Uncelebrated impacts of Nobel Prize-winning avermectins

Authors: Johannes Charlier1*, Georg von Samson-Himmelstjerna2, Eric Morgan3, Laura Rinaldi4, Johan Höglund5, Diana Williams6, Smaragda Sotiraki7, Edwin Claerebout8, Jozef Vercruysse9

Affiliations:
1 Avia-GIS, Risschotlei 33, 2980 Zoersel, Belgium.
2 Institute of Parasitology and Tropical Veterinary Medicine, Freie Universität Berlin, Robert-von-Ostertag-Str. 7-13, 14163 Berlin.
3 School of Veterinary Sciences, University of Bristol, Langford House, Langford, Bristol BS40 5DU, United Kingdom.
4 Department of Veterinary Medicine and Animal Productions, University of Naples Federico II, Via della Veterinaria 1, 80137 Napoli, Italy.
5 Department of Biomedical Sciences and Veterinary Public Health, Section for Parasitology, Swedish University of Agricultural Sciences (SLU), P.O. Box 7009, SE-750 07, Uppsala, Sweden.
6 Institute of Infection and Global Health, University of Liverpool, 146 Brownlow Hill, Liverpool, L3 5RF, United Kingdom.
7 Veterinary Research Institute, Hellenic Agricultural Organisation-Demeter, NAGREF Campus, 57001 Thessaloniki, Greece
8 Department of Virology, Parasitology and Immunology, Faculty of Veterinary Medicine, Ghent University, Salisburylaan 133, 9820 Merelbeke, Belgium.
9 Ghent University Global Campus, Incheon Global Campus Foundation, 119 Songdomunhwa, Yeonsu-Gu, Incheon, South Korea.

* Correspondence to:
J Charlier
jcharlier@avia-gis.com
Tel: +32 3 458 29 79
Abstract:
This year’s Nobel Prize in Physiology and Medicine goes to scientists that have revolutionized the treatment of parasitic diseases in the world’s poorest populations through the discovery of the avermectin drugs. However, the enormous impact these discoveries have in the world’s developed as well as developing regions through parasite control in animals is underestimated. Roundworm infections are a highly significant problem in livestock production around the world and efficacious treatment – through avermectins - contributes significantly to efficient production methods and food security. In companion animals, these same drugs are widely used for preventing the establishment of major zoonotic pathogens, thus reducing the disease risk for humans. There are also undesired consequences of intensive reliance on avermectins, the most important arguably being selection for resistant worm populations. Now that avermectins are applied at unprecedented scales on whole human populations, exchange of knowledge on best practice between veterinary and human medicine may improve the wellbeing of millions of people.

Main Text:
The 2015 Nobel Prize in Physiology and Medicine goes to scientists, who have revolutionized the treatment of parasitic diseases.\(^1\) After decades of global neglect, parasitic infections and the major problems they pose to global health are receiving the attention they deserve. This is corroborated by the renewed emphasis on these ‘neglected tropical diseases’ by the World Health Organization (WHO), the major focus that eradication of these diseases represents within the objectives of the Bill & Melinda Gates Foundation and now – the cherry on the cake - the Nobel Prize in Medicine. As mentioned in the official press release of the Nobel Prize Committee, “parasitic diseases affect the world's poorest populations and represent a huge barrier to improving human health and wellbeing”.
In the communications however, little to nothing is mentioned on the enormous impact the discoveries, recognized by the award, have also had in the so-called developed and more temperate regions, including Europe and the U.S.A. through parasite control in animals.\(^2\)
The drug – avermectin, a macrocyclic lactone - which William C. Campbell and Satoshi Ōmura discovered back in 1976 was, in fact, first used to control roundworm and other parasitic infections in livestock and companion animals.\(^3\) Unlike in humans, where only one derivative of this class of drug is currently available (ivermectin) and where this drug is typically given orally, in animal health, six other macrocyclic lactones have been developed and are today routinely applied in different formulations (i.e. oral, injection and topical treatment).\(^4\) These molecules have rapidly revolutionized parasite control in animals. For the first time, a single substance class that was safe, efficacious and easy to use against the majority of important endo- and ectoparasites of all livestock and companion animals was available.
Roundworm infections are a common and important problem in livestock production around the world. They usually do not provoke a risk for human health but impact on the production efficiency of the livestock sector. Current global trends including more outdoor ranging farm systems and increasing farm sizes as well as climate change are increasing the risk of parasitic disease.\(^5\) Since their first commercialization in 1981, veterinary science has developed strategic approaches to use these drugs in such way that they improved animal health and welfare and reduced the associated economic losses. As a result, clinical disease due to roundworm infections has become rare and this is considered as one of the success stories in animal health. Their strategic use
improves the production efficiency of meat, milk and animal fibre products and reduces green house gas emissions from livestock production by around 10% (Fig. 1). Although difficult to assess, this prevents economic losses which are likely to run into billions of dollars annually.

Less considered is that in the world’s developing regions, livestock parasites also profoundly affect human health. In subsistence economies, livestock plays a fundamental role in the production of food and generation of income. There have been recent calls for the need and opportunity to reduce poverty by greater investment in animal health. Also in companion animals ivermectin and related drugs have become critical in preventing the establishment of major zoonotic pathogens such as ascarid and filarial worms, thus reducing the disease risk for humans.

Veterinary science has also encountered the downsides of intensive use of these drugs. Reliance on the avermectins has selected resistant worm populations that are no longer killed and are now a real threat to sustainable livestock farming. Usage may also lead to leakage of bioactive residues in the environment which can reduce biodiversity by killing susceptible micro-fauna such as dung beetles. Consequently, current research is developing more sustainable, yet economically viable control methods based on a “diagnosis before treatment” philosophy and adopting selective anthelmintic treatment solutions.

The extensive experience that veterinary scientists have acquired with the macrocyclic lactone drugs is welcomed by the public health community now that the drugs are distributed on an unprecedented scale and applied in mass treatment delivery to whole human populations. This exchange of knowledge across disciplines, and learning the appropriate lessons from livestock, has helped to foresee the problems and may improve the health and wellbeing of millions of people.

The impact on society of these unique drugs is thus not only through the direct reduction of parasitic diseases in humans, but also through the reduction of these diseases in companion animals and livestock. Future benefits should be reinforced by a One Health approach uniting veterinary and human medicine.

Acknowledgements
This comment stems from discussions at the Livestock Helminth Research Alliance (LiHRA).

Reference and Notes:


**Fig 1.** Illustration of a roundworm infection, impacting the productivity of a dairy cow.