Review Article Compte rendu

Antimicrobial therapy of selected diseases in turkeys, laying hens, and minor poultry species in Canada

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Abstract — This paper identifies common poultry diseases requiring antimicrobial therapy, antimicrobials deemed efficacious to treat these diseases, and antimicrobial resistance (AMR) in these commodity-pathogen combinations, and describes current residue issues and minor use minor species (MUMS) guidelines. Veterinarians with turkey/layer expertise and diagnosticians were surveyed to determine the bacterial and protozoal diseases diagnosed in the last 5 years. Avian pathogenic *Escherichia coli, Staphylococcus aureus,* and *Ornithobacterium rhinotracheale* were the 3 most frequently diagnosed pathogens of turkeys. In layers, *E. coli*-peritonitis, and *Clostridium perfringens/Eimeria* spp. infections were the most common diagnoses. A literature review identified 32 antimicrobials as efficacious and/or recommended for treating these diseases. Surveillance and monitoring indicate the presence of enteric resistant organisms from some of these avian species (including resistance to antimicrobials of very high importance to human medicine). This paper highlights the need for surveillance of pathogen frequency, antimicrobial use (AMU), and AMR particularly in turkeys.

Résumé — Thérapie antimicrobienne pour des maladies sélectionnées chez les dindons, les poules pondeuses et les espèces mineures de volaille au Canada. Cet article identifie les maladies communes de la volaille exigeant une thérapie antimicrobienne, les antimicrobiens jugés efficaces pour traiter ces maladies et l'antibiorésistance dans ces combinaisons denrée-pathogène et il décrit les problèmes actuels liés aux résidus et les lignes directrices relatives aux utilisations mineures et aux espèces mineures. On a effectué un sondage auprès des vétérinaires possédant de l'expertise avec les dindons et les poules pondeuses et des diagnosticiens afin de déterminer les maladies bactériennes et protozoaires diagnostiquées au cours des 5 dernières années. *Escherichia coli, Staphylococcus aureus* et *Ornithobacterium rhinotracheale* aviaires pathogéniques étaient les trois organismes pathogènes les plus fréquemment diagnostiqués chez les dindons. Chez les poules pondeuses, les infections par *E. coli*-péritonite et *Clostridium perfringens/Eimeria* spp. étaient les diagnostics les plus fréquents. Un examen de la littérature a identifié 32 antimicrobiens comme étant efficaces et/ou recommandés pour traiter ces maladies. La surveillance et le suivi indiquent la présence d'organismes entériques résistants provenant de ces espèces aviaires (incluant la résistance aux antimicrobiens de très grande importance en médecine humaine). Cet article souligne le besoin de surveillance de la fréquence des pathogènes, de l'administration des antimicrobiens et de l'antibiorésistance, particulièrement chez les dindons.

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Introduction

Bacterial and protozoal diseases are continually diagnosed and new diseases have emerged in Canadian poultry, but there is a lack of newer efficacious antimicrobials to treat these diseases. Similarly in the United States (US), the lack of new antimicrobials has been recognized as the most important turkey health issue (1). Further, antimicrobial resistance (AMR) concerns arising in public health (2) are putting pressure on veterinarians and poultry producers to ensure antimicrobials are used prudently, from both animal health and food safety perspectives. Thus, it is important to understand why and how poultry producers are using antimicrobials. This can assist understanding

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the main drivers for use and whether these antimicrobials are the best therapeutic options given potential resistance in the animal pathogens they are intended for, and potential adverse effects on human health.

Turkey and chicken egg layers are important poultry species grown in Canada for meat and table eggs (3), respectively. Other species of poultry (e.g., ducks, geese, and game birds such as pheasants and quails) are raised for meat production in smaller volumes (4). As with chickens, turkeys carry antimicrobial resistant bacteria (5,6) to which humans can be exposed when consuming retail meat. Preliminary surveillance findings also indicate that minor poultry meats are carrying resistant bacteria (7).

Avian pathogenic *Escherichia coli* (APEC) and *Staphylococcus* spp. affect most poultry species of all ages (8,9). Historically they are the most frequently diagnosed bacterial diseases of turkey flocks in Canada (10–12). These diseases plus infections due to *Bordetella avium, Pasteurella multocida, Erysipelothrix rhusiopathiae,* and *Clostridium perfringens* have been continually diagnosed (10–14). *Ornithobacterium rhinotracheale* (ORT) infection is a relatively new disease in Canada; first diagnosed in 1997 in Quebec (15) and in 1998 in Ontario (16). Cellulitis, associated with *Clostridium septicum* and *C. perfringens* Type A, is an economically significant emerging disease of turkeys in the US (1,17–18); cellulitis lesions were the most frequent cause of turkey condemnation in Canadian processing plants in 2011 (19).

In layers, certain APEC strains (20) have been associated with sporadic egg yolk peritonitis (EYP), salpingitis, and salpingoperitonitis (8) leading to increased mortality (21). Spirochaetosis, an enteric disease of older laying birds (> 40 wk) (22), has been reported in Ontario flocks (23) and in the US (24).

The aim of prudent antimicrobial use (AMU) in veterinary medicine is to maximize the therapeutic efficacy of available antimicrobials and to reduce the animal/human health impact of usage. Prudent use may include valid veterinarian-client-patient relationship/client education, proper diagnosis of disease, and proper drug dosage/administration (25). These prudent AMU practices are similar to antimicrobial stewardship approaches described in human medicine (i.e., appropriate drug selection and optimizing dose and duration of therapy to reduce human health impact) (26). In Canada, the Canadian Veterinary Medical Association has produced prudent use guidelines (CVMA-PUG) which list antimicrobial options for treating common pathogens of turkeys and layers and include antimicrobials that are for label and off-label or extra-label drug use (ELDU) (25). Also, the Compendium of Medicating Ingredient Brochure (CMIB) produced by the Canadian Food Inspection Agency (CFIA) provides antimicrobial options for administration via feed, for treating commonly recognized disease syndromes such as chronic respiratory disease (CRD), non-specific enteritis, and synovitis (27). The CMIB emphasizes observance of residue withdrawal periods and acceptable drug compatibilities for approved in-feed antimicrobials (27). It does not include feeds prepared according to veterinary prescription/ELDU.

The Veterinary Drugs Directorate (VDD) of Health Canada approves and authorizes the sale of antimicrobials for use in animals in Canada and has established an ELDU policy (28), whereas provincial authorities determine how antimicrobials are used in animal production in their jurisdictions (e.g., over-the-counter sales, prescription requirements) (29).

Often it is not financially practical for a drug manufacturer to apply for a label claim for an antimicrobial that will be used in minor species or for treating minor diseases in major species. A minor use minor species (MUMS) policy/regulation has been developed in other countries to address this concern (30–32). A MUMS guideline is currently unavailable in Canada but has been prioritized by the VDD (33,34). Minor species include all animals other than one of the major species (i.e., cattle, pigs, turkeys, chickens, horses, dogs, and cats), whereas minor use, involves use of antimicrobials or other products in major species for diseases that occur infrequently or are detected in clusters of animals in limited geographic locations (30). Ducks, geese, and game birds are considered minor species.

This paper focuses on turkeys, layers, and minor poultry species. There is currently no national surveillance of antimicrobial use in these avian species or across pathogens or commensal bacteria isolated from these species. There is, however, national retail AMR surveillance of *Salmonella* and *E. coli* from ground turkey (35) and some provincial AMR activities for pathogens of avian species (36). In the absence of these data, the objectives of this study were to i) identify common diseases in Canada requiring antimicrobial therapy, ii) summarize the efficacy of antimicrobials based on *in-vitro* and *in-vivo* studies, and iii) provide guidance for antimicrobial therapy, including noting current Canadian approval status and potential food safety risks, such as residues and AMR, arising from the use of certain antimicrobials. This paper highlights the need for surveillance of pathogen frequency, AMU, and AMR particularly in turkeys, and serves as a starting point for the development of MUMS guidance.

Materials and methods

Poultry diseases diagnosed in Canada

In the absence of a national surveillance program for clinically relevant bacterial and protozoal diseases, a list of poultry diseases was created from publicly available Canadian laboratory reports, peer-reviewed publications and conference proceedings. The list formed the basis of a short survey (administered in English) sent electronically in the fall of 2012 to 10 veterinary practitioners with turkey and/or layer expertise, diagnosticians, and provincial poultry extension veterinarians. The survey aimed to determine the frequency of diagnosis and to identify diseases that were not in the original disease list. The survey was divided into frequency of detection for each disease during the last 5 y, and comment about the disease (e.g., lesions found, trends of occurrence). The frequency of detection was categorized and scored as follows: frequent (score = 3, if 3 or more cases were diagnosed per year), occasional (score = 2, if at least 2 cases were diagnosed per year), rare/sporadic (score = 1, if there was 1 case diagnosed per year or every other year), and not diagnosed (score = 0). Score averages were calculated and ranked as described in a similar US turkey health survey (1).

Table 1. Bacterial and protozoal diseases affecting turkey, layers, and minor poultry in Canada, based on a survey of poultry veterinarians, diagnosticians, extension veterinarians ($n = 9$)

Poultry host	Common disease manifestations	Primary etiologic agent	Score[a]	Rank
Turkeys	Colibacillosis (yolk sac infections/septicemia, airsacculitis, arthritis)	Avian pathogenic *E. coli*	2.8	1
	Staphylococcal infections (arthritis, septicemia, pneumonia, pododermatitis)	*Staphylococcus* spp.	2.3	2
	ORT infections	*Ornithobacterium rhinotracheale*	1.8	3
	Cellulitis	*Clostridium septicum/C. perfringens* Type A	1.5	4
	Coccidiosis	*Eimeria* spp.	1.4	5
	Necrotic enteritis[b]	*Clostridium perfringens*	1.2	6
	Erysipelas	*Erysipelothrix rhusiopathiae*	1.2	7
	Fowl cholera	*Pasteurella multocida*	1.0	7
	Bordetellosis	*Bordetella avium*	1.0	7
	Histomoniasis	*Histomonas meleagridis*	0.7	8
	Arizonosis	*Salmonella* Arizonae	0.7	8
	Mycoplasmosis (hatchability issues)	*Mycoplasma iowae*	0.5	9
	Mycoplasmosis (airsacculitis, abnormal development of the metatarsus)	*Mycoplasma meleagridis*	0.5	9
	Mycoplasmosis (synovitis)	*Mycoplasma synoviae*	0.2	10
	Enterococcosis/Vertebral Canal Stenosis/Osteomyelitis	*Enterococcus cecorum*	N/A	N/A
	Streptococcosis	*Streptococcus* spp.	N/A	N/A
Layers	Colibacillosis (mainly peritonitis, but septicemia, airsacculitis, pneumonia, and arthritis were also diagnosed)	Avian pathogenic *E. coli*	2.7	1
	Necrotic enteritis[b]	*Clostridium perfringens*	2.0	2
	Coccidiosis	*Eimeria* spp.	2.0	2
	Spirochaetosis	*Brachyspira*	1.1	3
	Mycoplasmosis (synovitis)	*Mycoplasma synoviae*	0.7	4
	Staphylococcal diseases	*Staphylococcus* spp.	0.5	5
Minor poultry				
Ducks	Riemerellosis	*Riemerella anatipestifer*	N/A	N/A
	Fowl cholera	*Pasteurella multocida*	N/A	N/A
Geese	Erysipelas	*Erysipelothrix rhusiopathiae*	N/A	N/A
Pigeon	Salmonellosis	*Salmonella* Typhimurium	N/A	N/A
Black Silkies	ORT infections	*Ornithobacterium rhinotracheale*	N/A	N/A
Partridge	Mycoplasmosis	*Mycoplasma gallisepticum*	N/A	N/A

N/A—not scored and ranked; not included in the survey list of diseases but were identified by veterinarian/diagnosticians.
[a] Diseases were scored according to observed occurrence (3 = ≥ 3 cases/year diagnosed, 2 = 2 cases/year diagnosed, 1 = 1 case/ year, 0 = not diagnosed) and ranked based on average scores.
[b] Frequently diagnosed concurrently with coccidiosis.

Efficacy studies

A literature search of *in-vivo* and *in-vitro* efficacy studies in 3 online databases, namely, PubMed, CAB Direct, and Scopus. The search was conducted in 2011–2012, using a specific search string, as previously described (37) [e.g., "*Bordetella* (or *Ornithobacterium*) and turkeys (or layer or ducks or geese or quail) and antimicrobial (or antibiotics or therapy or prevention or control)"]. Conference proceedings were also searched for available data on AMU. There was no exclusion for year of study.

Review of availability of antimicrobials for use in turkeys and layers

Information regarding the availability of antimicrobials for use in turkeys and other poultry in Canada was gathered from the Compendium of Veterinary Products (CVP) (38). The CMIB and the CVMA-PUG were consulted if the antimicrobials were included in the list of AMU options for the primary pathogen/condition. Antimicrobials were grouped according to their importance to human medicine, using the categorization system of Health Canada's VDD as follows: Category I — Very High Importance; Category II — High Importance; Category III — Medium Importance, and Category IV — Low Importance. Relevant label warnings/cautions by manufacturers were also noted.

Review of AMU in minor poultry — MUMS guidelines

Minor use minor species documents from the US, Australia, and Europe were consulted.

Current status of AMR and residue violations as indicators of food safety risk

Surveillance reports (36,39), peer-reviewed publications, and conference proceedings were accessed to determine the most current AMR profiles. The most recent CFIA's National Chemical Residue Monitoring Program (NCRMP) was consulted to assess residue violations (40).

Results

Survey of diseases

The survey response rate was 90% (9/10); one response was provided by 1 to 2 individuals in the same practice/laboratory. Table 1 summarizes average response scores and ranking of diagnosed bacterial/protozoal diseases. For turkeys, *E. coli*-associated diseases (i.e., yolksac infections, airsacullitis) ranked first. *Staphylococcus* spp.-associated diseases ranked second. Other diseases/conditions occasionally diagnosed (ranked 3rd to 7th) were ORT infection, cellulitis, necrotic enteritis, coccidiosis, erysipelas, fowl cholera, and bordetellosis. Sporadically occurring diseases (ranked 8th to 10th) included histomoniasis, arizonosis, and mycoplasmoses [i.e., detected by serology, real-time-polymerase chain reaction (RT-PCR)]. Histomoniasis was more frequently diagnosed in non-commercial/small flocks. Other pathogens identified in the survey (reported once) included *Enterococcus cecorum* and *Streptococcus* spp.

In layers, *E. coli*-associated egg yolk peritonitis (EYP) ranked first. Necrotic enteritis ranked 2nd, and was often diagnosed concurrently with coccidiosis. Veterinarians reported that NE-coccidiosis was relatively common in layer facilities with stacked-cage systems and affected birds were observed to be in cages located underneath manure belts with spots of wet manure. More recently, NE-coccidiosis was observed less frequently with the increasing use of a coccidiosis vaccine. Spirochaetosis (ranked 3rd), mycoplasmosis (ranked 4th), and staphylococcal infections (ranked 5th) were reported. Testing was not routinely done for *Brachyspira* spp., but was commonly detected in flocks with history of increased egg downgrades. *Mycoplasma* serological reactors were commonly detected in birds originating from multi-age facilities.

The laboratories diagnosed bacterial diseases of minor poultry/game birds at least once or twice in the last 5 years and included *R. anatipestifer, P. multocida, E. rhusiopathiae,* ORT*,* and *Mycoplasma* spp. Other diseases reported in the literature included: *S.* Typhimurium in racing pigeons in 2011 (41), *Clostridium colinum* (ulcerative enteritis) in quails in 1990 (42), *Chlamydophila psittaci* in breeder pigeons in Manitoba in 2008 (43) and ostriches in Alberta in 1998 (44), and *Mycobacterium avium* in rheas in Ontario in 1991 (45).

Efficacy studies

Over-all, 68 English articles from 1957 to 2010 were reviewed. Thirty-two antimicrobials were identified in the efficacy studies. These were grouped according to their category of human health importance and approval status in Canada (Table 2). Efficacious antimicrobials were identified for most of the common bacterial diseases in turkeys, layers, and ducks. One to four relevant studies were found for each antimicrobial-pathogen combination.

Review of antimicrobial use in major poultry species (turkeys and layers)

Turkeys

Table 2 included AMU options for the therapy of the 6 diseases listed in the CVMA-PUG including infections caused by APEC*, Staphylococcus* spp., *B. avium, E. rhusiopathiae, Mycoplasma* spp., and *Eimeria* spp., diseases included in the CMIB (i.e., CRD/synovitis/non-specific enteritis), and ORT.

At least 10 of the 32 antimicrobial listed in Table 2 are labelled for use in turkeys for oral administration (e.g., erythromycin, neomycin, penicillin-G, the tetracyclines and tetracycline-neomycin combinations, sulfamethazine, sulfaquinoxaline, amprolium). The label for at least 8 antimicrobials included a requirement for veterinary prescription. Other antimicrobials involve ELDU for any of the following reasons: species (e.g., broiler use only: amoxicillin, swine use only: tiamulin/tilmicosin), route of administration (e.g., subcutaneous route only: ceftiofur/gentamicin), growth or production phase (e.g., not to be used in poults $>$ 1 day for ceftiofur, not to be used in laying/breeding hens: various), and target pathogen/disease conditions (e.g., NE in broilers only: lincomycin, colibacillosis in broilers only: amoxicillin/florfenicol). To minimize AMR development, manufacturers included warnings and recommendations in the label for veterinarians to consider "previous clinical experience supported by pathogen culture and susceptibility testing" with the use of VDD's Category I (e.g., ceftiofur and enrofloxacin), VDD's Category II (e.g, amoxicillin, gentamicin, tilmicosin, tylosin), and VDD's Category III (e.g., florfenicol) antimicrobials (38).

Other diseases included in Table 2 were not included in the current versions of the CVMA-PUG/CMIB but Canadian/US information was available from the literature. For ORT treatment, a therapeutic regime consisting of neomycin-chlortetracycline in water concurrent with oxytetracycline in feed, followed by penicillin in water was found effective (16). The CMIB has not listed options for NE but included chlor-/oxytetracycline for the therapy of non-specific enteritis. Antimicrobials labelled for NE therapy in broilers, such as bacitracin and lincomycin are deemed ELDU if used to treat NE in turkeys. For cellulitis, AMU information was unavailable, but in the US, lincomycin, erythromycin, and chlortetracycline were suggested and a treatment regimen consisting of penicillin in water followed by chlortetracycline in feed was reported (18). For arizonosis therapy, spectinomycin and gentamicin are licensed in the US (46); the latter is also labelled for arizonosis treatment in Canada. Ormethoprim-sulfadimethoxine has been used historically in the US (47). Nitarsone (4-nitrophenylarsonic acid) is the only antimicrobial approved for use in turkey flocks in Canada for treating blackhead *(Histomonas meleagridis).*

Layers

Antimicrobial options for the therapy of *E. coli*-peritonitis, mycoplasmosis, and spirochaetosis in layers are listed in Table 2. The CVMA-PUG listed oxytetracycline, tetracycline, and tylosin for the treatment of *E. coli*-peritonitis and chlortetracycline and tylosin for mycoplasmosis therapy. However, the use of tetracycline and tylosin in layers is ELDU as egg Maximum Residue Limits (MRL's) are unavailable.

Information for the therapy of NE and spirochaetosis was not found in the CVMA-PUG and CMIB, but AMU experiences in other countries were available. Antimicrobials with anti-clostridial activity (e.g., bacitracin, penicillin, tylosin, ionophores) are largely labelled for use in broilers; these are ELDU in laying hens. For spirochaetosis therapy, tiamulin (ELDU) and lincomycin (ELDU) proved efficacious. Bacitracin was suggested but efficacy was found to be species-specific; it was

Table 2. Summary of literature review of antimicrobials used to treat selected bacterial and protozoal pathogens in turkeys, layers, and ducks and Canadian use guidelines

	Antimicrobial[a]	Target pathogen or condition	Number of studies[b]	Avian species	Identified in Canadian use guideline	Comments/cautions/current warning by manufacturer
I[c]	Ceftiofur[d]	*E. coli*	2	Turkeys	CVMA-PUG[e]	Rx. Label use: cattle, horses, swine, lambs, and dogs. ELDU if used in turkeys or any poultry. *In-ovo* administration is ELDU. "*The extra-label drug use of Excenel is not recommended.*"
		E. rhusiopathiae	1	Turkeys	NL	
		O. rhinotracheale	1	Turkeys	NL	
		P. multocida	1	Turkeys	NL	
		Staphylococcus spp.	1	Turkeys	NL	
		R. anatipestifer	1	Ducks	NL	
	Enrofloxacin	*E. coli*	2	Turkeys	NL	Rx. Label use: cattle and swine. ELDU if used in any poultry including broiler chickens/any route of administration. "*Do not use in an extra-label manner in cattle, swine or in any other species.*"
		E. rhusiopathiae	2	Turkeys	NL	
		O. rhinotracheale	3	Turkeys	NL	
		P. multocida	1	Turkeys	NL	
		Staphylococcus spp.	1	Turkeys	NL	
		R. anatipestifer	1	Ducks	NL	
II	Amoxicillin	*E. coli*	1	Turkeys	NL	Rx. Label use: *E. coli* and *Salmonella* in broilers, swine. ELDU if used in turkeys.
		O. rhinotracheale	2	Turkeys	NL	
	Ampicillin	*B. avium*	1	Turkeys	NL	Rx. Label use: swine. ELDU if used in any poultry/any route of administration.
		E. coli	2	Turkeys	NL	
		E. rhusiopathiae	2	Turkeys	NL	
		O. rhinotracheale	1	Turkeys	NL	
		P. multocida	1	Turkeys	NL	
		Brachyspira spp.	1	Layers	NL	
		R. anatipestifer	1	Ducks	NL	
	Apramycin	*E. coli*	1	Turkeys	NL	Label use: swine, poultry use is ELDU.
	Erythromycin	*E. coli*	1	Turkeys	CVMA-PUG	Label use: multiple species, respiratory diseases and complex syndromes/synovitis in turkeys, ELDU if used in ducks/minor poultry. "*Do not use in birds laying eggs for food purposes.*"
		E. rhusiopathiae	ND/p	Turkeys	CVMA-PUG	
		O. rhinotracheale	1	Turkeys	NL	
		Staphylococcus spp.	(1)	Turkeys	CVMA-PUG	
		R. anatipestifer	1	Ducks	NL	
	Gentamicin	*E. coli*	2	Turkeys	CVMA-PUG	Rx. Label use: multiple food animal species, SC administration in poults to treat *S.* Arizonae/*in-ovo* route and use in minor poultry is ELDU. "*Do not use in laying birds.*"
		B. avium	1	Turkeys	NL	
		S. arizonae	1	Turkeys	NL	
		P. multocida	1	Turkeys	NL	
		Staphylococcus spp.	(1)	Turkeys	NL	
	Lincomycin	*E. rhusiopathiae*	ND/p	Turkeys	CVMA-PUG	Label use: broilers, swine. ELDU if used in turkeys and minor poultry. Feed premixes are largely for use in swine.
		Brachyspira spp.	2	Layers	NL	
		R. anatipestifer	1	Ducks	NL	
	Lincomycin-spectinomycin	*E. coli*	(2)	Turkeys	CVMA-PUG	Label use: broilers and swine; ELDU if used in turkeys and minor poultry.
		R. anatipestifer	1	Ducks	NL	
	Neomycin	*E. coli*	2 (1)	Turkeys	NL	Label use: multiple species except layers.
	Penicillin-G	*E. rhusiopathiae*	2	Turkeys	CVMA-PUG	Label use: *E. rhusiopathiae* and other susceptible organisms. ELDU if used in minor poultry. "*Do not use in birds producing eggs for human consumption.*"
		O. rhinotracheale	1	Turkeys	NL	
		P. multocida	1	Turkeys	CVMA-PUG	
		Staphylococcus spp.	(1)	Turkeys	CVMA-PUG	
		R. anatipestifer	1	Ducks	NL	
	Penicillin-Streptomycin	*R. anatipestifer*	1	Ducks	NL	Label use: various species. ELDU if used in ducks/layers.
	Ormethoprim-sulfadimethoxine	*B. avium*	1	Turkeys	CVMA-PUG	Rx. Label use: *Aeromonas salmonicida* in salmonids. ELDU if used in any poultry.
		E. coli	1	Turkeys	CVMA-PUG	
		P. multocida	1	Turkeys	CVMA-PUG	
		Staphylococcus spp.	ND/p	Turkeys	CVMA-PUG	
		R. anatipestifer	1	Ducks	NL	
	Tiamulin	*Brachyspira* spp.	4	Layers	NL	Label use: swine. ELDU if used in any poultry. "*Do not feed to animals other than swine.*"
	Tilmicosin	*O. rhinotracheale*	1	Turkeys	NL	Label use: swine/feedlot beef. ELDU if used in any poultry. "*For use in swine or feedlot cattle feeds only.*"
		P. multocida	1	Turkeys	CVMA-PUG	

Table 2. Summary of literature review of antimicrobials used to treat selected bacterial and protozoal pathogens in turkeys, layers, and ducks and Canadian use guidelines *(continued)*

	Antimicrobial[a]	Target pathogen or condition	Number of studies[b]	Avian species	Identified in Canadian use guideline	Comments/cautions/current warning by manufacturer
	Trimethoprim-sulfadiazine	*B. avium*	1	Turkeys	CVMA-PUG	Rx. Label use: *Vibrio anguillarium* in salmon and multisystemic lesions in horses. ELDU if used in any poultry.
		E. coli	1	Turkeys	CVMA-PUG	
		Staphylococcus spp.	1	Turkeys	CVMA-PUG	
		P. multocida	1	Turkeys	CVMA-PUG	
	Tylosin	*Brachyspira* spp.	1	Layers	NL	Label use: swine, broilers and turkeys (infectious sinusitis). ELDU if used in layers/minor poultry. "*Do not use in laying hens.*"
		E. coli — peritonitis	1	Layers	CVMA-PUG	
		Mycoplasma spp.	1	Layers	CVMA-PUG	
		R. anatipestifer	1	Ducks	NL	
	Tylvalosin	*O. rhinotracheale*	(1)	Turkeys	NL	Label use: swine. ELDU if used in poultry.
III	Bacitracin, Zn	*Brachyspira* spp.	3	Layers	NL	Label use: swine, broilers and turkeys. ELDU if used in layers.
	Chlortetracycline	*E. coli*	(1)	Turkeys	CVMA-PUG	Label use: multiple species (including layers)/multiple pathogens. ELDU if used more than the approved dosage of 110 ppm in feed.
		B. avium	ND/p	Turkeys	CVMA-PUG	
		E. rhusiopathiae	1	Turkeys	NL	
		Mycoplasma spp.	1	Turkeys	CVMA-PUG	
		P. multocida	3	Turkeys	CVMA-PUG	
		Staphylococcus spp.	(1)	Turkeys	CVMA-PUG	
		CRD/enteritis synovitis/sinusitis	(3)	Turkeys	CMIB	
		Mycoplasma spp.	1	Layers	CVMA-PUG	
	Florfenicol	*E. coli*	2	Turkeys	NL	Rx. Label use: (for water soluble formula): broilers, swine. ELDU if used in other poultry. Feed medication is ELDU for any poultry.
		E. rhusiopathiae	2	Turkeys	NL	
		O. rhinotracheale	2	Turkeys	NL	
		P. multocida	1	Turkeys	CVMA-PUG	
		R. anatipestifer	1	Ducks	NL	
	Neomycin-oxytetracycline[f]	*R. anatipestifer*	1	Ducks	NL	Label use: multiple species/pathogens. ELDU in ducks/minor poultry and layers.
	Neomycin-tetracycline[f]	*O. rhinotracheale*	1	Turkeys	NL	Label use: multiple species/pathogens. ELDU in minor species/layers.
	Novobiocin	*P. multocida*	2	Turkeys	NL	Previously used to treat Staphylococcal synovitis in turkeys/currently unavailable.
		R. anatipestifer	1	Ducks	NL	
	Oxytetracycline	*E. coli*	(1)	Turkeys	CVMA-PUG	Label use: multiple species (including layers)/multiple pathogens. ELDU if used in minor poultry.
		B. avium	3	Turkeys	CVMA-PUG	
		E. rhusiopathiae	1	Turkeys	CVMA-PUG	
		Mycoplasma spp.	1	Turkeys	CVMA-PUG	
		O. rhinotracheale	1	Turkeys	NL	
		P. multocida	1	Turkeys	CVMA-PUG	
		Staphylococcus spp.	ND/p	Turkeys	CVMA-PUG	
		CRD/enteritis/synovitis/sinusitis	(4)	Turkeys	CMIB	
		E. coli — peritonitis	1	Layers	CVMA-PUG	
		R. anatipestifer	1	Ducks	NL	
	Spectinomycin	*E. coli*	2	Turkeys	NL	Label use: swine < 4 weeks/6.8 kg. ELDU if used in any poultry.
		R. anatipestifer	1	Ducks	NL	
	Sulfadimethoxine	*E. coli*	1	Turkeys	NL	Label use: dogs and cats. ELDU if used in any poultry.
		Eimeria spp.	1	Turkeys	NL	
		P. multocida	2	Turkeys	NL	
	Sulfamethazine	*E. coli*	1	Turkeys	CVMA-PUG	Label use: turkey coccidiosis and various respiratory diseases, duck *Riemerella* and *P. multocida* infections. ELDU in layers.
		Eimeria spp.	1	Turkeys	CVMA-PUG	
	Sulfaquinoxaline	*E. coli*	(1)	Turkeys	CVMA-PUG	Label use: turkey coccidiosis/fowl cholera and fowl typhoid. ELDU for other turkey pathogens, use in minor poultry and layers.
		R. anatipestifer	1	Ducks	NL	

Table 2. Summary of literature review of antimicrobials used to treat selected bacterial and protozoal pathogens in turkeys, layers, and ducks and Canadian use guidelines *(continued)*

	Antimicrobial[a]	Target pathogen or condition	Number of studies[b]	Avian species	Identified in Canadian use guideline	Comments/cautions/current warning by manufacturer
	Tetracycline	*E. coli*	1	Turkeys	CVMA-PUG	Label use: multiple species/multiple pathogens. Not to be used in layers.
		B. avium	1	Turkeys	CVMA-PUG	
		P. multocida	1	Turkeys	CVMA-PUG	
		Staphylococcus spp.	1	Turkeys	CVMA-PUG	
		Brachyspira spp.	2	Layers	NL	
		E. coli — peritonitis	1	Layers	CVMA-PUG	
N/A	Amprolium	*Eimeria* spp.	1	Turkeys	CVMA-PUG CMIB	Label use: broiler/turkey coccidiosis. ELDU in minor poultry/layers.

Rx — prescription required, ELDU — Extra-label Drug Use, SC — Subcutaneous route, CVMA-PUG — Canadian Veterinary Medical Association — Prudent Use Guidelines, CMIB — Compendium of Medicating Ingredient Brochures, NL — not listed in Canadian antimicrobial use guidelines, ND/p — no data for poultry was found, CRD — Chronic Respiratory Diseases, number in parenthesis broiler data only. N/A — Not applicable (importance to human health not yet determined).

[a] Cited by various authors and available in Canada regardless of their common pattern of use/approval status; some label information may have been updated since the time of writing (38). Full reference list is available from the corresponding author.

[b] Total number of *in-vitro* susceptibility testing and/or *in-vivo* efficacy/pharmacokinetic studies identified per pathogen-antimicrobial combination.

[c] Roman numeral I to III indicate the ranking of antimicrobials based on importance in human medicine as outlined by the Veterinary Drugs Directorate (VDD), Health Canada (http://www.hc-sc.gc.ca/dhp-mps/consultation/vet/consultations/amr_ram_hum-med-rev-eng.php).

[d] Beginning December 1, 2012, the approved indication for use in day-old turkey poults was removed from the product label (Source: Health Canada Drug Database http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php).

[e] CVMA-PUG recommends use only in recurrent omphalitis problems related to a breeder flock or in very hot weather and poor shell quality.

[f] Aminoglycosides generally belong to Category II, however, neomycin is essentially used in humans for topical products and for this reason, the VDD recommends that Category III is the most appropriate classification for this combination.

effective against *B. intermedia* infections (48) but not effective against *B. pilosicoli* infections (49,50). Re-colonization has also been reported in flocks previously treated with bacitracin and tetracyclines (24).

Review of antimicrobial use in minor poultry species and MUMS practices

Sixteen antimicrobials were found to be efficacious against *R. anatipestifer*; 1 antimicrobial, sulfamethazine, is labelled for the treatment of riemerellosis in ducks in Canada. Other antimicrobials historically used for the therapy of diseases in minor poultry in Canada included oxytetracycline for the treatment of ulcerative enteritis caused by *C. colinum* in pigeons (42), chlamydophilosis in pigeons (43) and ostriches (44), and amoxicillin for the treatment of salmonellosis in pigeons (41). In the US, some common antimicrobials used to treat similar diseases in chickens and turkeys have MUMS designations including bacitracin (for the therapy of *Clostridum colinum* in quails) and chlortetracycline (for the therapy of *C. psittaci* in ducks). Coccidiostats (VDD Category IV) that have MUMS designation in the US include lasalocid (against *Eimeria legionensis*) and ormethoprim-sulfadimethoxine (against *E. kofoldi* and *E. legionensis*) for use in chukar partridges, amprolium (against *E. cochici, E. legionensis,* and *E. phasiani)* for use in pheasants, and monensin and salinomycin (against *E. dispersa* and *E. lettyae)* for use in quails (51).

Minor use minor species guidelines and policies are available in some countries. The MUMS Act in the US allows pharmaceutical industries to extend approved drug indications such as species and reasons for use without the lengthy and costly approval process of routine drug submissions. This Act, effective in 2004, aimed to address the severe shortage of approved new animal drugs for MUMS (30). The National Research Support Project 7 (NSRP-7), a multi-discipline/multi-stakeholder collaborative program was subsequently formed. One of the projects arising from NSRP-7 was the Minor Use Animal Drug Program (MUADP), a program collaboration involving the Food Animal Residue and Depletion Program (FARAD) and the College of Veterinary Medicine, University of Florida, US (http://www.nrsp-7.org/mumsrx/) (51). The MUADP lists approved antimicrobials for the therapy of bacterial/protozoal diseases of minor poultry including ducks, pheasant, partridges, and ratites. Similar policy/guidelines are currently implemented in Europe (32) and Australia (31).

In the absence of MUMS guidelines and antimicrobial options, poultry practitioners in Canada manage diseases in minor species with regard to ELDU practices, previous experience in treating minor species, and comparisons to treatments in related major species. The Canadian Association of Poultry Veterinarians Web site (www.capv-acva.ca/), in consultation with the Canadian Global Food Animal Residue Avoidance Databank (CgFARAD) provides an AMU Web resource for licensed veterinarians which is updated annually (52).

Review of Canadian foodborne hazards monitoring activities

AMR

Table 3 summarizes the most recent AMR findings from various surveillance and monitoring programs available in Canada (36,39). Of importance is the current level of ceftiofur resistance among retail *Salmonella* isolates (i.e., 29%, 9/31 in 2011) (35). This level is higher compared to 2 earlier research studies: 14% (14/102 isolates) in 2003–2004 in Ontario (5), and 25% (6/24) in 2007–2008 in Alberta (6). In clinically sick turkeys, the ceftiofur resistance prevalence was higher (39%, 16/39), though this may reflect previous drug use. Gentamicin resistance in retail *E. coli/Salmonella* has remained relatively low ($\leq$ 5%), but was higher in isolates from clinically sick turkeys (17%, 7/41). As shown in Table 3, the avian [i.e., turkeys

Table 3. Summary of antimicrobial resistance in diagnostic submissions and passive surveillance of turkeys/avian species across Canada

		Gram-negatives				Gram-positives	
		E. coli		*Salmonella*		*Clostridium perfringens*	*Staphylococcus* spp.
		Clinical (MAPAQ)[a] *n* = 253 *(% Resistant)*	Retail (CIPARS)[b] *n* = 295 *(% Resistant)*	Clinical (CIPARS)[c] *n* = 41 *(% Resistant)*	Retail (CIPARS)[b] *n* = 31 *(% Resistant)*	Clinical (AHL)[d] *n* = 50 *(% Resistant)*	Clinical (MAPAQ)[a] *n* = 46 *(% Resistant)*
I[e]	Ceftiofur	49	12	39	29	—	0
	Ciprofloxacin	—	0	0	0	—	—
	Enrofloxacin	0	—	—	—	—	2
II	Amoxicillin	60	—	—	—	—	0
	Amoxicillin-clavulanic acid	—	—	32	—	—	—
	Ampicillin	—	34	39	29	—	—
	Erythromycin	—	—	—	—	0	26
	Clindamycin	—	—	—	—	0	26
	Gentamicin	45	6	17	3	—	0
	Neomycin	10	—	—	—	—	6
	Penicillin	—	—	—	—	—	9
	Streptomycin	100	32	41	26	—	100
	Trimethoprim-sulfa	14	7	7	3	—	0
	Virginiamycin	—	—	—	—	8	—
III	Bacitracin	—	—	—	—	60	—
	Florfenicol	17	—	—	—	0	22
	Novobiocin	100	—	—	—	—	9
	Oxytetracycline	65	—	—	—	—	37
	Spectinomycin	68	—	—	—	—	100
	Sulfadimethoxine	69	—	—	—	—	2
	Sulfathiazole	69	—	—	—	—	7
	Sulfisoxazole	—	26	24	19	—	—
	Tetracycline	65	56	34	29	88	35

— not tested/may not be included in the panel of antimicrobials.

[a] MAPAQ — Ministère de l'Agriculture, des Pêcheries et de l'Alimentation du Québec, passive surveillance of avian [i.e., consisted of turkeys (14%), broiler chickens (67%), and other poultry type/species (19%) including broiler breeders, egg layers, breeder layers and game birds] clinical *E. coli*/*Staphylococcus* isolates in Quebec in 2011, using AVIAN1F plates, Sensititre®, Trek Diagnostic Systems; clinical breakpoints were used (36).

[b] CIPARS — Canadian Integrated Program for Antimicrobial Resistance Surveillance, preliminary data, retail ground turkeys purchased in British Columbia, Saskatchewan, Ontario and Quebec (2010–2011) using CMV2AGNF, Sensititre®, Trek Diagnostic Systems, clinical breakpoints were used (35).

[c] CIPARS — Canadian Integrated Program for Antimicrobial Resistance Surveillance, passive *Salmonella* surveillance (i.e., clinically-sick turkeys submitted by veterinarians/producers to participating provincial diagnostic laboratories (2011), using CMV2AGNF, Sensititre®, Trek Diagnostic Systems; clinical breakpoints were used (39).

[d] Animal Health Laboratory — diagnostic submissions (i.e., clinically-sick turkeys), Ontario, Canada in 2005, using plates custom-made for AHL by Trek Diagnostic System, epidemiological breakpoints were used (14).

[e] Roman numerals I to IV indicate the ranking of antimicrobials based on importance in human medicine as outlined by the Veterinary Drugs Directorate, Health Canada (http://www.hc-sc.gc.ca/dhp-mps/vet/antimicrob/amr_ram_hum-med_intro-eng.php).

(14%), broiler chickens (67%), and other poultry type/species (19%) including broiler breeders, egg layers, breeder layers, and game birds] clinical *E. coli* isolates in Quebec, CIPARS turkey clinical (i.e., from passive surveillance of clinically sick turkeys submitted to participating provincial diagnostic laboratories), and CIPARS turkey retail meat (i.e., purchased in 4 provinces) *E. coli*/*Salmonella* isolates also exhibited resistance to other VDD Category II-III antimicrobials. Antimicrobial resistance data for *Staphylococcus* spp. isolated from clinically sick avian species (i.e., from the multiple poultry species described) in Quebec in 2011 and *C. perfringens* isolated from clinically sick turkeys submitted to the Animal Health Laboratory, Guelph, Ontario, in 2005 (14) also exhibited resistance to various antimicrobials. Canadian AMR profiles of *B. avium, P. multocida,* and *E. rhusiopathiae* were unavailable. In 1998, isolates from 1 case of ORT in Quebec exhibited susceptibility to enrofloxacin (15).

Preliminary AMR data in 1 minor poultry species (i.e., Black Silkies), selected to represent the game bird population included ceftiofur-resistant *Salmonella* (1/5) and ciprofloxacin-resistant *Campylobacter* spp. (2/16) (7). Antimicrobial resistance data from bacteria from layer chickens are not currently available.

Residues

The CFIA's 2009 NCRMP (40) reported 100% compliance (i.e., within established threshold limits or not detected for residues), to VDD's Categories I and II antimicrobials in all types of poultry meat. Violations were reported for some VDD Category III antimicrobials (tetracycline: 2% of ducks; macrolides: $< 1\%$ of fowl and game birds) and Category IV antimicrobials (clopidol: 2.08% of game birds; ionophores: 29.23% or 19 positives/65 samples of game bird meats); violations for ionophores in game birds was up by 7% from the previous sampling year. Residue violations were negligible in turkey meats for the last 5 y.

The NCRMP reported high compliance rates to VDD's Category I to III antimicrobials in eggs; however, compliance rates for ionophore anticoccidials were lower for domestic (88.10% compliant) compared with imported eggs (96.28% compliant).

Discussion

Ranking of common bacterial and protozoal illnesses which require treatment with antimicrobials in Canada is one first step in understanding AMU and potential areas on which to focus surveillance of pathogens. Knowing what has been identified as clinically effective for treating these diseases and current rates of resistance in Canada, both in animal pathogens and foodborne zoonotic organisms, can provide a scientific basis for therapeutic decision-making and also are important for highlighting critical data gaps.

The survey indicated that historically diagnosed bacterial diseases persist in Canadian turkeys and new diseases have emerged. Yolksac infections/omphalitis and septicemia were commonly diagnosed in poults/growing turkeys. A chronic multisystemic lesion is a sequel to neonatal APEC infections (8). *Klebsiella, Staphylococcus,* and *Pseudomonas* (12) are environmental/opportunistic organisms that may contribute to the severity of the disease. Ceftiofur, known to have good tissue distribution and good spectrum of activity (53,54) was described in the literature to treat neonatal infections. However, ceftiofur, a VDD Category I antimicrobial, is no longer labelled for use in turkey poults in Canada. Further, surveillance has highlighted emerging resistance to ceftiofur (36,39) (Table 3). Gentamicin, a VDD Category II antimicrobial, is labelled for use in day-old poults. Indicator and zoonotic organisms have remained susceptible to this drug; however, the field efficacy of gentamicin under Canadian conditions is unknown. It largely targets Gram-negative organisms (55). To reduce AMR, the practice of continuing AMU, regardless of its importance to human medicine, in young poults/embryonating eggs should be re-evaluated as this routine may result in persistence of resistant strains/genetic elements throughout the growing period beyond the residue withdrawal time recommended, as described in a broiler drug exposure study (56). It may also impact clinical outcomes of subsequent therapy (i.e., when same class antimicrobials are used) and may result in downstream dissemination of resistant organisms [e.g., at retail/further processing (5,6,36,39)], potentially posing a food safety risk (2).

Though clinical isolates remained susceptible to antimicrobials commonly used for treating *Staphylococcus* in turkeys (e.g., penicillins, potentiated sulfonamides) (36), it is unclear if these *in-vitro* results correlate with field efficacy. Staphylococcal diseases are therapeutically challenging, as the localized lesions (i.e., arthritis, osteomyelitis) are hard to reach by oral antimicrobials (57).

The respiratory pathogens that were diagnosed in turkeys (e.g., APEC, *B. avium, P. multocida,* ORT, *Mycoplasma* spp.) can be clinically challenging when 2 of these pathogens occur concurrently such as in APEC-ORT (58), APEC-*B. avium,* or APEC-*Mycoplasma* spp. (CRD complex) infections (59). Intermediate to broad-spectrum antimicrobials that can penetrate the infected sites (i.e, the upper and lower respiratory organs) including aminopenicillins, potentiated sulfonamides, and the tetracyclines were the common AMU options for most of these respiratory diseases (55). Florfenicol is an additional option cited for APEC-ORT (58). However, surveillance indicates that *E. coli* populations have developed resistance to most of these antimicrobials. Because clinical outcomes as a result of AMU and current AMR profiles of most respiratory pathogens in Canada are not documented, options should be based on clinical experience in treating respiratory disease and its complications and supported by susceptibility-testing, as suggested in various AMU guidelines for poultry (25,38,55). Antimicrobial resistance in *E. rhusiopathiae* is also unknown but the literature suggests that the penicillins/aminopenicillins remain efficacious (55,60).

Necrotic enteritis and coccidiosis were the only enteric diseases of turkeys reported in the survey. In an Ontario study, turkey clinical *C. perfringens* isolates had a high prevalence of resistance to tetracycline (88%) and bacitracin (60%) but lower levels to virginiamycin (ELDU) (8%) (14) *in-vitro*, similar to a US study (61). In light of the potential removal of growth promotion claims of certain antimicrobials (33) that may be efficacious against *C. perfringens*, more research is required towards non-antimicrobial alternatives/novel technologies to reduce NE. Another clostridial disease, cellulitis, was diagnosed but Canadian information regarding AMU approaches and AMR were unavailable. In the US, a therapeutic regimen consisting of penicillin and chlortetracycline was cited (18), suggesting that multiple antimicrobials might be required due to its complex etiology.

For histomoniasis, other than nitarsone, no antiprotozoal drugs are available in Canada, but managing the cecal worm, *Heterakis gallinae* (intermediate host for *Histomonas meleagridis*), by administration of benzimidazole compounds was suggested (62); use in turkeys, however, is ELDU in Canada.

In summary, various AMU guidelines recommended that drug choices should be based on detection and susceptibility testing of primary/concurrent pathogens, previous clinical experiences in treating the disease, and human health considerations, such as AMR and residues. On-going surveillance of the prevalence of clinically relevant/enteric pathogens, their resistance profiles, antimicrobial use on the farm, and clinical outcomes following therapy would help detect emerging trends in turkey health and provide valuable information for prudent use guideline refinement. Other flock health management that could curb AMR are: selecting quality hatching eggs and turkey poults (i.e., important for APEC and *Staphylococcus* spp.); effective cleaning and disinfection of egg/poult contact surfaces; vaccinations (e.g., to enhance protection against *B. avium, E. rhusiopathiae, P. multocida* and poult immunity against APEC); and managing overcrowding, presence of abrasive surfaces, and excessively wet litter (i.e., to reduce mechanical damage to the skin and immunosuppression that may predispose birds to *Staphylococcus* spp., *E. rhusiopathiae,* and *C. septicum* infections).

Published field experiences for treating layer diseases and AMR information from bacterial pathogens of layers were generally limited or unavailable. *E. coli*-associated EYP was the most frequently diagnosed disease of layers but Canadian resistance profiles of this pathogen-commodity combination were unavailable, though 3 antimicrobials were listed in the CVMA-PUG for therapy. The disease occurs sporadically throughout the laying period and may mimic disease patterns/syndromes of some viral and other bacterial and viral diseases that may not

necessarily require AMU. Knowledge of flock-level baselines for *E. coli*-associated reproductive diseases under normal operating conditions may help, through the process of exclusion, detect conditions associated with *Salmonella* (63), avian influenza (e.g., H6N2) (64), and a newly identified pathogen in laying hens in Ontario, *Gallibacterium anatis* (65), all known to cause similar reproductive/multisystemic lesions and impact on flock mortality/egg production.

Necrotic enteritis and coccidiosis were the 2nd most frequently diagnosed disease of layers and might explain the detection of ionophore residues in domestic eggs. It is possible that CgFARAD or manufacturer recommended withdrawal times were not properly observed (or that CgFARAD data may not be available for layers), or other pathways such as cross-contamination with other medicated feed, may have played a role. As noted in the field, coccidiosis was observed less frequently with the increasing use of coccidiosis vaccines, thus, could be included in routine pullet health programs to curb AMU. As with broilers (66,67), NE vaccinations of pullets to protect flock during the laying phase or in layer breeders to protect progeny flocks could be explored. Regular cleaning/running the conveyor belts and checking nipple drinkers may reduce wet spots that may predispose to sporulation of *Eimeria* spp.

Antimicrobial resistance information and experiences in treating spirochaetosis in layers under Canadian conditions have not been documented, but in other countries such as Australia (68), resistance to antimicrobials known to be efficacious against spirochaetosis has been reported, including tiamulin, lincomycin, tetracycline, and ampicillin, and in Europe, resistance to lincomycin, tylosin, and tilmicosin was detected (69). Given the limited AMU options in layers, good biosecurity/containment and pest control programs should be enhanced, as swine, rodents (70), and wild waterfowl (71) could harbor *Brachyspira* spp. and spread it to flocks. Further, installing hygiene barriers and reducing personnel traffic between flocks in multi-age managed facilities [identified as a risk factor (23)] are efforts to reduce flock-to-flock transmission. Vaccination may be explored, to reduce the potential economic impact of this disease, including a 5% drop in egg production and up to 9% mortality (72). Human *Brachyspira* cases linked with exposure to layer flocks have not been reported in Canada; however, the potential role of layer flocks in the epidemiology of human spirochaetosis (i.e., reservoir and subsequent re-introduction of *Brachyspira* in human population) (73) needs to be elucidated.

Overall, very few antimicrobials are labelled for use in egg-producing chickens in Canada, consistent with the US and European countries (reviewed in 74). Data on MRL's or acceptable/safe concentrations of antimicrobial dosages in eggs are scarce (75). As a precaution, manufacturers included warnings in the label not to use their products in egg-producing chickens. As in turkeys, management efforts such as vaccination against *E. coli,* C. *perfringens/Eimeria,* and *Brachyspira* should be explored to reduce AMU at the laying phase.

Clinically relevant and zoonotic diseases were diagnosed in minor poultry/game birds and resistant organisms were also detected, highlighting the importance of these species in the larger ecology of AMR organisms and zoonotic pathogens.

The detection of ionophore residues in game bird meats may indicate ionophore exposure as a result of clinical cases of coccidiosis/NE problems in the field. As in layers, pharmacological studies in minor poultry have been lacking, hence, appropriate antimicrobials, dosage recommendations, and MRL's in minor meat are largely unavailable in Canada, limiting informed AMU options. Inappropriate therapeutic choices and under/over dosing may prolong the course of infection and may lead to residues in meat products, as reported in the NCRMP. Dose calculations in minor species could be extrapolated from available turkey and chicken data; however, this practice may reduce efficacy and could result in levels of residues in meats/eggs that may be unsafe for humans (76). Further, subpopulations of the intestinal flora evolve as resistant (77), enter the food chain or potentially carry over to succeeding flocks and become disseminated in the environment, as noted in AMR organisms detected from minor species. In Canada, more data are required (e.g., prevalent coccidial species and bacterial pathogens in game birds, efficacy of available antimicrobials) to guide veterinarians in their AMU choices, and to ensure observance of residue withdrawal periods. A MUMS program similar to the MUMS program in the US, resulting from a compilation of existing information, would be useful for identifying efficacious and prudent AMU options in minor poultry.

Summary and recommendations

This paper identified the primary diseases requiring antimicrobial therapy in turkeys, layers, and minor avian species, reviewed currently available antimicrobials for the therapy of these diseases, and existing AMR profiles and residue concerns. This paper is a summary resource document, with the intent to update the contents as new information becomes available. This review found that, first, historically diagnosed diseases have persisted in turkeys, layers, and minor species and new diseases have emerged. Secondly, antimicrobials are available to treat these diseases but most of the efficacious antimicrobials belong to higher VDD categories and would have to be used in an ELDU manner in Canada. Thirdly, surveillance and monitoring indicate the presence of enteric AMR organisms (including resistance to Category I antimicrobials), but few residue violations of higher category antimicrobials. Producers may be using the antimicrobials, particularly the coccidiostats, according to current residue withdrawal standards, or in the case of egg layers and minor species, withdrawal information may be unavailable. This review highlights data gaps in pathogen frequency, AMU, commodity-bacterial combination AMR profiles, and outcomes of therapy. The authors recommend the implementation of an integrated and on-going surveillance of AMU and resistance in clinically relevant pathogens, indicator and zoonotic species, and other risk factors (e.g., viral diseases, flock management practices), in turkeys, with periodic monitoring in laying/breeding hens and minor poultry species. This would improve the understanding of current and emerging issues in the field that may impact food safety. Antimicrobial resistance and AMU data, in addition to data on residue monitoring will help to refine and hone prudent AMU, MUMS guidelines, and animal/human health risk management.

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