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# Nutrition: From the First Medicine to the First Poison

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## Abstract

Severe adverse reactions of the organism to environmental elements have been dizzily rising in humans and pets over the last 50 years. Such reactions can be expulsive (vomit, diarrhea, dandruff, and abundant secretion or excretion) or driven by an inflammatory process (which has been considered as healing process) in charge to destroy every toxic introduced into the body. Thus, it is clear that if a contaminated food is assumed daily, the inflammatory process becomes inevitably chronic. Most common inflammatory processes of dogs and cats originate from this condition, which we observed to be frequently caused by well-defined contaminants: toxic residues of oxytetracycline (OTC). In fact, once everything containing in this compound is eliminated, all inflammatory processes tend to rapidly and spontaneously regress. Here, we reviewed and discussed the problem related to the amount of pharmacological and chemical substances, which are used to increase the production of fruits, vegetables, intensive farming-derived meat and fish, milk, eggs, and grain. Such substances can persist within the products in variable amount and, gradually or rapidly (often in a few hours), poison the organism causing reactions such as allergies, anaphylactic shocks (not so frequent), autoimmune diseases (fortunately not so frequent but continuously increasing), and inflammatory processes, the most common reaction. In this context, nutrition, as a daily and frequent habit, should be taken seriously into account; given that wild animals do not seem to have the same pathologic reactions, there are no doubts that many foods deriving from intensive farming have become a poison rather than a remedy.

**Keywords:** food intolerances, food as carrier of chemical and/or pharmaceutical residues, oxytetracycline, increase of excretions and secretions, inflammatory processes, adverse food reactions

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## 1. Introduction

Pathologic reactions of the organism to environmental elements sharply rose in humans and pets in the last 50 years. In this context, nutrition, as a daily and frequent habit, should

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seriously be taken into account. Moreover, given that wild animals do not have the same pathologic reactions, there are no doubts that food has become a poison rather than a remedy. Here, there are few simple reflections.

To preserve pet's oral health cavity, the use of a toothbrush and toothpaste is quite frequently necessary recommended in veterinary clinical practice [1]. It is the same for the ear and body cleaning where the weekly use of an ear cleaner and a dandruff shampoo is even more used [2].

The final reason of all these precautions is the owner desire to have "normal" dogs, with an oral cavity free of plaque, a tartar, and a clean fur, as normally occurs in wild environment without any care.

The only real difference is that wild animals eat naturally available foods, while domesticated ones, and also their owners, are daily bombarded by high amounts of pharmacological and chemical substances, which are used to increase the production of food (fruits, vegetables, meat, milk, eggs, or grain).

Such substances can remain within the food and, gradually or rapidly, poison the organism causing two kinds of reactions: one very negative and abnormal, represented by allergies, anaphylactic shocks (not so frequent) [3], and autoimmune diseases (unfortunately even more frequent and dramatic) [4, 5], and one "positive," represented by food intolerances [6].

The reason why we defined "positive" food intolerances is in the definition, which unequivocally identifies foods as normal, and the reactions to these as abnormal. On the contrary, foods result as abnormal because they systematically contain chemical and pharmacological residues and can cause symptoms related to damage induction and to the defense reactions triggered by the host. Such reactions can be expulsive (vomit, diarrhea, dandruff, and abundant secretion or excretion) or driven by an inflammatory process (which should be considered the healing process) in charge of destroying toxins introduced into the body.

Thus, it is clear that if a contaminated food is consumed daily, the inflammatory process becomes inevitably chronic.

Most common inflammatory processes of dogs and cats, but also humans, originate from this condition and it has been hypothesized and partially demonstrated that can be caused by a well-defined contaminant derived by the intensive farming: the oxytetracycline (OTC) [7–9].

## 2. Oxytetracycline

OTC, a widely and legally used antibiotic for intensive farming still used worldwide, can unfortunately reach the food chain supply (pet and human food) and then become the enhancer of inflammatory processes [7, 8].

We have also observed that its toxicity is exerted once bound to the bone of intensive farming-treated animals, e.g. chickens and turkeys [10]. Also, fat is considered an OTC deposit, but its role is less prominent.

It is not a case that chicken, at different concentrations, is the most used raw material in pet food [11].

It is important to point out that in vitro experiments showed a cytotoxicity of OTC even at lower concentrations with respect to minimal residual limits [7, 10, 12].

Both OTC (in its liquid form at 20%) and bone meal with OTC induced a significant release of interferon (IFN)- $\gamma$  from human peripheral blood lymphocytes [7] and DNA damage features, such as the activation of ataxia-telangiectasia-mutated (ATM) protein and p53 oncogene, the phosphorylated histone H2AX ( $\gamma$ H2AX), the modifications of histone H3 methylation of lysine K4 in the chromatin, and an increased expression of type 1 superoxide dismutase (SOD1) [13].

Moreover, current regulatory authorities do not contemplate the evaluation of bone because considered not eatable, while widely present in most of meat meals [10].

Providing a well-balanced food without the overdose of raw materials and toxic compounds able to promote inflammatory processes allows the organism to reach homeostasis, thus removing the inflammatory process. The restoration time is almost immediate depending on symptoms.

Therefore, we claim that the immune system is absolutely involved in the inflammatory and deregulatory process induced by OTC rather than in the allergic one [10, 14].

## 2.1. Antibiotic resistance

Already in 2014, the Food and Drug Administration (FDA) has published three papers aimed at reducing the use of antibiotics in animal nutrition [15]. According to experts, the habit of adding to the antibiotic feed used in humans has also led to an increase in bacteria resistant to their action, endangering human health seriously [16]. Hence, there is a need for conscious use of these drugs, which should be limited to cases where it is necessary to cure animals and not to increase their weight or make them more resistant to disease. Eighteen of these antibiotics, approved decades ago, have been judged by new FDA studies as being at high risk for humans because their use in feed promotes the development of resistant bacteria that can be transmitted to humans through the food chain. For the other 12 antibiotics, the producers had submitted safety records that would today be considered insufficient to obtain authorization. Nine are still used in herds. Among them, the tetracyclines are still heavily used. Europe's antibiotic resistance data provided by the EARS-Net Surveillance Network show a rather uncomfortable panorama: the resistance of the two types of bacteria under surveillance, *Escherichia coli* and *Klebsiella pneumoniae*, has increased considerably during the last 4 years. For this reason it is important to be alert because antibiotic resistance has become one of the major public health problems that threaten the health of European citizens. Antibiotic resistance causes difficulty or inability to effectively treat some bacterial infections, with increased hospitalization times, healthcare costs, and mortality. European data confirm the increase in resistance to the two types of bacteria under surveillance: *E. coli* and *K. pneumoniae* [17]. These two species are responsible for urinary infections, sepsis, and other nosocomial

infections. The World Health Organization (WHO) describes a rather reassuring scenario regarding the antibiotic resistance phenomenon: it is a serious threat to public health, which could lead to post-antibiotic age in the next few years, in which simple surgery, common infections, and minor injuries will be able to kill again. Only in our country, every year, they die from 5000 to 7000 people because of the antibiotic resistance with an annual cost of more than 100 million euros. The problem has long been known and has to do with intensive breeding. The overcrowding conditions of farms and stables of companies that have adopted an industrial production model make animal health precarious: excessive density and contiguity between garments make developing pathologies more likely. And, to prevent them from spreading throughout the game, the massive use of antimicrobial drugs is being resorted to. Many breeders argue that there is no preventive and default use and that pharmacological intervention only occurs in the presence of illness. But, even if only one animal has pathologic symptoms, it becomes necessary to subject all the garments to pharmacological treatment to avoid the risk of contagion. This systematic use of drugs has favored the prevalence of treatment-resistant bacteria, with serious risks also for people's health as some families of these pathogens, as described above, may also attack humans, who would find themselves without effective antibiotics. Basically, if antibiotics lose effect because the bacteria learn to overcome them, when they really do, they do not work anymore.

## **2.2. Allergies and intolerances: new elements for a differential diagnosis**

Pharmacological intolerances are defined as pseudoallergic reactions due to their clinical similarities with IgE-mediated allergies. Food intolerances and their symptomatic manifestation are always dose dependent, and this helps in distinguishing them from real allergies, where symptoms are related to the intake of even small quantities of the responsible food [18, 19].

Until fairly recently, it was widely accepted that 90% of the adverse food reactions were allergies. We retain that 90% of the adverse food reactions are intolerances. Who is right? We believe that the answer can be given by the privation diet approach that, by means of a rapid disappearance of symptoms (within a few days for intolerances), can clarify the allergic or intolerance origin of suspected symptomatology. It is well known that food allergies are frequently caused by immune system food reactions (IgE release), with related symptomatology, that try to counteract the allergen within food culminating with an histamine release which in turn triggers the inflammatory process [20]. In fact, in most of "supposed" food allergies, the symptomatology is related to the administration of incorrect diets with an overdose of raw materials and toxic compounds, specifically OTC, frequently present within pet food [21].

## **2.3. Undefined food intolerances**

"Mere" food intolerances are ascribed to the incessant consumption of some foods, are not IgE-mediated, and are characterized by a delayed onset once starting the accused food intake [22]. Related symptoms concern the gastroenteric apparatus (diarrhea, constipation, IBD, and eczema) [23]. Many foods are able to induce intolerances, but recent studies revealed the unexpected and toxic role of the OTC and its residues as one of the main triggering factors. This antibiotic, apparently harmless to chickens, turkeys, pigs, and cows,

becomes unexpectedly toxic once bound to the bone, promoting apoptosis and inflammatory processes related to the increased pro-inflammatory cytokine release. The overall result is the onset of several immune-mediated pathologies in dogs and cats [10, 14, 24]. It is worth noting that a rapid disappearance of clinical symptoms (otitis, conjunctivitis, keratitis, gingivitis, stomatitis, dermatitis, hot spot, pyoderma, gastritis, enterocolitis, colitis, enteritis, nephritis, cystitis, pancreatitis, and other inflammatory processes) with a privation diet without oxytetracycline and without therapy is a clear demonstration of our researches. Thus, OTC toxicity is exerted through apoptosis induction and interferon- $\gamma$  release [7, 10]. We just listed that there are many inflammatory and reactive processes induced by OTC (generally those related to the intolerances), which can involve each organ. So far, the most effective tool, with respect to other unreliable commercially available tests, is the privation diet, which allows us to easily distinguish between intolerance and allergy. Moreover, such tests provide qualitative but not quantitative results. Thus, it is of relevance to distinguish, among food intolerances, between pharmacological and the so called “undefined” intolerances [25]. We can now refer these latter to OTC adverse reactions (OAR), which are characterized by physicochemical reactions without allergic reaction, but with immune-mediated inflammatory process implication; response times to privation diet between 3 and 10 days; localized itch on the neck and lumbar region and ear (less frequently in both ears), chin, neck, armpits, croup, thighs, volar carpus, and hot spot lesions; sensitization times of few hours; fundamental apparatus involvement, also with inflammatory, phenomena, and/or increase in excretions and secretions; and rapidly and strongly dose-related reaction. Reactions to such molecule can be accompanied by an increase in secretions and excretions, which should be considered as natural mechanisms of toxic expulsion.

#### 2.4. Food residue syndrome in dogs and cats

By “food residue syndrome” (FRS), we mean the sequence of symptoms that develops in a sensitive subject following to the ingestion of foods that contain pharmacologically active molecules. These symptoms affect especially the gastrointestinal system, the skin, and the eyes, but the reaction could appear everywhere (mouth, pancreas, bladder, kidney, behavior, immune, and reproductive system):

- **Miliary dermatitis (cats and dogs):** it has no precise cause. Several causes are just supposed, from flea allergy (that was recognized as the most frequent and most convenient cause, though the advent of new flea repellent with total efficiency did not alter the incidence of the disorder, thus contradicting this origin) to fungal, parasitic, and bacterial infections (all these elements are effects and nearly never the cause of the disorder). Atopic dermatitis is called into question too. It is another disease whose origin is often impossible to identify. The whole neck area is affected, and local hair loss may occur. The skin can be slightly thickened and wrinkled. The possible dermatitis will be characterized by thin dandruff. It is possible to observe the characteristic pannicular wave movement (looking back as if someone had stung it with a nail), annoyed licking (without the typical relaxation of normal cleaning activities), and biting of the concerned part; these are all symptoms that cannot be attributed to simple itching, but seem to show paraesthetic phenomena and possible neurologic reactions [21].

- **Granuloma (cats and dogs):** possible onset of very itchy granulomas, with scratching injuries. The most frequent location is between the corner of the eye and the mouth of the cat, even though it can appear as a line on the distal part of the thigh or the foot.
- **Chin pyoderma (cats):** it is relatively frequent in cats due to the presence of tetracycline residue in pet food. It always localizes near the chin. It appears with black scabs that strongly adhere to the skin. Chin pyoderma is associated with itching, which causes the partial detachment of the scabs, with bleeding and pus.
- **Repeated fasting vomiting (especially cats):** the most characteristic manifestation of the food residue syndrome is fasting vomiting. It can occur at night or early in the morning, and it is very unpleasant, as the cat systematically identifies the fabric that is more similar to the ground or the grass and inevitably chooses carpets, rugs, and sofas, where it regurgitates yellowish stomach acids that leave permanent stains.
- **Malabsorption disorders (cats and dogs):** these manifest through belching, borborigmo, feces of variable volume, consistence, color and smell, flatulence, and up to chronic or recurrent diarrhea. The clinical picture is usually characterized by the absence of high temperature and general signs. Dogs and cats can live rather well with the pathology, with no particular signs of dehydration even in lack of parenteral rehydration [26].
- **Forms of colitis (cats and dogs):** these can be even very severe and characterized by vomiting, blood vomiting too, colic, pain, and profuse diarrhea, often hemorrhagic diarrhea, and can develop in the second part of the digestive tract. As it is known, there are no efficient treatments for chronic colitis (IBD), and symptomatic treatments often are nearly ineffective. On the contrary, a specific diet we developed for such disorder can be very effective.
- **Halitosis (cats and dogs):** FRS causes several reactions in the oral cavity, from halitosis to dental plaque hyperproduction, tartar development, gingivitis and even to more serious forms of stomatitis [27].
- **Chronic interstitial nephritis (cats and dogs):** although at present the FRS-related disorders cannot be distinguished from those with a different origin.
- **Idiopathic cystitis (cats and dogs):** it is often labeled that way because it does not have an identified cause. It often arises from FRS [28].
- **Constant lachrymation (cats and dogs):** numerous cats and small dogs, especially the breeds with brachygnathia, suffer from constant lachrymation, with secretions that are from transparent to brown or reddish. Even the consistency of secretions can vary from liquid to dense, with the accumulation of eye discharge that tends to dry. Very often, fair-haired cats have a real colored strip from the corner of their eyes.
- **Conjunctivitis (cats and dogs):** these are characterized by the fact of being unilateral (just like paw-licking and ear infections). The manifestation is not dissimilar to the typical cases of conjunctivitis.

- **Keratitis (cats, but especially dogs):** there is a growing awareness that keratitis in cats, that are not particularly frequent but are often autoimmune, can be attributed to FRS. It is now certain that *Keratoconjunctivitis sicca* in dogs is worsened and in some cases is caused by OTC only. Published studies on more than 50 chronic subjects clearly show: with numerous before and after pictures: the partial or total regression of the disease thanks to an elimination diet supplemented with immune-modulating herbal extracts [29]. In a large number of these cases, the regression occurs even without any drug. Even in this case, the manifestations are typical and unilateral.
- **Behavioral disturbances (cats and dogs):** home cats apparently are less affected than dogs by the presence of the pollutant. In any case, similar to dogs, behavioral unbalance concerns all anxiety-related disorders and certain forms of exasperated or unjustified aggression. This could be the case of unjustified aggressive assaults to the members of one's family. The most common manifestations in dogs are aggression attacks, marking, anxiety, diffidence, irregular biorhythm, reactivity, activation, irritability, alertness, paw licking, environmental exploration, and attention requirement [30, 31].

## 2.5. Conclusions

The only effective treatment for FRS consists of the definitive elimination from the diet of all the foods that could contain the harmful pharmacological residues such as OTC, even in the smallest quantity. The various inflammatory phenomena that could affect different organs spontaneously regress, because they are the expression of the body's defense mechanisms. The dietary pattern that leads to the best results is based on residue-free foods and on the total elimination of all can have bones and fat from industrial farming. The food which proved to be the best both during the trial period and throughout the following maintenance diet is sea-caught fish: a very small number of dogs showed adverse reactions while eating fish constantly, even for a very long period. In cats, however, it is quite a common fish allergy.

Other foods that constantly proved to be free from this harmful residue are pasta (with the exception of egg pasta); rice; all fresh, frozen, and deep-frozen vegetables; all fruits; organic food meat of strictly wild animals; sheep meat that does not come from industrial farming; and vegetable fats.

Summer relapses are observed in those subjects who do not continue the prescribed privation diet in winter too, when there is a spontaneous, partial, or total regression of itching and skin disorders. You can likely assume that these improvements are connected with the seasonal disappearance of allergens that in spring and summer contribute to develop the disorder in question.

So, we reiterate that, in order to assist to a definitive remission of the FRS symptoms, the right diet must be constantly followed. It is extremely important to underline that, in the first phase, since each time you bend the rules, the effects last on average 4–5 days, two tidbits per week are enough to undermine all the efforts. In our experience most of the failures result from the owner's difficulty in following strictly the privation diet in the first 5–10 days. The success rate is objectively very high.



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