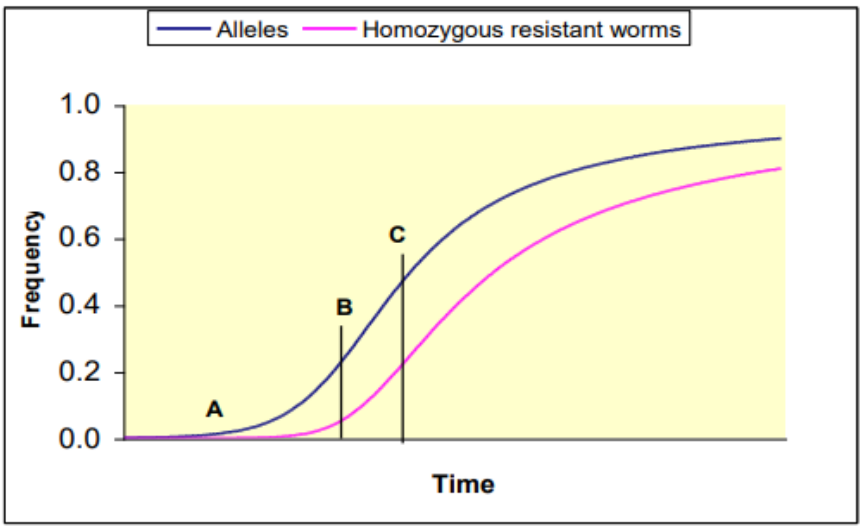
What is anthelmintic resistance (AR)?

A parasite is considered resistant if it survives exposure to the standard recommended dose of the anthelmintic and the ability to survive is passed on to the parasite's offspring. AR is defined as "the heritable reduction in the sensitivity of a parasite population to the action of an anthelmintic". Resistance has been shown to result in significant production losses due to ineffective worm control, particularly young stock but also in older stock with concurrent infections. (See chapter 3. Internal parasites & diseases, section 3.2 Diseases)

We can measure AR in a number of ways. These include indicative field tests, such as a simple post drench efficacy test, to more accurate Faecal Egg Count Reduction Tests (FECRTs) and laboratory assays such as Larval Development Tests (LDT) and Egg Hatch Tests (EHTs) (See chapter 2. SCOPS Principles, section 2.6 Test for AR). A fully effective anthelmintic is expected to reduce the FEC of an animal to zero after administration. If the reduction is 95% or less, then resistance is suspected, pending further investigation.

The development of resistance is, however, an insidious process. Under field conditions this means that anthelmintics will apparently continue to give clinical efficacy in parasitised sheep even if the reduction in faecal egg count (FEC) is substantially lower than 95%. Only when the reduction falls below 80% does it start to become clear that the worm burden has not been controlled effectively. Consequently, many sheep farmers remain unaware that resistance to an anthelmintic is present until resistance reaches a high prevalence. By this stage it is too late for them to undo.

Figure 4. The rate at which AR appears in a flock



Point A, resistance alleles are at very low levels; B, resistance detectable in tests (95%); C, resistance apparent as a clinical problem (<80%)

It is vital to understand the distinction between the ***detection*** of resistance at the 95% level, and farmers seeing apparent clinical failure if we are to slow the development of AR. If AR is detected at an early stage, then sheep farmers can implement the SCOPS principles which are designed to reduce the selection pressure on the worm population. The effect of this is to extend the time taken for the worm population on their farm to move from point B to point C on figure 4 above. This means the activity of the wormer group(s) concerned can be maintained for longer. This is why early detection and the implementation of practices which reduce the selection pressure for resistance are essential if we are to sustain the efficacy of anthelmintics.

The Genetic Basis for Anthelmintic Resistance

Alleles, loci and genes

The different forms of a gene at a specific position on a chromosome is called an allele. The position at which it occurs is called a locus (Latin for 'place'). The word gene can refer to either the locus or the allele. Generally, it is acceptable to substitute the word gene for allele. Worms are diploid creatures – meaning they have paired chromosomes. When both alleles at the same locus on each pair of chromosomes are the same, the worm is homozygous for that gene. When they are different (e.g., one allele for resistance to anthelmintic, and the other for susceptibility), the worm is heterozygous.

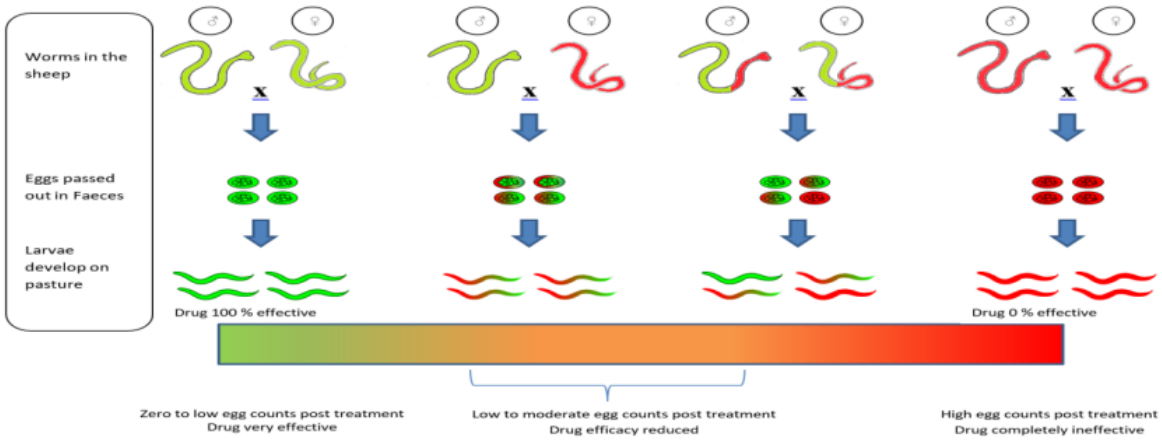
Resistance alleles pre-exist in worm populations

Anthelmintic resistance is now accepted as a pre-adaptive phenomenon, in that the allele or alleles that confer resistance already exist within the worm population before it has ever been exposed to the anthelmintic in question. In the absence of the anthelmintic, natural selection keeps the resistance alleles at a very low frequency because, presumably, the resistance alleles make the worms carrying them less fit for survival than fully susceptible worms.

The introduction and continued use of an anthelmintic, however, confers a survival advantage on the resistant worms. This allows them to reproduce at higher rates than susceptible worms, and their frequency within the population increases. Eventually the frequency of worms with a resistant phenotype becomes so high that anthelmintic resistance is said to have 'appeared' or to have 'developed' in the flock. This is likely to be the time at which resistance to anthelmintics is first detected in laboratory or field tests, or when the anthelmintic fails to cure clinically affected sheep. In fact, by that time, AR has already been present in the population for a substantial period, as the current methods of detection are relatively insensitive.

When anthelmintic resistance in worms behaves as a dominant trait then worms that have either one or both resistant alleles, will not be killed by a full dose of anthelmintic. When resistance behaves as a recessive trait, only homozygous worms survive a full dose of anthelmintic and heterozygous parasites are still killed by the anthelmintic. However, when a sub-optimal dose of anthelmintic is given, it may allow the heterozygotes to survive even though the trait is recessive.

Figure 5. Diagrammatic representation of examples of mating events that may occur in sheep, giving rise to varying populations of resistance in worms.



Diagrammatic representation of examples of mating events that may occur in sheep. Mating fully susceptible (green) male and female worms produces **SUSCEPTIBLE** eggs that become **SUSCEPTIBLE** larvae. Mating a homozygous susceptible (green) worm with a homozygous resistant (red) worm produces heterozygous (red and green) eggs and larvae. Heterozygous (red and green) worms mate to produce fully susceptible, fully resistant and heterozygous eggs and larvae. Fully resistant (red) worms can only produce **RESISTANT** eggs and larvae.

FACT CHECK:

- It is worms that are resistant to anthelmintics NOT the sheep.
- Resistant worms produce resistant offspring and is specific to a worm species
- A farm may have some resistant worm species while other species remain
- susceptible to the class of anthelmintic
- Testing efficacy of different anthelmintic classes at different times of year is
- necessary to provide an overall picture for a farm.
- Resistance is specific to an anthelmintic class. Resistance of a worm species to one
- class does not mean it is resistant to others. It is important to test anthelmintic
- efficacy to all the broad-spectrum classes.