NUTRITION Perspective

Nutrition Perspective is a series of practical resources for professionals on health issues of importance to Canadians. It is brought to you by the Registered Dietitians at the Beef Information Centre.

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Understanding Use of **Antibiotic** and **Hormonal** Substances in Beef Cattle

This issue of Nutrition Perspective addresses common questions and concerns that you or your clients may have about antibiotic and hormone use in cattle in Canada.

This brief overview will focus on:

- the regulatory system in place to protect our health;
- the use of antibiotics and hormonal substances in cattle; and
- some of the health related questions linked with antibiotic and hormonal substance use.

Veterinary Drug Regulation in Canada

The federal, provincial and municipal governments work together to implement the Canadian food inspection system to ensure that Canadians enjoy a safe and wholesome food supply. The regulation of veterinary drugs used in livestock production, specifically antibiotics and hormonal substances, is the responsibility of the following two federal government agencies:

- Health Canada (HC) sets the standards and policies for food safety and nutrition, outlined in the *Food and Drugs Act and Regulations.*
- The Canadian Food Inspection Agency (CFIA) enforces these standards and policies.[1,2]

Veterinary drug use in food animals is controlled by the *Food and Drugs Act and Regulations* which stipulates:

- The drugs permitted for use, must:[1,3]
  - be effective for their purpose
  - be safe for the animal, and
  - result in food products that are safe for human consumption;[41]
- The appropriate withdrawal period prior to slaughter;[3]
- The acceptable levels of residues in food of animal origin.[1,3]

The withdrawal period is identified on the label of each drug. It indicates the minimum length of time between the last drug treatment and slaughter, in order to reduce possible residues to levels that are safe for humans.[4,5]

Maximum Residue Limit

The Maximum Residue Limit (MRL) is the maximum amount of a drug residue that may remain in a food product at the time of human consumption.[6] Consumption of a food of animal origin that contains a drug residue level at, or below the MRL, is not considered a risk to humans. If the amount of drug residue in the food is higher than the MRL, the food is considered to be adulterated and not fit for human consumption.[5] Codex Alimentarius Commission (Codex) establishes MRLs required for international trade of drugs used in food animals.[2]

In This Issue

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Health Canada's Veterinary Drugs Directorate is the federal agency responsible for approving new drugs and setting MRLs in Canada.[5]

Testing for Drug Residues

Testing for drug residues is part of meat inspection carried out by the CFIA at federally registered meat plants under the *Meat Inspection Act and Regulations*.[3,6] Residue testing also takes place at the provincial level.

Canada's sampling and testing protocols, which are based on standards set by Codex, include three components:

1. Monitoring – random samples are obtained on an ongoing basis from apparently healthy animals. This provides information on the residue concentrations in predetermined populations.
2. Surveillance – additional samples are collected from animals that are considered suspect. The carcasses are held until results are determined.
3. Compliance – once identified as adulterated, the products are prohibited from entering the food supply. Producers are contacted and measures are taken to prevent re-occurrence of the problem.

Once samples are collected, they are sent to government laboratories for testing. In addition, suspect animals – those with signs of injection marks or chronic conditions such as arthritis – are given the Swab Test On Premises (STOP) to detect any antibiotic residues in kidney tissue.[5]

Maximum Residue Limits and Health Risks

To determine whether there is a health risk associated with exposure to a particular substance, such as an antibiotic or a hormonal substance, a risk assessment is conducted. Risk assessment involves determining the probability that an adverse health effect will occur in the individual or the population following exposure.

Risks are assessed through a thorough evaluation of the hazards, or toxicity of the substance, and the amount required to induce an adverse effect. This is then compared to the actual amount to which people are typically exposed over their entire lifetime through the food supply.

Toxicology tests determine if a substance is a potential hazard. Many substances can cause adverse effects at high levels but do not cause any adverse effects at much lower levels, typical of exposure through the food supply.[7]

Acceptable Daily Intake (ADI)

The risk that an adverse health effect will occur is a function of the hazard in a food and the extent of exposure to the hazard. The Acceptable Daily Intake (ADI) level is determined from toxicology studies to be the highest amount of a substance that can be consumed daily throughout a lifespan without causing adverse effects.[8] The MRLs for antibiotics or hormonal substances represent the exposure to those products. In simple scientific terms, risk can be expressed as a relationship between exposure and the ADI:

$$\text{Risk} = \frac{\text{Exposure (MRL of residue in meat x the amount of meat consumed)}}{\text{Acceptable Daily Intake}}$$

The lower the value is for exposure relative to the ADI, the smaller the risk. For antibiotics approved for use in Canada, the MRLs are set by Health Canada's Veterinary Drugs Directorate. These values are well below the ADI. For approved hormonal growth substances, the MRL is set at zero.

Monitoring

Positive tests for drug residues can occur when withdrawal periods are not followed or when drugs are not used according to label instructions. The Canadian Food Inspection Agency releases an annual report on the monitoring results for pesticides, agricultural chemicals, veterinary drugs and environmental contamination in products of animal origin, including beef. Each year from 1994 to 2001, between 99.9-100% of the beef samples tested were in compliance with respect to antibiotic residues and between 97.0 -100% with respect to hormonal substances. Random tests on imported meat and poultry products are also conducted.[9,10]

Antibiotic Use in the Cattle Industry

Antibiotic Use

Antibiotics are metabolites produced by microorganisms that inhibit other microorganisms. They are commonly used drugs designed to reduce the incidence of non-viral infectious disease. Antibiotics are used at both therapeutic and subtherapeutic levels in animals raised for human consumption. The purposes of antibiotic use include:

1. Therapeutically – for treatment of infections after diagnosis;
2. Prophylactically – for disease prevention, especially during times of stress (e.g., when calves leave their mothers and are transferred to feedlots); and

3. As growth promoters – to increase efficiency of feed use (such that nutrients are used for growth rather than to fight infection).[11] However, medically important antibiotics are not used as growth promoters in beef cattle production.[12]

To treat infection, levels of antibiotics are given to the animal in accordance with the instructions on the drug label.[11] Amounts higher than label dosages require a prescription from a veterinarian. Subtherapeutic levels of antibiotics may be given to animals through feed or water at dosages below those required to treat infection.

Antibiotic Resistance

Antibiotic resistance is the ability of certain bacteria to survive exposure to an antibiotic, which is normally able to destroy or limit the growth of the bacteria.[13] This can occur from exposure to the antibiotic or through the transfer of resistance genes.[14] Bacteria have the ability to adapt to their environment. The use of antibiotics may create an environment that favours one type of bacterium over another, allowing it to multiply. In addition, bacteria can adapt to their environment by genetic mutation – one or two mutations can allow the bacteria to become resistant to the antibiotic or they can acquire resistance genes from another organism.[15] These resistant strains survive and reproduce transferring resistance to future generations of bacteria.[14]

Antibiotic resistance can occur in a number of ways:

1. Naturally occurring phenomenon;[16]
2. Over-use and/or inappropriate use of antibiotics in human medicine;[14,16,17]
3. Use in agri-food industries to treat specific diseases or to prevent illness and/or to promote growth;[14,16,18,19]
4. Use of antibacterial cleaning products; e.g., community or household disinfectants or antiseptics;[14]
5. Use of cleaning and disinfection products in farm and veterinary practices.[14]

The use of antibiotics does not necessarily lead to the evolution of resistant bacteria.

Antibiotic resistance is a complex process.

For example, the bacterium *Streptococcus pyogenes* has never become resistant to penicillin even after 50 years of use.[16] Conversely, some bacteria are able to adapt to the presence of an antibiotic almost immediately. In 1940, when penicillin was introduced, *Staphylococcus aureus* resistance to penicillin was 1%, by 1946 it was 14% and currently about 90% of the bacterium isolates are resistant.[16] In addition, the occurrence of antibiotic resistance varies between countries.

In Canada, *Salmonella enterica* and *Campylobacter jejuni* are two bacteria that cause infections in humans primarily through consumption of contaminated food or water. Many of these infections are resistant to antibiotics. Although the cause of this resistance is unknown, antibiotic use in animals might be a factor.[15]

Since antibiotic residues in animals raised for human consumption are almost non-existent as determined by assessing the MRL, the concern is not the residues but rather the potential emergence of resistant pathogens. While it is plausible to link the use of antibiotics at subtherapeutic levels in the feed of food-producing animals to the transfer of resistant bacteria to humans, the evidence is incomplete, uncertain and highly controversial. This has led some scientists to conclude that a cause and effect relationship cannot be proven or disproven.[20] However, some organizations take a more conservative approach. A report of the World Health Organization indicates that there is sufficient evidence to recommend terminating the use of antimicrobials (antibiotics and other substances that destroy microbes) for growth promotion.[21] Part of the controversy is the lack of information, coordination and monitoring on antibiotic use and antibiotic resistance within and between countries.

In Canada, the Advisory Committee on Animal Uses of Antimicrobials and Impact on Resistance and Human Health recommends that antimicrobials used for growth promotion or feed efficiency be evaluated using sound risk analysis principles. It recommends the elimination of those not fulfilling the following criteria:

- "demonstrably effective,
- involving products rarely, if ever, used in human therapy, and
- not likely to impair the efficacy of any other prescribed antimicrobial for human infections through the development of resistant strains".[15]

In addition, the Committee is calling for a permanent national surveillance system for antimicrobial resistance.[15] Beef production will be impacted to a lesser degree than some other agricultural sectors, as medically important antibiotics are not used for growth promotion in beef cattle.[12]

Minimizing Antibiotic Use in Animals

Use of antibiotics in animals cannot be eliminated entirely since they are needed to treat diseased animals and, in some cases, to control the spread of infection to humans (who are in contact with animals). However, antibiotic use can be minimized. There are many organizations working with livestock producers and processors to reduce the use of antibiotics.

These include:

1. Canadian Cattlemen's Association has developed the Quality Starts Here® program that outlines best management practices for beef cattle producers.[22]
2. Canadian Veterinary Medical Association encourages veterinarians to follow the guidelines on the prudent or judicious use of antimicrobials and provides advice on the alternatives to antibiotics.[20,23]
3. Health Canada is involved in a number of initiatives including:

- Financial support to the Canadian Committee for Antimicrobial Resistance and the development of a national antimicrobial resistance surveillance system; and
- Participation on the CODEX Committee on Residues of Veterinary Drugs in Food.[14]

4. CFIA Chemical Residues: Residue Trace Back program investigates the source of the adulterant and offers a producer education component.

Cattle producers are encouraged to work with veterinarians to reduce the therapeutic use of antibiotics by preventing the occurrence of disease through immunization and/or control of the spread of disease by the quarantine of infected animals. Subtherapeutic use of antibiotics can be reduced by:

- optimizing the nutritional quality of the feed; and
- reducing stress so that natural immunity is enhanced through measures such as minimizing transport stress, providing adequate water, and proper housing.

Hormonal Substance Use in the Cattle Industry

The hormonal substances used are either natural sex steroids (e.g., estrogen, progesterone and testosterone) or their synthetic derivatives.[24] They are administered via implants in the ear of the animal or as feed additives.

Hormonal substances are used in livestock production to ensure that feed is used efficiently by the animal and nutrients are absorbed. Benefits include: [24,25,26]

- an increased rate of lean muscle development;
- improved carcass quality by decreasing fat deposits;
- increased efficiency of feed use so that there is more growth on less feed;
- reduced costs for cattle producers and less expensive beef for the consumer.

Steers (young castrated male animals) are given hormonal substances to replace the growth stimulating effect of testosterone that is lost as a result of castration.[24] Male animals are castrated to prevent dangerous behaviour and control bleeding. Heifers (female animals) are given hormonal substances to ensure a leaner product.[27]

Hormone Levels

The levels of hormones such as estrogen or estrogen-like compounds found in animal and plant foods vary tremendously depending on the food. The greatest level of hormones is from daily human production of hormones and from the use of oral contraceptives or hormone replacement therapy. Although hormones are present naturally in all animals, exposure from consumption of beef is minimal compared to other sources. Amounts are similar when beef comes from implanted or non-implanted cattle. In addition, estrogen, progesterone and testosterone are inactivated by the human gastrointestinal tract and the liver, resulting in very small amounts (less than 10%) being bioavailable after oral ingestion.[28]

Tables 1 and 2 compare the levels of naturally occurring hormones and external sources of hormones.

Table 1—Amounts of Endogenous Hormones

Total Daily Production	Estrogen (nanograms)*	Progesterone (nanograms)	Testosterone (nanograms)
Prepubescent girls	54,000	250,000	32,000
Prepubescent boys	41,600	150,000	65,000
Non-pregnant women	192,000 – 1,192,000	420,000 – 19,600,000	240,000
Men	136,000	410,000	6,400,000

Table 2—Amounts of Exogenous Hormones

	Estrogen (nanograms)	Progesterone (nanograms)
Oral Contraceptive (per pill) (low-dose ethinylestradiol with levonorgestrel) (e.g., Alesse™ is an example of the lowest levels)	20,000-50,000	100,000-500,000
Hormone replacement therapy (per pill) (conjugated equine estrogens with medroxyprogesterone acetate) (e.g., PremPlus™)	625,000	2,500,000
Beef from non-implanted steers 100 g	1.5	27
Beef from implanted steers 100 g	2.2	44
Milk, 250 mL	35.9	Not applicable
Cabbage, 100 g	2,381**	Not applicable
Wheat germ, 30 g	600**	Not applicable
Soybean oil, 15 mL	28,773**	Not applicable

* 1000 nanograms = 1 microgram (µg)
**nanograms of estrogen equivalent activity (i.e., in the form of phytoestrogens).
Note: Table 2 - Testosterone for beef from non-implanted steers (100 g) is 10 nanograms. The amount for implanted steers is not available. Testosterone is not applicable to the other items in Table 2. References for values in tables: 28, 29, 30, 31

Hormonal Substances and Health Risk

The two perceived health concerns regarding the use of hormonal substances in animals arise from whether these products possibly have a role in the etiology of cancer and in human development.

Cancer

The quantities of hormones found in a serving of meat are far below the level considered to be a risk to the development of cancer. Moreover, the World Health Organization noted that the use of natural hormone implants results in hormone levels that are indistinguishable from those in non-implanted animals and has, therefore, concluded that MRLs need not be established in animals implanted with natural hormones.[28] Similarly, while Health Canada has established MRLs for the synthetic hormones, these hormones are typically not found in beef samples monitored by the CFIA.[10]

Human Development

Another question that has arisen is whether hormone use in animals may alter the rates at which girls and boys mature. Trends have shown that puberty (for eg. may be characterized by a growth spurt or breast development in girls) may be starting earlier, however, age of menarche and completion of puberty have remained constant over the past 30 years.[32,33,34] The appearance of earlier onset may be a result of:

- lack of standardized definitions and assessment of early stages of puberty;[33,34]
- improved nutrition over the past 60-70 years;[35,36] and
- increase in the number of over weight and obese children.[32,36]

Current scientific evidence does not support the role of hormonal substance use in animals as a factor in pubescent maturation.

The contribution of estrogen, progesterone and testosterone from beef is miniscule compared to the quantities produced naturally in the body.

European Union Ban on Hormone Implanted Beef

In 1988 the European Community prohibited trade of meat and meat products obtained from animals treated with hormonal substances. After receiving science-based submissions opposing the ban, the World Trade Organization (WTO) confirmed that this practice does not constitute a health risk.[37]

Organic Beef

In order for beef to be labelled organic, it must meet the minimum conditions for the production, processing, packaging, and distribution of organic food products as outlined in the *National Standard for Organic Agriculture*, set out in *Canada's Guide to Food Labelling and Advertising*, and enforced by the Canadian Food Inspection Agency.[38,39] In addition, a producer may have their farm operation certified by an accredited certifying body to ensure the National Standard is being met. In Canada, there are approximately 45 certifying bodies.

The key differences between organic beef and non-organic beef are primarily in the way cattle are fed and in the use of veterinary drugs. In organic beef production, the cattle must:

- be completely segregated from conventionally managed farms;
- receive 100% of their feed from organic sources;
- be born and raised in an organic production unit, although up to 10% of the breeding livestock can be obtained from non-organic operations; and
- not be given growth or reproductive hormones; however, antibiotics can be used to treat sick animals and vaccines are permitted that target communicable diseases.[40]

Although hormonal substances are not given to cattle raised organically, all cattle produce hormones. Levels of naturally occurring hormones are similar in organic and non-organic beef.

Living conditions for both organic and conventional production are similar in that the cattle are allowed free movement as well as access to fresh air, natural daylight, fresh water and high quality feed. In organic production, the grazing pasture must be certified organic, which means no chemical fertilizers or pesticides are used. However, these products are rarely used on pastures in conventional production.

Regardless of production method, 94% of all beef – organic or non-organic – undergoes federal inspection. Provincial and municipal inspection programs are in place to inspect the remainder.

For more information on meat inspection, see Nutrition Perspective: **"Beef Up Food Safety from Gate to Plate"** *at* www.beefinfo.org (visit the Order Center).

Conclusion

The aim of the beef industry and the regulatory system in Canada is to provide a safe and wholesome product to consumers. Regulations on veterinary drug use in food animals and the drug-residue testing program ensure that the product in the grocery store is free of residues from antibiotics or synthetic hormones used in livestock.

Currently, there is no evidence that the use of antibiotics pose any health risk to consumers. However, new surveillance systems, both in Canada and worldwide, will assist in identifying specific practices that may contribute to antibiotic resistance. In addition, new programs and guidelines by the Canadian Cattlemen's Association, the Canadian Veterinary Medical Association, and the federal government will assist producers in minimizing antibiotic use in animals.

At present, there is no evidence linking the use of hormonal substances in cattle to a health risk in humans. The Canadian regulatory bodies as well as the World Trade Organization support this view. However, if consumers want to consume beef that has not been given hormonal substances, they have the choice of purchasing certified organic beef.

Regardless of the choice made, consumers can be assured that the beef purchased will be a safe product, providing essential nutrients to their diet.

Beef Information Centre

Questions about Beef?
Visit www.beefinfo.org or call
1-888-248-BEEF
Beef Information Centre has offices in North Vancouver, Calgary, Winnipeg, Mississauga, St. Laurent and Halifax.

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Understanding Hormone Use In Beef

What are hormonal substances?

"Hormonal substances" is a term used to describe sex hormones given to cattle. Health Canada has approved three natural hormones and three synthetically produced hormones for use in cattle in Canada.

Why are they used in the cattle industry?

Hormonal substances are used so that the animal uses its feed efficiently. The use of hormonal substances results in:

- Development of more lean meat with less fat deposited in the meat
- More growth using less feed
- Reduced cost for the cattle producer and less expensive beef for the consumer

Does hormone use affect the safety of beef?

The safety of hormone use has been reviewed by many experts and agencies, including Health Canada, the World Health Organization and the Food and Agriculture Organization of the United Nations. All have concluded that hormones can be used safely in beef production.

Research has shown that very high levels of hormones taken for a long time (such as those levels found in oral contraceptive pills or hormone replacement pills) may be a risk factor in some kinds of cancer. However, the levels found in food products, such as beef, are too low to be of risk to human health.

How do we know that the hormones are safe?

Health Canada, through the Food and Drug Act and Regulations, determines what hormonal substances can be used in animals and how these substances are to be used. In order for the hormone to be approved for use it must:

- Be effective for its purpose (do what it is suppose to do);
- Be safe for the animals;
- Result in food products that are safe for humans to eat.

Who makes sure that beef producers use the appropriate level of hormonal substances?

The Canadian Food Inspection Agency makes sure that beef producers follow the Food and Drug Act and Regulations. They do this by inspecting the meat and testing it for residues. In Canada, the level of synthetic hormones that can be left in beef is zero. A review of the data from this testing program shows a near perfect record, that is, no hormonal residues in the beef.

Are all cattle given hormonal substances?

No, each beef producer makes a business decision on the use of hormonal substances. This decision is based on many factors, including the cost/benefit of purchasing and administering the hormone. However, since cattle are bought and sold, there is only one way to ensure that a beef product has never received any hormonal substance. One must purchase beef, which has appropriate verification that it has been sourced from cattle that have been raised without the use of hormonal substances, such as certified organic beef.

Understanding Hormone Use In Beef

There is no such thing as hormone-free beef. Even beef raised organically will contain hormones. All animal products contain hormones because all animals produce hormones naturally. The hormone levels found in a sample of organic beef are similar to beef from animals given hormonal substances.

How much hormones are in beef?

Cattle, like humans, are mammals. All mammals have naturally occurring hormones. The level of hormones in beef from cattle given hormonal substances is no different that the level found in beef from cattle not given hormonal substances. Studies also show that there is more variation in hormone levels of animals of different sexes than between treated and untreated animals.

In addition, the level in a serving of beef is very low compared to other sources of hormones in our body.

Table 1—Hormones we produce naturally in our bodies

Total Daily Production	Estrogen (nanograms)	Progesterone (nanograms)	Testosterone (nanograms)
Prepubescent girls	54,000	250,000	32,000
Prepubescent boys	41,600	150,000	65,000
Non-pregnant women	192,000 – 1,192,000	420,000 – 19,600,000	240,000
Men	136,000	410,000	6,400,000

Table 2—Hormones we may consume in food

	Estrogen (nanograms)	Progesterone (nanograms)
Oral Contraceptive (per pill)	20,000-50,000	100,000-500,000
Hormone replacement therapy (per pill)	625,000	2,500,000
Beef from cattle not given hormonal growth promotants 100g	1.5	27
Beef from cattle given hormonal growth promotants 100g	2.2	44
Soybean oil, 15 mL	28,773**	Not applicable
Cabbage, 100 g	2,381**	Not applicable
Milk, 250 mL	35.9	Not applicable

***estrogen equivalent activity (i.e. in the form of phytoestrogens)*

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