use of drugs on farms is one of the duties of the vet. Measures taken to prevent diseases will play an increasingly important role in animal welfare. The necessity to vaccinate food producing animals against animal diseases common in other parts of the world can be disregarded in Finland, since such diseases have not occurred in this country. Many vaccines used in Europe are, in fact, prohibited in Finland, and the prohibition is based on the fact that Finland is disease-free and on the effective prevention measures applied in the country.

The isolation of Finland before joining the EU has saved the country from many animal diseases and also from many unwanted features in the medical treatment of animals. Threatening scenarios include drug smuggling and the black market trade of illegal drugs, which would jeopardise both the purity of foodstuffs and the control of animal diseases. The Veterinary and Food Department of the Ministry of Agriculture and Forestry actively aims to deal with any illegal use and other misuse of drugs in Finland both by means of advice and training, and supervision. Co-operation between different authorities, the industry and animal owners is necessary to maintain the well-managed use of veterinary drugs.

# Summary

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## Medication compliance in pediatric practice

*Medication compliance is a characteristic of the studied subject and implies the subject's willingness and ability to follow the instructions for treatment that are given to her/him. The instruction or recommendation for treatment may concern medication, follow-up or the patient's way of living.*

Good compliance is characterised by certain behaviour, which follows the instructions, and poor treatment compliance is characterised by deviation from the instructions.

Depending on the definition of compliance, the variations of good compliance in various studies have been between 5 and 90%. The prevailing opinion in literature is that medical treatment of long-term illnesses in adults results in 1/3 of the patients showing good compliance, 1/3 of them are poor and the rest somewhere in between. Poor compliance is very difficult to predict in advance. The prescribed medication is most likely to be ignored if the illness is symptom-free and the drugs are difficult to obtain and administer. The severity and concrete symptoms of the illness do not predict good compliance.

Unsuccessful medical treatment due to poor compliance may have both financial effects and effects on patient care (Table). It is important to achieve good compliance among those diseases, which if left untreated would impose a serious health risk.

There is evidence that doctors prescribe their patients unnecessary drugs, too, in which case poor compliance makes sense. Previously, acute infections were treated with antibiotics for 10 days given in four daily doses. A 100% compliance was rarely achieved in practice, but a course of only 5–7 days was adequate to treat the infection, and therefore, a 100% compliance would

have been unnecessary. Shorter courses of antibiotics and less frequent doses are increasingly administered nowadays. There are also antimicrobials that can be administered as a single oral or intramuscular dose for the treatment of certain infections. In this case the patient either receives the medication or does not, and the compliance is either 0 or 100%.

### Special features affecting compliance in children

To a certain extent, compliance in children is influenced by different factors than those in adults. The responsibility of medication in a child's case lies with the child's guardian. As the child grows up, the responsibility of his/her medical treatment increasingly shifts to the adolescent him/herself.

The attitude of adults to their child's medical treatment is most often similar to that of their own. When parents were asked for reasons for failure in the treatment of their child the most common reasons were: forgot to give the medicine, stopped giving the medicine once the symptoms disappeared, misunderstood the instructions for administration, child was unwilling to take the medicine, medicine caused adverse effects and the medicine was supposedly ineffective.

### Age and development of the child

The age of the child is significant

with regard to treatment compliance. A weak sense of taste and a sucking reflex in infants make the administration of a liquid medicine easier. Problems in administration occur in certain stages of development such as at the age of 2–3 when the child is less willing.

A school-age child has the ability to understand the importance of her/his medical treatment, and compliance in this age group is usually good. For example, compliance was found to be the best in child cancer patients of the age of 9.5 years and worst at the age of 17.4 years.

In the age of puberty, an adolescent has a need for independence with associated desire to take care of his/her own affairs, including medical treatment. An adolescent's need to identify with his/her peer group in puberty is negatively affected by restrictions imposed by a chronic illness (e.g. diabetes or epilepsy) and associated treatment. An adolescent may ignore his/her medical treatment and probably deny the whole illness, this resulting in reduced compliance.

### Illness of the child

The more severe the symptoms of the illness and the shorter its duration, the better the compliance. Medical treatment will be more successful if the family is already familiar with the illness, such as acute inflammation of the middle ear. Compliance will be reduced, however, as the symptoms of the illness disappear, and a large

Table. Examples of problems caused by unsuccessful treatment due to poor compliance.

- ◆ Expected result of treatment is not achieved.
- ◆ The efficacy of drug is misjudged.
- ◆ The consequences of poor compliance to the individual patient include unnecessary examinations, follow-up treatment, and increased doses of drug or supplementary medication.
- ◆ The relationship between the doctor and the patient is not good; the patient is unsatisfied with his/her treatment and the quality of treatment suffers.
- ◆ Time and money are wasted.
- ◆ The patient may be hospitalised, although he/she could have been treated as an out-patient.
- ◆ Dangerous unused drugs accumulate in homes with small children.
- ◆ Misuse of antimicrobials, mainly disruption of a course of treatment, may develop resistant strains of microbes.

number of courses of antibiotic treatment prescribed for children's infections is interrupted prematurely. Parents should understand the positive effects of treatment and the risks involved in abandoning treatment, and they should get information on the possible adverse effects associated with a given medical treatment.

A severe illness does not necessarily predict good compliance. Korsch et al. studied the compliance associated with immunosuppressive treatment in 152 children who had had a kidney transplant operation. The treatment was discontinued by 14 children (9.2%), 13 of which were adolescents at the age of puberty. Six of the children lost their transplant and eight of them developed renal insufficiency.

### Relationship between patient and doctor

The important factor influencing compliance is that the patient and his/her parents have understood the doctor; in other words, why and how the medicines should be taken. Successful treatment is best achieved if the child is treated by a doctor familiar to the family. The doctor is then familiar with the family background and the child's previous medical history, and it is easier for him/her to prescribe a drug that has previously been appropriate for the child. A doctor with a warm and caring attitude, and who takes the patient seriously will win the patient's confidence. If parents are left with the feeling that the doctor is not fulfilling their expectations, poor compliance will follow.

When patients trust and understand their doctor they also follow his/her instructions for treatment. A

doctor again should be able to assess the parents' ability to pick up information. Irrespective of education, the parents of a child who has suddenly fallen ill may have a limited ability to understand or remember afterwards what the doctor advised them to do.

### Medication

The choice of medication is an important part of compliance. The doctor should select a drug appropriate for the child patient by listening to the family's own experiences and wishes. The form of drug or its taste may be crucial from the point of view of successful administration. Administration of antibiotics to small children is easier in the form of sweet mixtures than in tablet form. The drug may be spat out or vomited by a child, and many drug mixtures should be kept in the refrigerator to retain their efficacy. Accurate measures such as by syringe or measuring spoon should be used in the administration of drug mixtures instead of normal household spoons. Parents using syringes have been found to be more accurate in their administration of antibiotic mixtures to their child than parents using other methods of administration.

Administration via intramuscular or subcutaneous has the same benefits as rectal administration, but the pain caused by injection is a drawback. Repeat injections in particular should be avoided in children. According to one study, however, parents prefer a single intramuscular injection as the form of administration of antibiotics to their child rather than oral administration. Adverse drug effects result in reduced compliance, and the rare occurrence of them will certainly improve compli-

ance, particularly if the patient has previous unpleasant experiences of adverse effects.

The price of a drug is often decisive for parents in their choice of drug. Drugs which are too expensive, but effective, may not be bought even though a more suitable alternative from the price point of view may be found among synonymous preparations. The convenient location and suitable working hours of a pharmacy (even in the middle of night at times) are also contributory factors to successful medical treatment.

### How can compliance be improved?

The doctor should make sure that the patient has understood the necessity of medical treatment and the instructions given, which should preferably be in writing, as well as any possible adverse effects of the drug. The drug administration should be kept as simple as possible: as small amounts and as few doses as possible; infrequent administrations should be aimed at and times of administration inconvenient to the patient should be avoided.

Poor compliance in some patient groups is more likely than others. These include adolescents and the elderly, patients living alone, patients with a hostile attitude towards medical science or their illness and patients who have "adopted the role of an ill person" and do not even want to get better. It is detrimental to the relationship between the doctor and the patient if the doctor suspects or detects poor compliance in the patient. When poor compliance is suspected the doctor should be particularly tactful about it and criticism of the patient should be avoided.

When poor compliance is found to be the reason for unsuccessful medical treatment, the doctor should find out why the patient is not taking the drug prescribed to him/her. Is an adverse reaction caused or suspected to have been caused by the drug the actual underlying reason? Is it a question of involuntary forgetfulness, ignorance or a result of a poor relationship between the doctor and the patient, misunderstood instructions for treatment or suspicion towards the prescribed medical treatment?

# Summary

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ADR News

## Less reports on adverse reactions of oral cephalosporins

The rapidly increasing use of second-generation oral cephalosporins in the beginning of the 1990s was distinctly reflected in the number of reports received and included in the register of adverse drug reactions. During peak years, the number of reported reactions of urticaria/arthritis – similar to serum sickness – associated with cefaclor reached over 20 per year. This rare adverse reaction also occurring in association with many other  $\beta$ -lactam compounds is significantly more frequently associated with the use of cefaclor than with any other drugs. Reports on adverse reactions also peaked on another drug, cefuroxime axetil, regarding diarrhoea *Cl. difficile*. During the same period, a very small number of reports were received on first-generation cephalosporins, even though their sale was almost equal (Figures 1 and 2).

The discussion started on the choice of antimicrobials and the adverse reactions associated with second-generation cephalosporins also initiated a downward trend in the use of cefuroxime axetil as early as in 1993, with the use of cefaclor starting to decline a year later. The number of reports of adverse reactions to cefuroxime axetil started to decrease at the same time, but the number of reports on cefaclor did not peak until 1995, although its sales had already dropped the previous year. The delayed peak is probably partly explained by the attention received by the reactions of urticaria/arthritis, which increased the inclination to report. Another notable phenomenon is that the in-

creased use of cephalexin, which replaces the diminished use of second-generation cephalosporins, has only insignificantly increased the number of reports of its adverse reactions.

Figure 1. Consumption of cephalosporins

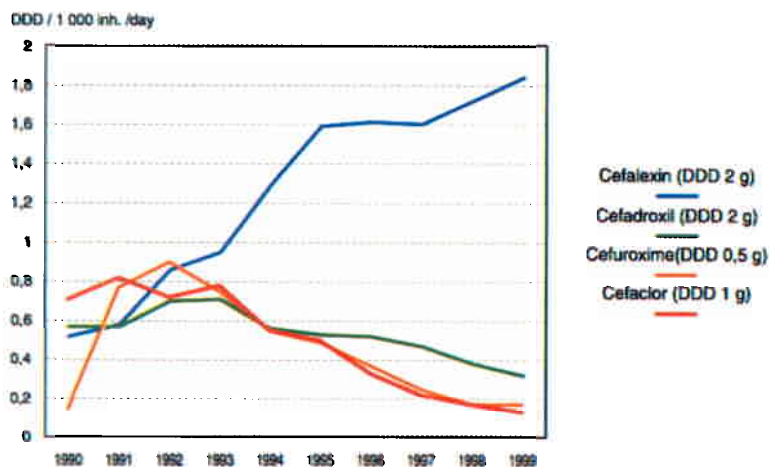


Figure 2. Reports on adverse drug reactions of cephalosporins

