Anthelmintic Resistance in poultry

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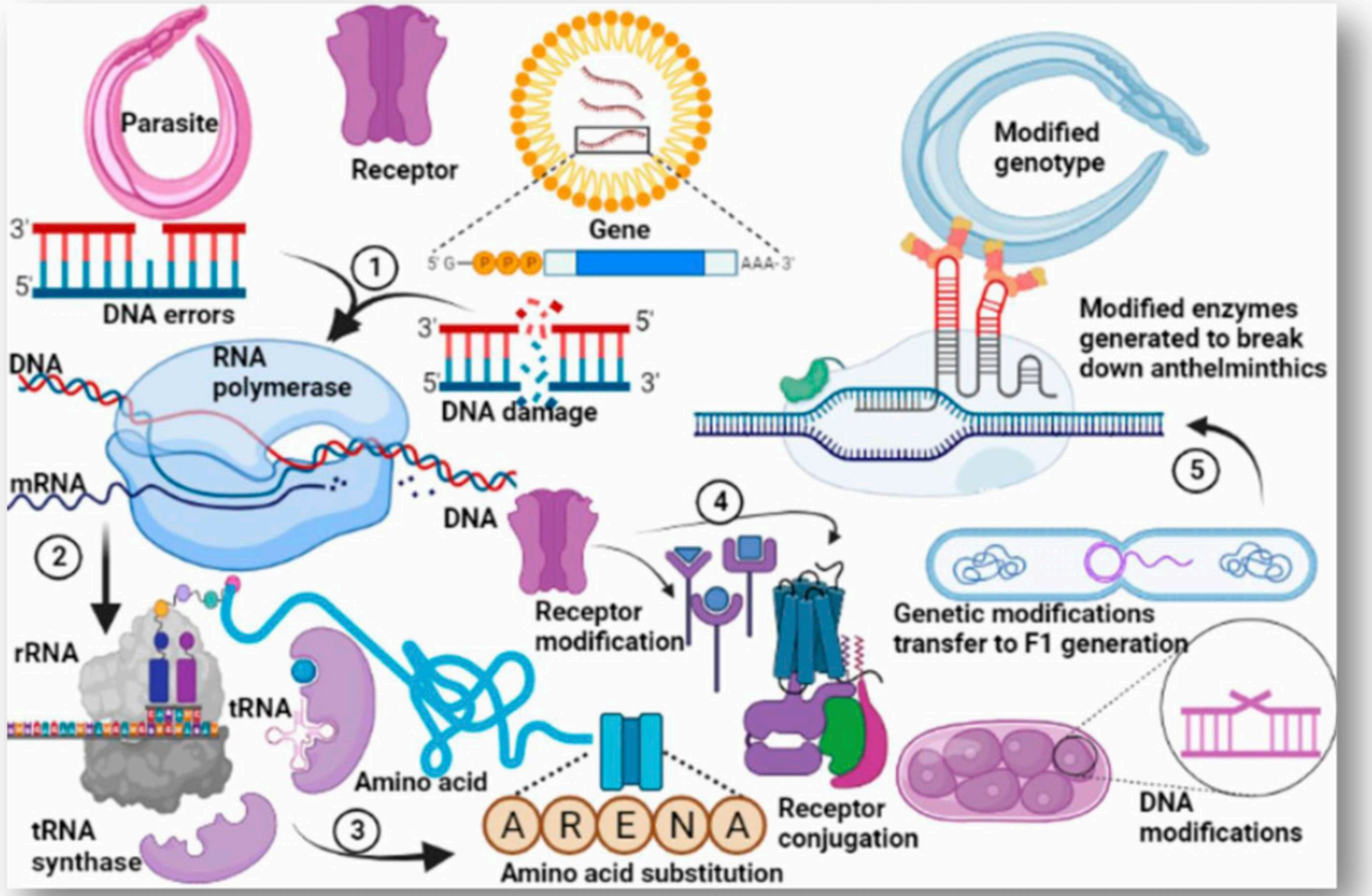
Learning Objectives

- Genetic Basis of Anthelmintic Resistance
- Types of Anthelmintic Resistance
  - -Cross Resistance
  - -Side Resistance
  - -Multiple Resistance
- Status of Anthelmintic Resistance in Livestock, Poultry and Pet animals
- Factors contributing for the development of anthelmintic resistance

Genetic basis of Anthelmintic Resistance

- Main cause is change in allele frequency of resistant gene that confers resistance to anthelmintic
- Anthelmintic resistance is the result of drug selection in the parasite population
- Resistant parasites survive and pass the genes to the next generation
- Nematodes have great genetic diversity and large population size resulting in high mutation rates and rapid evolution

Genetic Modification occurs in parasites following decades of anthelmintic exposure



(1) Transcription (2) Translation (3) Substitution of primary amino acids associated with susceptibility with those which favour resistances against anthelmintics (4) Protein modifications favours expression of receptors which inhibit or reduce anthelmintic binding (5) Production of metabolic enzymes which degrade anthelmintics

(Zirintunda et al., 2022)

Types of Anthelmintic Resistance

There are three types of anthelmintic resistance *(Nipane et al.*, 2002)

1. Cross Resistance
2. Side Resistance
3. Multiple Resistance

Cross Resistance

- Resistance in which a parasite strain is able to tolerate the therapeutic doses of anthelmintics having different mechanism of action

Side resistance

- Resistance to anthelmintics that are having similar mechanism of action. Eg. Resistance among Benzimidzole anthelmintics

Multiple Resistance

- Resistance to two or more anthelmintic drugs having similar or different mechanism of action

Geographical distribution of AR

Country	Anthelmintic drugs
Argentina	BZs, LEV, IVM
Australia	Ops, BZs, LEV, TBZ, OXF, Closantel, Morantel
Belgium	BZs
Brazil	BZs, LEV, IVM, Closantel
France	BZs, LEV
Germany	IVM,BZs, Pyrantel tarterate, FEN, Febantel, OXF, LEV, TBZ, ALB, MBZ
India	BZs, IVM, FEN, Morantel, Closantel, LEV, Thiophanate,
Kenya	BZs, LEV, RAF, FEN, IVM
Malaysia	BM_Z, LEV_S, IVM, Moxidectin, Closantel
Netherlands	OXF_S, LEV_S, BM_Z, IVM
New Zealand	BM_Z, LEV_S, IVM
Pakistan	OXF_S, LEV_S, ALB, IVM
Paraguay	BM_Z, LEV_S, IVM
South Africa	BM_Z, IVM, RAF, Closantel
Uruguay	BM_Z, LEV_S, IVM
United State of America	FEN, IVM, Pyrantel pamoate, LEV_S, TB_Z,
Zimbabwe	RAF, BM_Z, LEV_S,

Prevalence of Anthelmintic Resistance in India *(Verma et al., 2018)*

Anthelmintic	Generic drug name	Host	Species	Place
Benzimidazole		Sheep	Strongyles	Karnataka
		Goat	*H. contortus*	Uttar Pradesh
		Horse	Equine Cyathostomins	Uttar Pradesh
		Goat	Strongyles	Kerala
		Goat	Strongyles	Madhya Pradesh
		Sheep	*H. contortus* and *Teladorsagia* spp.	Tamil Nadu
	Albendazole (ALB)	Sheep	*H. contortus*	Rajasthan
		Sheep	*H. contortus*	Tamil Nadu
		Goat	Strongyles	Gujarat
		Goat	Strongyles	Chhattisgarh
	Fenbendazole	Sheep	*H. contortus*	Haryana
		Goat	*H. contortus*	Haryana
		Sheep	*H. contortus*	Haryana
		Sheep	*H. contortus*	Tamil Nadu
		Goat	Strongyles	Madhya Pradesh
	Mebendazole	Goat	*H. contortus*	Haryana
Tetrahydopyrimidines	Closantel	Sheep	*H. contortus*	Tamil Nadu
	Morantel	Goat	*H. contortus*	Haryana
		Sheep	*H. contortus*	Haryana
Imidazothiazoles	levamisole (LEV)	Goat	*H. contortus*	Haryana
		Sheep	*H. contortus* and *Teladorsagia* spp.	Tamil Nadu
		Sheep	*H. contortus*	Haryana
		Goat	Strongyles	Madhya Pradesh
		Goat	Strongyles	Gujarat
		Goat and Cattle	Strongyles	Chhattisgarh
Macrocyclic lactones	Ivermectin (IVM)	Goat	Strongyle	Gujarat
		Goat and Cattle	Strongyles	Chhattisgarh
		Sheep	*H. contortus*	Haryana

AR in Cattle and Buffaloes

- AR is an emerging problem in all parts of the world in gastrointestinal nematodes of cattle
- AR in Cattle GI Nematodes :

  -Haemonchus spp.,

  -Ostertagia spp.,

  -Trichostrongylus spp.,

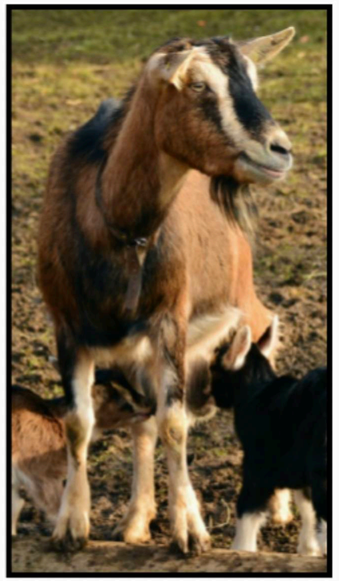
  -Cooperia spp.

  -Oesophagostomum spp.

- Systematic review and meta-analysis suggested that AR in cattle is present on several continents (Baiak et al. 2018)
- Study in buffaloes a Possible AR in *Toxocara vitulorum* for Benzimidazole and Levamisole (Biswas et al., 2022)

Anthelmintic Resistance in Small Ruminants

- **Drench-and-shift:** A common practice where the sheep are drenched with anthelmintic drugs immediately before moving them to clean pastures, thus reducing GIN reinfection. This practice has been found to be positively associated with the development of resistance



- Use of **long acting anthelmintic and mixed species grazing** (Falzon et al., 2014) also favours AR development

Anthelmintic Resistance in Small Ruminants

BENZIMIDAZOLE RESISTANCE
Haemonchus contortus
Nematodirus spathiger
N. filicollis
N. abnormalis
Teladorsagia circumcincta
T. trifurcata
T. davtiani
Trichostrongylus axei
T. colubriformis
T. vitrinus

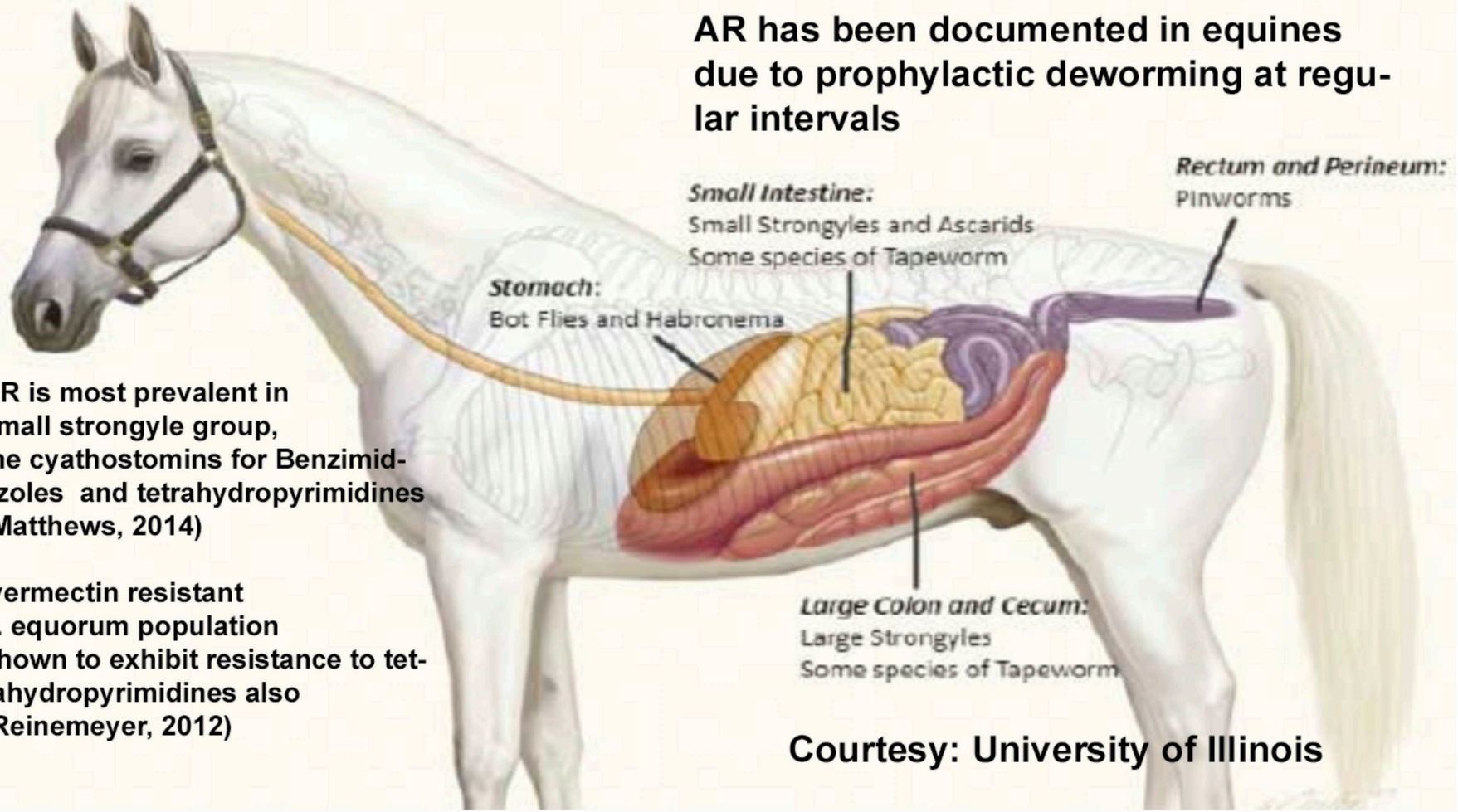
MACROCYCLIC LACTONES RESISTANCE
Haemonchus contortus
Trichostrongylus axei

LEVAMISOLE RESISTANCE
Teladorsagia spp.,
Trichostrongylus colubriformis
Trichostrongylus vitrinus

Holm et al., 2014
Untersweg et al., 2021

Anthelmintic Resistance in Horses

AR has been documented in equines due to prophylactic deworming at regular intervals



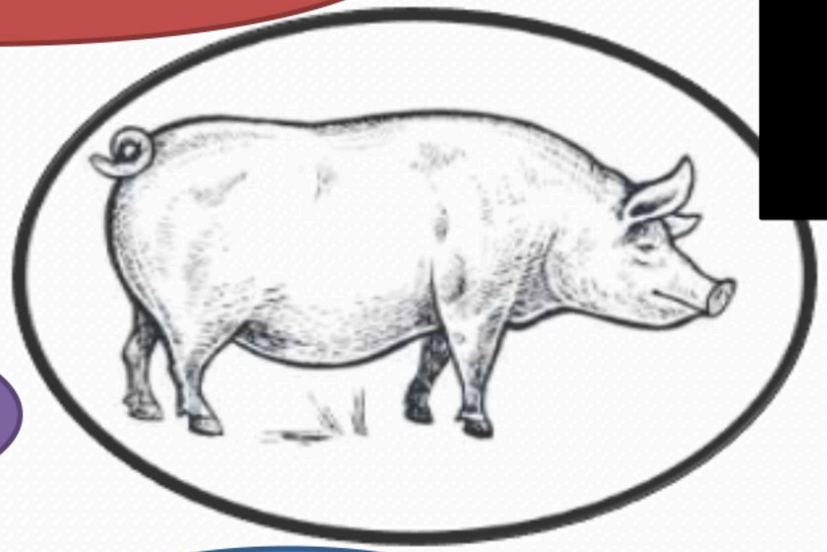
Courtesy: University of Illinois

AR is most prevalent in small strongyle group, the cyathostomins for Benzimidazoles and tetrahydropyrimidines (Matthews, 2014)

Ivermectin resistant P. equorum population shown to exhibit resistance to tetrahydropyrimidines also (Reinemeyer, 2012)

Anthelmintic Resistance in Pigs

Oesophagostomum dentatum



Trichuris suis

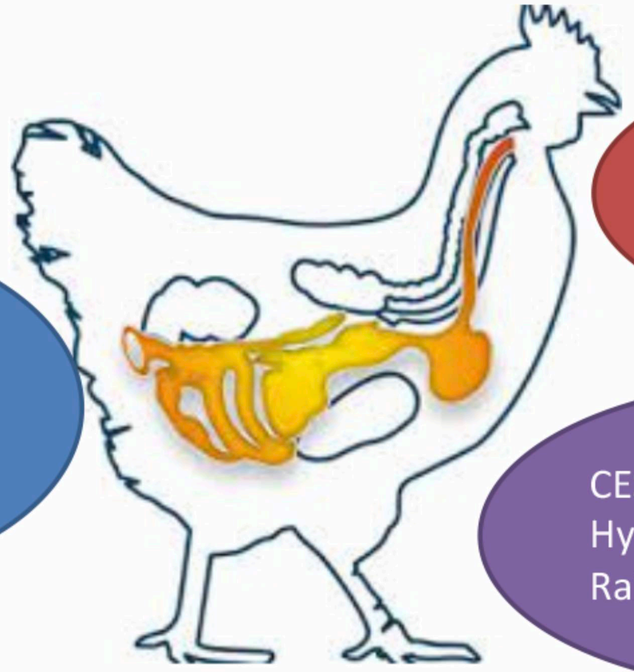
Ascaris suum

RESISTANCE TO

BENZIMIDAZOLES
LEVAMISOLE
IVERMECTIN

(Thamsborg *et al.*, 2013)

Anthelmintic Resistance in Poultry



NEMATODES
Ascaridia galli
Hetarakis gallinarum
Capillaria spp.

TREMATODES
Prosthogonimus spp

CESTODES
Hymenolepis spp.
Raillientina tetragona

Ascradia galli has shown resistance to benzimidazoles (Tarbiat 2018).

Change in β-tubulin genes leads to either the deactivation of receptors or decrease in affinity of receptors to bind with the benzimidazoles (Keri et al. 2015)

Anthelmintic Resistance in Dogs and Cats

NEMATODES
Toxocara canis
Ancylostoma sp.
Trichuris sp.
Dirofilaria immitis

CESTODES
Multiceps spp.
Taenia spp
Dipylidium spp.

A. caninum causes the greatest morbidity and mortality though blood loss.

There are multiple reports and clinical studies demonstrating *A. caninum* infections refractory to treatment with one or more anthelmintics
(Jimenez Castro and Kaplan, 2020; Marsh and Lakritz, 2023)

Factors contribute for development of Anthelmintic Resistance

1. **Frequent use of same anthelmintic drug for treatment of helminths**

- More than three treatments per year
- More frequent treatment-faster development of resistance

Factors contribute for development of Anthelmintic Resistance

- **Administration of incorrect and inadequate anthelmintic dose**

-Visual weight estimation to determine the dose rate on an anthelmintic leads to inappropriate dosing and underdosing

-Underdosing favours the survival of heyterozygous resistant worms and contributes to selection of resistant gene

-Variation in the bioavailability of anthelmintic in different host species also plays a crucial role in calculating correct dose

-Example: Bioavailability of anthelmintics in goats is lesser than sheep. Hence the benzimidazole drugs in goats should be double than the sheep dose

Factors contribute for development of Anthelmintic Resistance

3. Mass prophylactic anthelmintic dosing without assessing the need for treatment and parasitic load

- Treating all animals at the same time favours development of resistance
- It is possible to delay the development of resistance by treating only 80 per cent of the flock

Factors contribute for development of Anthelmintic Resistance

4. Parasites with resistance genes are preexisting in the population of parasites

- Resistant alleles are present in parasite population before it ever exposed to anthelmintics
- Continuous use of anthelmintics allows the resistant worms to reproduce at faster rates than susceptible worms resulting in an increased in the frequency of worms with resistant phenotype
- Treating and moving to clean pasture favours the development of resistance at faster rate.

Thank you