CHEMICAL CONTAMINANTS IN FOODS OF ANIMAL ORIGIN

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ABSTRACT : *Residues of chemical contaminants in foods are no longer of major public health concern, but they are important with respect to international trade and consumer confidence. The most contentious residues that occur in meat, milk and eggs are antibacterial drugs, hormonal growth promoters, and certain pesticides, heavy metals and industrial chemicals.*

RESUME : *Les résidus de contaminants chimiques apparaissant dans les aliments ne suscitent plus autant d'intérêt dans le domaine de la santé publique, mais sont par contre importants en ce qui concerne le commerce international et la confiance des consommateurs. Les types de résidus soulevant le plus de litiges et apparaissant dans la viande, le lait et les œufs sont les antibactériens, les promoteurs de croissance hormonale et certains pesticides, métaux lourds et composés chimiques industriels.*

In the last several decades, there have been a number of incidents that have heightened public concern about chemical contaminants in foods. Publication of the book "Silent Spring" by Rachel CARSON drew public attention to the dangers of pesticides in the environment and food. The association of DES with cancer in the daughters of women treated with the hormone raised questions about its safety as a growth promoter in animals [28]. The banning of several artificial sweeteners in the 1970's due to evidence of carcinogenicity in laboratory animals raised questions about the safety of food additives, and questions about the role of laboratory animal testing for food safety evaluation. In addition, there have been incidents of illegal use of hormones in animal production, media reports of drug residues in milk, and considerable public debate about BST use in dairy cattle. Until very recently, the principal food safety issue in the mind of the public was chemical residue contamination and food additives [24]. Very recently in North America, concerns about chemical residues have been surpassed by fear of microbial contamination of foods, largely due to the shock of the 1993 *E. coli* O157:H7 outbreak in the northwestern United States. In this large multi-state outbreak, there were hundreds of cases of hemorrhagic colitis and hemolytic uremic syndrome, and some of the affected children died [5]. For years, scientists have been telling the public that their fears of chemical contamination of foods have been misplaced, that it is microbial contamination of foods that is the real public health problem. Nevertheless, the current debate in Europe over removal of the ban on hormonal growth promoters in livestock, and the debate in North America and elsewhere about BST indicates that these issues have not gone away.

Foods from animals (mainly meat, milk and eggs in the context of this paper) could potentially be contaminated with one or more of the thousands of man-made chemicals that are used for various purposes in society. Among the thousands are relatively few that occur as residues with any regularity in foods from animals, and the most contentious are antibacterial drugs, hormonal growth promoters/production adjuncts, polyhalogenated hydrocarbon pesticides, industrial chemicals and heavy metals. However, it is important to recognize that foods from animals may also be contaminated with naturally-occurring toxic substances, including bacterial toxins (eg botulinum toxin, staphylococcal enterotoxin), mycotoxins (eg aflatoxin and ochratoxin), and algal toxins (eg. saxitoxin in shellfish [5, 24].

Among man-made chemicals that occur in foods are a large number of additives that are intentionally used for production, processing or preservation purposes. A few of these, for example nitrite, are of concern if their toxic metabolites (eg nitrosamines) are allowed to form in foods prior to ingestion.There are also chemical residues (eg chlorine) which are minor contaminants of sanitation procedures, and some (eg aluminium and styrene) that occasionally migrate from packaging materials.

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In general, chemical contaminants in foods from animals are infrequently found at concentrations that could be hazardous to the people ingesting them, and it is therefore tempting to conclude that they are not very significant from the public health standpoint. Nevertheless, they remain very significant from the perspective of consumer confidence and international trade [7, 24]. As tariffs are removed and goods flow freely between countries, importing countries must be confident that the foods they purchase are safe, and in addition to this, there is from time to time pressure to use chemical residues as non-tariff barriers to importation.

I - RISK ASSESSMENT OF CHEMICAL RESIDUES IN FOODS

The characterization of potential human health risks associated with chemical residues in foods is not as straight forward as it is for microbiological hazards in foods, which tend to produce acute symptoms of gastrointestinal disease that can readily be attributed to an infection or microbial toxin [5]. While very high concentrations of chemicals in foods will produce recognizable symptoms in patients, long term exposures to low doses of residues in foods, if they have any negative health effects at all, are likely to be chronic [24]. Risk assessment is a process that has evolved over the last couple of decades to assist in the characterization of risks due to low-level exposure to environmental contaminants and other hazards. Used in this context, the term risk connotes both the probability of occurrence and the magnitude of the negative health outcome from exposure to the chemical residue in food. Hazard identification and dose-response assessment are components of the US National Research Council model of risk assessment that entail description of the negative outcomes (types of disease ; eg cancer, allergic reaction) that can be attributed to the chemical and the threshold dose at which toxic effects begin to be observed. These determinations are sometimes based on evidence from case reports or epidemiological studies in people, when they are available. More often, the results of animal bioassays are used to identify both the outcomes and threshold doses. Together with safety factors to account for the various types of uncertainties in the process (eg human-animal differences and differences within the human population) these threshold doses are used to establish acceptable daily intakes (ADIs) of chemical residues in foods consumed over a lifetime [24, 14]. In the case of veterinary drugs, it is possible to use the ADI estimates to establish milk and meat withholding times for animals treated with these compounds, which are intended to ensure that harmful residues do not appear in edible products. In the case of carcinogenic substances, ADIs are sometimes based on doses of chemical estimated to pose a human cancer risk in the order of one in a million over a lifetime of exposure [24].

An important aspect of assessing the risk of chemicals to human health is estimating the quantities of chemical residues which consumers are exposed to in foods. Exposure assessment is sometimes achieved by measuring the quantities of residues within people (eg measurements of organochlorines in blood or body fat), or by measuring residue levels in foods and then estimating the amounts of the food eaten by people in society [29]. The results of monitoring are usually expressed in terms of maximum residue levels (MRLs) or in some cases « tolerance » or « legal » levels. MRLs are usually derived as functions of ADI of the compounds, together with the estimated consumption quantities of various foods that may contain the residue [14, 24]. Characterization of the risk of individual chemical residues in foods is essentially an attempt to put together the information from hazard identification, dose-response assessment and exposure assessment to estimate the type and magnitude of the public health problem posed by that chemical, in the concentrations it is found, and in the frequency that it occurs in various foods. In some cases, risk (frequency and impact of adverse health effect) posed by various chemical residues can be ranked by priority for action by risk managers.

II - AGRICULTURAL PESTICIDE RESIDUES

Although most of the pesticides used in agriculture are herbicides (and residues of these have been reported in fruits and vegetables and occasionally in foods from animals), it is the insecticides and fungicides that have been of most concern in meat, milk and eggs [19, 22, 25]. Among these, the organochlorine pesticides (such as DDT, heptachlor and hexachlorohexane or lindane) cause the most concern, because they are lipid soluble, persistent and therefore prone to bioaccumulation. Although there is some suggestion that these substances are carcinogens, there appears to be insufficient human and animal data to be sure of this. Recently, the presence of organochlorine residues in blood was associated with breast cancer in a large cohort of American women. The role, if any, of these residues in human cancer is under debate [29]. Organochlorine pesticides are sometimes found in milk and meat, but in general, the levels found are below those considered safe. In recent years since these compounds have been withdrawn from use in many countries, the residue concentrations in foods have been steadily declining [25].

Animals may become contaminated with pesticides when they are treated with these compounds to rid them of insect pests, or through exposure to contaminated water, buildings or pastures. Contamination of feed may also be important and heptachlor contamination of animal feed has resulted in major episodes of meat and milk contamination. Milk residues of these compounds are of special concern because milk is consumed in relatively large quantities by children and organochlorines tend to concentrate in the milk fat. Overall, it has been estimated that approximately 40 p. cent of pesticides in the human diet are found in meat, milk and eggs, and that this exposure has decreased in the past few decades, with the exception of occasional outbreaks, such as the heptachlor contamination of milk [25].

III - INDUSTRIAL CHEMICAL RESIDUES AND HEAVY METALS

Industrial chemicals and heavy metals that are not used for agricultural purposes can contaminate animal feeds or their environment and thereby gain access to milk, meat or eggs. Some of the contaminants in this category are fungicides, for example, pentachlorophenol and hexachlorobenzene, which have been used as wood preservatives and seed grain fungicides, respectively. Wood preservatives, such as pentachlorophenol may contaminate animals housed in pens made of treated wood or bedded on treated wood shavings. Seed grain fungicides may contaminate animals if treated grains are mistakenly used as animal feeds [26].

Some industrial chemicals have become widespread environmental contaminants and as such find their way into foods. Polychlorinated biphenyls (PCBs) are examples of compounds that were widely used in industry until, like DDT, their tendency to persist in the environment and bioaccumulate became apparent and the compounds were banned. Although PCBs are believed to be toxic in high levels, their significance at low levels is doubtful, other than their ability to bioaccumulate in tissues. Since their use has been banned in most countries, residue concentrations have been decreasing in monitored foods, although trace levels are still apparent in many food commodities, especially fish and to a lesser extent milk and dairy products [26]. Cadmium, mercury and lead occasionally contaminate meat and milk, particularly from animals pastured or housed in areas of industrial contamination, or in the case of cadmium in particular, where soils naturally contain significant levels of the element. While the toxicity of lead has been well known for many years, there is growing concern that low levels of lead may be important, especially in children where low-level exposure may result in impaired cognitive development. Livers and kidneys from cattle and horses sometimes contain sufficient cadmium to render them unsuitable for consumption ; lead levels are rarely elevated above MRLs in meats and milk, even in animals with clinical evidence of lead toxicity. Iodine concentrations in milk have in some countries reached levels that cause concern, and have resulted, at least in Canada, of a withdrawal of licensure of iodine-based medicines from feeds of food-producing animals [25].

IV - RESIDUES OF EXOGENOUS HORMONES

It is now an understatement to say that the use of hormones in food animal production is controversial. The controversy over the use of these compounds for growth promotion or increased milk production centres on two main points: (1) the effects of residues of these chemicals on human health ; and (2) economic, social and political implications of using these compounds in agriculture. At present, these compounds are used legally to a varying degree in many countries ; the European Community is considering a repeal of the ban on hormone use that was instituted a few years ago in the face of public and political pressure.

Historically, some of the public health concern over these compounds emerged out of the observed association of DES treatment of women with reproductive problems and cancer in some of their female offspring. Secondly, there have been a few (generally unconvincing) reports in the literature of precocious sexual development in children and possible exposure to foods contaminated with hormonal residues in foods [28].

In the context of food safety, it is useful to consider the hormonal substances used in food animals to fall into two main groups: those that are naturally occurring in animals (and therefore humans also) and those that are synthetic compounds or do not occur naturally in animals (so-called xenobiotics). Among the naturally occurring compounds are testosterone, progesterone, estrogen and somatotropin, although it should be noted that for commercial purposes bovine somatotropin in particular has been genetically engineered (recombinant bovine somatotropin, rBST), with minor structural differences from the natural hormone. As a general rule for risk assessment, if the concentrations of the exogenous, naturally occurring hormone in edible tissues from treated animals do not significantly differ from those in untreated animals, the presence of residues of the active hormone in foods should be no cause for concern with regard to public safety. This can be justified even though it has been shown that some of these compounds (ie the sex steroids) can act as tumour promoters [28].

It is generally accepted that residues of bovine somatotropin are not public health hazards for several reasons: bovine somatotropin is not metabolically active in humans ; it is inactivated by heat treatment during pasteurization ; it is a protein and therefore degraded by the digestive process, and concentrations of the hormone in milk from treated animals are no higher than in untreated ones. The remaining minor public health concerns about the use of this compound are based on the increase in insulin-like growth factor that has been observed in milk of treated animals, and the greater frequency of mastitis in treated animals. It has been argued that an increase in mastitis may lead to a coincident increase in risk of drug residue contamination of milk [4, 8, 28].

Xenobiotic compounds (including trenbolone acetate, zeranol and melangestrol acetate) by definition do not occur naturally in animal tissues. For these compounds, safe levels have been established in foods through the means of risk assessment described above, and withdrawal times have been established to prevent harmful residues in foods. Most surveys for the presence of these compounds in foods from animals show that they are rarely present at illegal levels [28].

V - ANTIBIOTIC RESIDUES IN MEAT AND MILK

Although antibiotic residues in foods can have a detrimental effect on processing of cultured products such as cheese and are important in terms of consumer confidence, there are also significant public health concerns about residue concentrations of some of these compounds in foods [27]. Most of the antibiotic drugs currently used in animal agriculture are relatively non-toxic, even at high concentrations, but there are a few antibiotic residues that pose a small, but significant threat to public health. Among these is chloramphenicol, which has been associated (in a non-dose related manner) with aplastic anemia due to bone marrow depression in a small proportion of human patients administered the drug for therapeutic purposes. Some of the patients surviving the bone marrow depression have developed leukemia, raising concerns about possible carcinogenicity. Based on animal bioassay data, there is also some concern of carcinogenicity with regard to nitrofurans and some of the anti-parasitic drugs, such as dimetridazole [27]. Some antibiotics have been associated with allergic reactions of varying severity in people. It has been estimated that between 4-10 allergic reactions occur per 100 000 courses of penicillin treatment given, but actual incidents of allergic reaction to penicillin residues in foods are few and poorly documented [27]. Although sulfonamides and tetracyclines administered to people at therapeutic concentrations may have toxic and allergic consequences, there is little evidence that these consequences occur at the concentrations that residues are encountered in foods. Based on experimental evidence, however, there is concern that residue concentrations of antibiotics have the potential for encouraging the development of antibiotic resistance in the microbial flora of people eating contaminated foods [10].

Monitoring of milk, meat and eggs for antibiotic residues occurs in most countries and the incidence of residues at violative levels is very low and has been declining in recent years [6, 9, 11, 13, 15]. When they do occur, illegal residues of these drugs are a consequence of their use in food animals for treatment of clinical or subclinical infectious disease, or for disease prevention or growth promotion [17, 18, 20, 23]. A wide variety of antibiotics and sulfonamides are used in animal agriculture, including penicillins, tetracyclines, aminoglycosides, sulfonamides and others [16, 20, 21]. Because of the temporal proximity of treatment with one or more of these antibiotics to the time of slaughter, certain types of animals, such as cull dairy cows, certain types of veal calves, down or disabled animals and young swine are at greater risk of residues than others [23]. Due to their pharmacokinetic or physical properties, certain drugs are more likely than others to result in violative residues at slaughter. Some of the aminoglycosides for example, may be found for prolonged periods after treatment in kidneys. Sulfamethazine residues have been a problem in the swine industry, partly because the drug is relatively stable and traces can be transferred between treated and untreated animals through feces or feed [23, 27]. Another factor that is frequently associated with residues in meat and milk is the practice of "extra-label" treatment, whereby antibiotics (or other drugs for that matter) are administered in a manner (with respect to dose, frequency of administration, route, animal species or type) that differs from the drug label instructions [16, 17, 21]. Withdrawal times are calculated on the basis of the label treatment conditions, thus deviation from these conditions may lengthen the time that potentially harmful residues of drug are present in edible tissues.

There are also other types of human error that lead to residues in foods. People sometimes forget to withhold the milk of cows treated for mastitis with large quantities of penicillin, thereby contaminating the milk from their own farm and perhaps other farms as well after the milk is mixed for transport or processing. It has been shown that some people simply do not know the proper withholding times for meat or milk that apply to the antibiotic products that they use [18, 23]. Although a wide variety of antibiotics may be used on farms, methods for detection of residues of these compounds in foods vary considerably in their ability to detect them. In general, the microbiologically-based screening methods are reasonably useful for detecting the penicillins, but are less effective for some of the other compounds. Fortunately, the penicillins are among the most commonly used drugs on farms [20, 21, 16], and there have been technological advances in recent years that enable detection of a wider range of antibiotic residues in large numbers of samples of food [1, 11]. Regulatory agencies use risk-based monitoring strategies to select screening tests and to determine sampling strategies for detection of drug residues in foods from animals [27].

Of all of the chemical residues that occur with some frequency in foods from animals, antibiotic residues are arguably the most preventable because these drugs must be deliberately administered to animals during production. Industry recognition of this coupled with increased awareness of the importance of this type of contamination to consumer confidence and international trade has led to concerted efforts to reduce residues. Several food animal producer groups have instituted on-farm quality assurance programs that are intended to reduce the risk of drug residues in their products. The pork quality assurance program and the 10-point dairy quality assurance programs are notable examples in the US [3, 7]. Among other things, these programs are designed to ensure that farmers use antibiotics in a safe and responsible manner which is unlikely to result in residues. These programs are in many respects analogous to hazard analysis - critical control point (HACCP) programs that are becoming prevalent in other sectors of the food industry.

Since human error, lack of knowledge and faulty treatment practices are so often associated with residue violations, formal education programs for farmers who are legally able to treat their own animals with antibiotics are useful. In Ontario, a livestock medicines course has been administered to approximately 1 500 farmers in the past two years, and has been shown to increase their understanding of the rationale for wise and safe use of antibiotic and other drugs in food animals [2]. Finally, although the move to HACCP has in some respects resulted in less reliance on end-product testing to assure food safety, the monitoring of milk, meat and dairy products by government still has a very important place in risk assessment (exposure assessment is largely based on these data), and in some cases to enforcement of legal limits on residue concentrations [6, 9, 11, 12, 13, 22].

Residues of chemical contaminants in foods are no longer of major public health concern, but they are important with respect to international trade and consumer confidence. Continued vigilance is required to ensure that hazardous residues do not contaminate our foods.

VI - REFERENCES

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ACKNOWLEDGEMENTS : Preparation of this paper was supported in part by the Ontario Ministry of Agriculture and Food.