Importance of Anti-Parasitic drugs in Animal Health and Production

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Introduction

Parasitism: A two-species association in which one species, the parasite, lives on or in a second species, the host, for a significant period of its life and obtains nourishment from it.

- Important features of the host-parasite relationship:
  - Parasitism always involves two species, parasite and host.
  - Many parasitic associations produce pathological changes in hosts that may result in disease.
  - Successful treatment and control of parasitic diseases requires not only comprehensive information about the parasite itself but also a good understanding of the nature of parasites' interactions with their hosts.
  - The parasite is always the beneficiary and the host is always the provider in any host-parasite relationship.

Source:
Parasites and Parasitic Diseases of Domestic Animals
Dr. Colin Johnstone (principal author)
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Introduction

Traditionally regarded as parasites:
• protozoa, arthropods, helminths

Broader definition of parasites:
• all infectious agents of animals, i.e. viruses, bacteria and fungi as well as the arthropods, helminths and protozoa; can be further divided into microparasites and macroparasites

Source:
Parasites and Parasitic Diseases of Domestic Animals
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A female **mosquito** blood feeding. Mosquitoes serve as intermediate hosts of other parasites such as **Dirofilaria immitis** the dog and cat heartworm and **Plasmodium** species causing malaria in humans and birds. They are also vectors of viruses causing yellow fever and encephalitis.

A cluster of **nematodes**, the roundworm of dogs, **Toxocara canis**. This parasite is common in puppies and may be transmitted transplacentally as well as to nursing pups in their mother's milk. This parasite has public health importance as a cause of visceral larva migrans in man.

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Fleas are common parasites of dogs and cats. They bite their hosts and feed on blood. Fleas are intermediate hosts of the tapeworm Dipylidium caninum and the filarid nematode Dipetalonema reconditum. The cat flea is a vector of feline parvovirus.

Fasciola hepatica, the liver fluke of ruminants. The parasite has a complex life cycle involving snail intermediate hosts. Migration of developing flukes in the host liver provokes an intense inflammatory reaction with severe liver damage.
**Hematopinus suis**, the blood-sucking louse of swine is common in pigs raised indoors with transmission readily occurring from pig to pig. Infested pigs are restless and rub their skin frequently to relieve the itching.

**Anoplocephala perfoliata**, a tapeworm of horses, is often found in clusters at the ileo-cecal junction. It is widespread in distribution and usually benign. However, cecal abscesses, and intussusceptions have been reported.

Source:
*Parasites and Parasitic Diseases of Domestic Animals*
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The nematode *Dirofilaria immitis*, the heartworm, has a complex life cycle involving mosquitoes as intermediate hosts. These worms are found in the cardio-pulmonary circulation and may cause severe heart disease in dogs and cats.

The protozoan *Giardia* is important as a cause of diarrhea in dogs and cattle but is also found in other domestic animals as well as man. The trophozoite stage, shown here, attaches to the mucous epithelium cells of the small intestine.
Parasites in fish include external parasites (shown above: isopod *Anilocra gigantea*), leeches, nematodes, cestodes, flukes, carp lice and salmon (sea) lice. *Tetracapsuloides bryosalmonae*, a myxozoan parasite causes Proliferative kidney disease (PKD) in salmonids.

Sea lice are marine ectoparasites (external parasites) that feed on the mucus, epidermal tissue, and blood of host marine fish. *Lepeophtheirus salmonis* and various *Caligus* species are adapted to saltwater and are major ectoparasites of farmed and wild Atlantic salmon. Several antiparasitic drugs have been developed for control purposes.
Not all parasites are equally parasitic – parasitism can be seen as a spectrum

- Free living, seeking a host only to feed
- Cannot survive without a host at any stage of their life cycles

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Why Do Parasites Matter?

- Disease and Death
- Production Loss
- Zoonotic Potential
- Animal welfare

(OIE logo)
Consequence of parasite infections - animal health and productivity

- Reduced growth rates (including meat production)
- Reduced reproductive rates
- Reduced milk production
- Reduced fleece weight, fibre diameter and staple strength
- Behavioural changes, e.g. through flies, which annoy animals, causing reduced grazing behaviour and agitation
- Condemnation of carcase parts at slaughter
- Damaged hides and fleeces
- Increased maintenance feed consumption
- Increased susceptibility to infections
- Diseases transmitted by the parasite
- Pain
How big is the loss?

- Experimental infection in sheep with *Trichostrongylus* and *Ostertagia* – influence on weight gain over study period

(Tc = *T. colubriformis*; Oc = *O. circumcincta*. Data from Steel et al. 1982, Aust J Agric Res, 33, 131)
How big is the loss?

- Fasciolosis: Worldwide losses in animal productivity in 1999 estimated at over US $ 3.2 billion per year
- Ticks: estimated productivity losses caused each tick

<table>
<thead>
<tr>
<th>Tick species</th>
<th>Live-weight-gain loss (g)</th>
<th>Milk loss (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amblyomma hebraeum (Conway et al., 1989)</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>Amblyomma variegatum (Pegram &amp; Oostenrijk, 1990)</td>
<td>65-60^</td>
<td>-</td>
</tr>
<tr>
<td>Amblyomma americanum (Baumard, 1985)</td>
<td>16-29</td>
<td>-</td>
</tr>
<tr>
<td>Amblyomma maculatum (Williams, Hair &amp; McNew, 1970)</td>
<td>33</td>
<td>-</td>
</tr>
<tr>
<td>Boophilus microplus (Sutherst et al., 1993)</td>
<td>0.6-1.5</td>
<td>-</td>
</tr>
<tr>
<td>Rhipicephalus appendiculatus (Conway et al., 1986)</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Rhipicephalus appendiculatus (de Castro et al., 1985)</td>
<td>NSD</td>
<td>-</td>
</tr>
</tbody>
</table>

- Cattle - worldwide: 80% of the population at risk from ticks and tick-borne diseases; losses: US $7 billion (McCosker, 1979).
How big is the loss?

• Ticks, USA: eradication campaign for *B. microplus* and *B. annulatus* successfully completed in 1947, at a cost of US $53.5 mio (at 1953 prices). Estimated benefit-cost ratio of the eradication: 140:1

• Ticks in cattle, Argentina (1992): cost of tick infestation: US $154.6 mio for weight loss, death and hide damage, cost of tick control and tick fever vaccine: US $34.9 mio

• Parasitic diseases in sheep and cattle: the annual cost in Australia estimated at US $1 billion (2010)

• Africa and Middle East: estimated losses
  Endoparasites: > 3 billion US $/Year direct and indirect losses
  Ectoparasites: > 2 billion US $/Year direct and indirect losses (incl. tick borne diseases)
Controlling parasites

Different strategies in livestock and companion animals

- **Companion animals**: most owners do not tolerate any parasites - chemotherapy
- **Livestock**: not economical or even possible to prevent all parasites. Aim is to minimise parasites to reduce economic loss
Controlling parasites

**Prevention** of parasitic infections
- Management of pastures and animals, including monitoring of resistance
- Vaccines
- Routine chemotherapy treatment

**Treatment** of manifest infections
- Curative treatment - chemotherapy
Antiparasitic drugs

- Ectoparasiticides
- Endectocides
- Ectoparasiticides

Requirements
- Effectively kill or remove adult and immature parasites
- Safe
- Easy to administer
- Economic for the producer
- Practical withdrawal periods
Ectoparasiticides

Chemical control of Ectoparasites

- Organochlorines
- Organophosphates (e.g. Coumaphos, Trichlorfon)
- Carbamates (e.g. Propoxur)
- Synthetic pyrethroids (e.g. Flumethrin, Cypermethrin, Deltamethrin)
- Amidines (e.g. Amitraz, Cymiazole)
- Macro cyclic lactones (e.g. Ivermectin, Doramectin, Moxidectin)
- Insect Growth Regulators (e.g. Fluazuron)
- Pyrazole group (e.g. Fipronil)
- Spinosad
Endoparasiticides

Chemical control of Endoparasites - Anthelmintics

Antinematodes

• Benzimidazoles and Pro-benzimidazoles (e.g. fenbendazole, albendazole, oxibendazole, febantel)
• Imidazothiazoles (e.g. levamisole)
• Tetrahydropyrimidine (e.g. pyrantel)
• Piperazines
• Organophosphates (e.g. trichlorphon)
• Octadepsipeptides (e.g. emodepside)
• Aminoacetonitrile derivatives (nonepantel)
• Spiroindoles (derquantel, only in combination with abamectin)
Endoparasiticides

Chemical control of Endoparasites – Anthelminthics

Anticestodes
- Praziquantel
- Epsiprantel
- Benzimidazoles

Antitrematodes
- Clorsulon (benzenesulphonamide)
- Nitroxynil (halogenated phenols)
- Salicylanilides (e.g. closantel, rafoxanide)
- Triclabendazole
Endoparasiticides

Chemical control of Endoparasites

Anticoccodials

- Ionophores (e.g. monensin, lasalocid)
- Amprolium
- Diclazuril
- Toltrazuril
- Quinolones (e.g. decoquinate)

Antiproteozoals

- Imidocarb dipropinate
- Diminazene acetuarate
- Isometamidium
- Quinapyramine
- Pantamidines*
- Buparvaquones*

* human medicines
Endectocides

Chemical control of endo and ectoparasites (chemical group available: Macrocyclic lactones)

- Ivermectin
- Doramectin
- Eprinomectin
- Moxidectin
- Abamectin
- Selamectin
- Milbemycin oxime

Large spectrum:
- intestinal worms, lung worms,
- ectoparasites: mange, lice,
- oestus ovis, parafilaria,
- Thelazia, Horn flies
- (Cochliomiya), Hypoderma bovis, Ticks (Boophilus spp)
Antiparasiticide administration

Available formulations

- Oral suspensions (individual animal or herd treatment)
- In feed formulations (herd treatment)
- Dips (herd treatment)
- Spray (spray races - herd treatment, hand sprayer - fewer animals)
- Dust (few animals)
- Pour-on (herd treatment)
- Injectables (herd treatment)
- Ear tags (herd treatment)
- Pheromone or acaricide impregnated devices, e.g. tail band (few animals)
Ectoparasiticides
Challenge

Development of resistance

- Few *new* classes of antiparasitics have become available (emodepside – cats only, monepantel – sheep, derquantel – sheep)
- Monepantel-resistance is already emerging
Vaccines

- Anticoccidial vaccines for poultry
- Antileishmanial vaccine for dogs
- Antitick vaccines
  - Historically: Recombinant vaccine against *Boophilus* TickGARD, TickGARD Plus (Australia), Gavac, Gavac Plus (Cuba)
  - Current: None
  - Future: research ongoing
Global animal health market in 2013

- Total value in 2013: 23 billion US $
- Antiparasitics part of Pharmaceuticals, traditionally about 28%, i.e. 6.4 billion US $
- Americas region represents nearly half the global market
- Food animals account for 59% of the global market

Source: IFAH Annual Report 2013 at www.ifahsec.org
Thank you for your attention!