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Parasitic disease of livestock is costly to the agriculture industry. It is estimated that losses resulting from nematode infections of beef and dairy cattle in the United States alone will reach the $600 million mark by the end of the decade. Farmers try to prevent losses by administering anthelmintic drugs, which are expensive, and through pasture rotation, which is labor intensive. An added problem is that some parasite populations are resistant to a number of commonly used anthelmintics.

Researchers, in the field and in the laboratory, have been studying means of controlling parasite infections for many years. Now, with the advent of powerful computers, these studies have taken on an added dimension. Computers can be used to develop mathematical models which can examine different means of parasite control. "We can use mathematical models of parasite population biology to see how the disease status of the infected livestock alters in time and space," explained Dr. Gary Smith, assistant professor of population biology and epidemiology at the University of Pennsylvania School of Veterinary Medicine. "Such models also allow us to examine different strategies for parasite control before they are tested in the field."

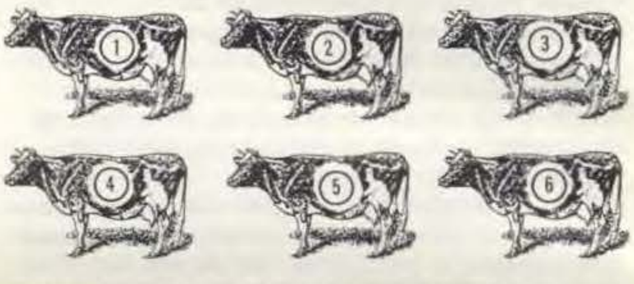
Dr. Smith pointed out that the modeling technique is the same whether the researcher is dealing with macroparasites (roundworms, tapeworms, flukes) or microparasites (viruses, bacteria, protozoa). "In the case of parasitic disease caused by worms, we construct an equation for each stage in the life cycle and simulate the course of infection during a grazing season for specific climatic conditions. We know the time needed for the development of infectious larvae, how long they can survive in the pasture, and bow long it takes the worm to reach adulthood once ingested. To study the effect of an anthelmintic drug, we can alter the equations to reflect the drug's action on specific stages of the parasite and then determine the likely reduction in worm burden."

One such study examined different protocols to combat *Ostertagia ostertagia* (stomach worm) infection in grazing calves and yearlings in Europe and temperate regions in North America. Normally, the infection peaks in August and September and declines on its own, without drug intervention. "Traditionally farmers used to wait until the cattle showed signs of disease before treating them with anthelmintic drugs," said Dr. Smith. "Such a regimen works but requires repeated administration of the drug." The computer model simulated six protocols: a) no anthelmintic therapy; b) therapeutic administration of anthelmintic A at the time of peak infection; c) prophylactic administration of A at three, six, and nine weeks after turnout to pasture; d) movement of calves to a second pasture immediately following a prophylactic dose of anthelmintic A; e) prophylactic administration of anthelmintic B three and eight weeks after turnout to pasture; and f) prophylactic administration of anthelmintic C via an intraruminal time release device (bolus), which releases effective quantities of the anthelmintic for 80 to 100 days.

The model generated information demonstrating the impact of the various protocols on the worm burden in the cattle. All the prophylactic protocols (c to f) significantly reduced the worm burden at midsummer. Dr. Smith pointed out that these protocols work by reducing the number of infectious larvae in the pasture. "The model allows us to study an approach in detail without doing a field study," he said. "It allows us to think about different approaches and examine the problem in depth prior to embarking on a field study." The model did not examine the costs of treatment and the financial return realized by the use of each of the different protocols.

Resistance to drugs is a big problem in parasite control. "Drug resistance is highest where long-term routine dosage is practiced," said Dr. Smith. "Resistance typically appears within ten to 50 generations of the routine application of a drug." It appears that parasites are always one step ahead of the drug companies. Resistance is a vexing problem for horse owners, as seven out of ten of the small strongyles have demonstrated drug resistance. Australian sheep farmers also have tremendous difficulties with drug-resistant sheep nematodes, which reduce the yield of wool and meat significantly. It is important to slow down the spread of such resistant strains, and mathematical models can help. "We suspect that within each parasite population there may be individuals which are wholly resistant, not resistant, and partly resistant. If we assume that the wholly resistant and the non-resistant strains are homozygous for the trait and that the partly resistant strain is heterozygous, we can develop a model for each of these populations and can investigate when resistance is likely to appear." The model then can be used to determine the most efficient method of utilizing a drug without encouraging the rapid spread of resistant strains.

Dr. Smith pointed out that parasite populations are regulated by a number of natural processes. "For example, cattle will develop a natural immunity during each grazing season, and this causes a decrease in the worm burden later in the season." Dr. Smith is incorporating these natural regulatory processes in his models since they influence drug strategies. "The natural regulatory processes render the host-parasite system more or less refractory to perturbation, and so they tend to oppose the effects of anthelmintics."

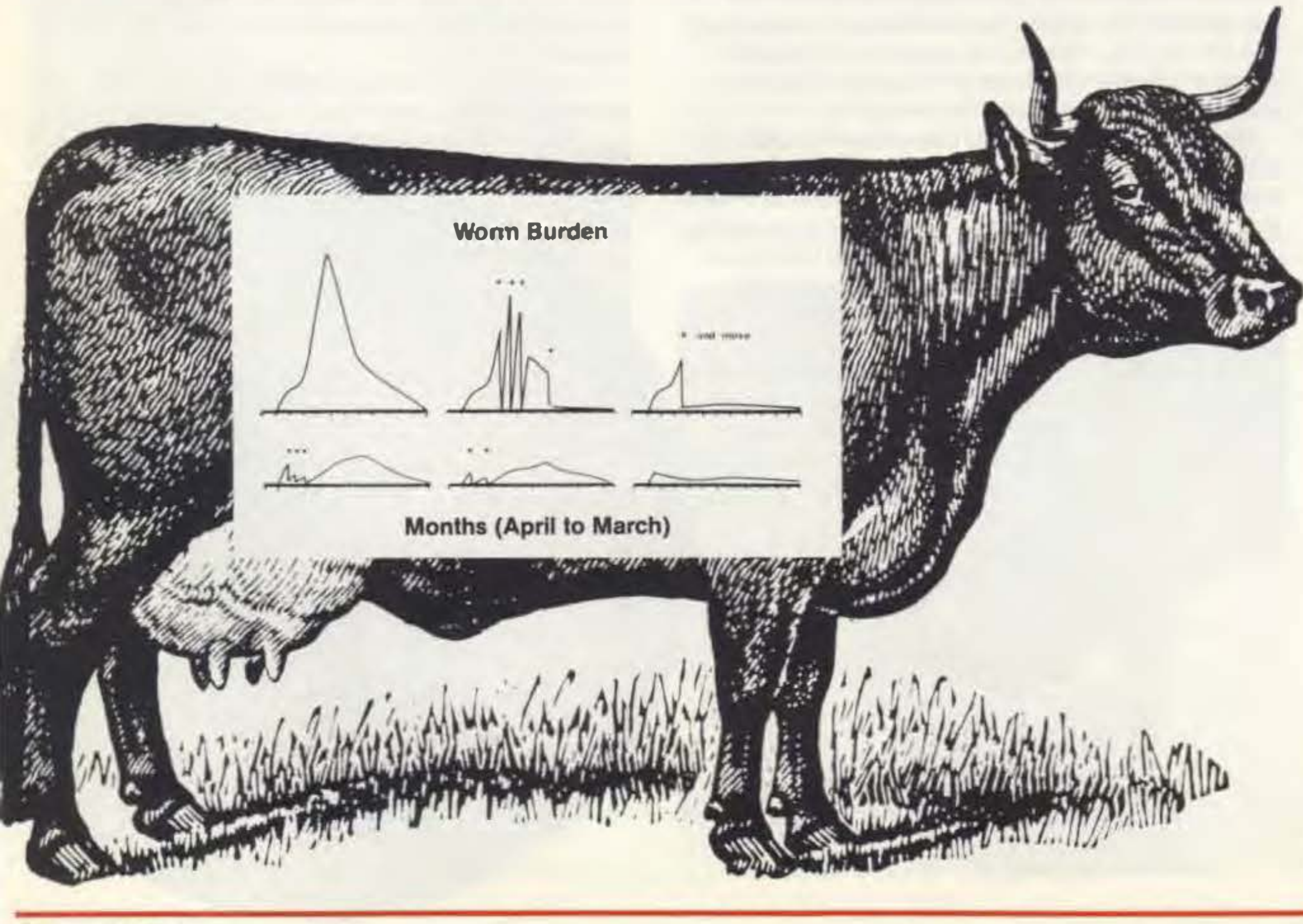


Use of mathematical models can reduce the number of field tests and make these more efficient. Such models also reduce the number of animals needed for field studies, though they will not entirely eliminate the need to use animals in such studies. "The model frees the researcher from the need to think about three or four things at once. Each variable and its impact can be examined methodically in a controlled situation without using animals. In essence, a model can be a rehearsal for a field study with animals, making the field study much more efficient."

Mathematical models can also be used to examine vaccination strategies prior to field testing. For example, it is possible to determine the number of vaccinated animals needed to halt the spread of an infectious disease such as rabies.

The economic benefits of a given strategy can also be examined using models. "We hope to be able to estimate the expected return from specific protocols and so assess the specific worth of veterinary intervention together with the risks involved." Dr. Smith is collaborating with Dr. David Galligan in the development of such a model.

Dr. Smith is a member of the Center for Animal Health and Productivity at New Bolton Center, and his research is funded by a grant from the Pennsylvania Department of Agriculture. He came to Penn from England in 1986.



Effects of protocols (a) to (f) on the average number of worms (*O. ostertagia*) per calf. Top left to bottom right, protocol (a), no treatment, to protocol (f), time release bolus.