

# STANDARD DEVIATIONS: A Worm and Baloney Sandwich

Greetings,

Got head lice? Maybe headed to a country endemic for River Blindness? Or, perhaps, your pet Appaloosa is complaining of pinworm, lungworm, or intestinal hairworm?

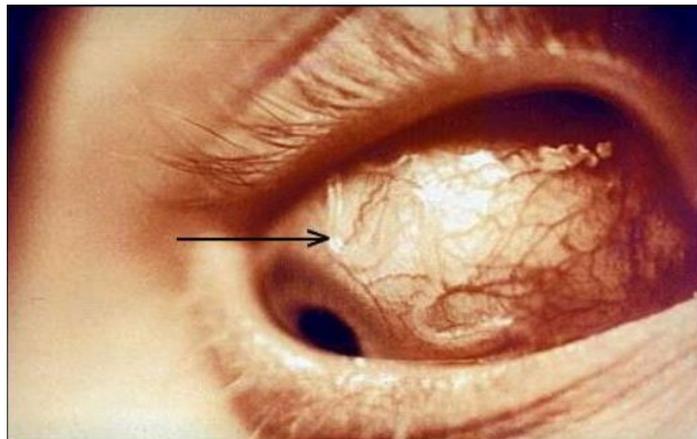
You need **ivermectin!** STAT!

Looking for a COVID-19 remedy? Yeah, not so much.

What's the deal here? What is this drug and why do folks think the antiparasitic is also antiviral?

Ivermectin is the commercial drug (Merck) of compounds known as avermectins (*Lat, a + vermis*, "without worms"). They were isolated from *Streptomyces* bacteria in Japan (1970) and shown to kill roundworms in mice. This led to a 2015 Nobel in Medicine for Satoshi Ōmura, a Japanese biochemist, and William Campbell, at Merck.

Ivermectin has been used safely by *hundreds of millions* of people to treat [onchocerciasis](#) (river blindness), [lymphatic filariasis](#) (elephantiasis), and other parasitic maladies. It is a common prescription for treating heartworm in pets and helminth (worm) parasites of livestock (for years, *ivermectin was the bestselling veterinary medicine in the world*). It's on the WHO List of Essential Medicines and FDA approved as an antiparasitic. Besides helminths, it is also used to treat infection with parasitic arthropods (i.e., mites in scabies and lice).



{River Blindness}





{Elephantiasis}

These are fairly large compounds that act by interfering with nerve and muscle function of helminths and insects. They bind and block anion transport ([chloride channels](#)) across the membranes of invertebrate nerve and muscle cells. Ivermectin blocks the gate open and the unrestricted flow of anions hyper-polarizes the cell membrane, wreaking all kinds of havoc and paralyzing the tissue which leads to death of the invertebrate.

In mammals, these specific anion channels only occur in brain and spinal cord and are protected by the blood-brain barrier. Most vertebrates (fungi and bacteria, too) have a glycoprotein efflux pump that can kick these molecules out. Now, **if you dump enough ivermectin into a dosage it will saturate the pump, cross the barrier, and affect the tissue. This is where people are getting into trouble when they take dosages that are meant for large equines.**

{Okay, here is a little sidebar. This efflux pump, P-glycoprotein, is not found in the tortoise. You'll kill a tortoise with ivermectin.}

So, at *recommended* doses, ivermectin kills the parasite but does not cross the blood-brain/testis barrier. In endemic areas the drug must be taken repeatedly to constantly suppress infection. For insects, adult mites die but the nits/eggs have to be treated again and again as they hatch.

What's the COVID connection?

Researchers are always looking to re-purpose (drug repositioning) compounds that show promise against other pathogens. SARS-CoV2 is certainly no exception. *In silico* modeling leads to *in vitro* experimentation leads to *in vivo* investigation (i.e., hydroxychloroquine, dexamethasone, Remdesivir, Valproic Acid, etc.). The thinking is that ivermectin disrupts the viral hijacking of the cellular transcription process by inducing conformational changes that prevent [nuclear import](#) of key viral and host proteins, stopping viral replication. The actual mechanism is not fully understood.



In April of 2020 a [study](#) found that ivermectin inhibited SARS-CoV2 replication *in vitro*. This finding jump-started a bunch of **small** clinical trials. *None have been statistically significant in showing efficacy*. Several “meta-analysis” studies have popped up on different [websites](#) that do not include critical information about the data (methods, inclusion criteria, quality assessment, etc.). One meta-analysis study was [withdrawn](#) following evidence of data fabrication and plagiarism. Another was pushed in pre-print that claimed the data showed ivermectin dramatically reduced mortality in COVID-19 patients. Peer review questioned the findings and the paper was [retracted](#), but social media [promotion](#) and government authorization in Latin America has caused a huge spike in people taking ivermectin, at dangerous dosages.

(Okay, here is another sidebar. The same group retracting their ivermectin study was responsible for initially promoting [hydroxychloroquine](#) (and then [also retracting that study](#)); and one of the authors is an adjunct faculty member at the University of Utah.)

Despite the lack of evidence to suggest any efficacy and advice to the contrary, some governments have allowed its off-label use for prevention and treatment of COVID-19. Peru and India have since rescinded their approval, but Mexico, Slovakia, and the Czech Republic still okay it. A black market has evolved in countries where official approval has not been granted.

This month (September, 2021) US health experts expressed concerns from reports of sharp increases in outpatient prescribing and dispensing of ivermectin with respect to levels before the pandemic. The CDC has not authorized or approved ivermectin for the prevention or treatment of COVID-19. Ivermectin is not approved by the U.S. Food and Drug Administration (FDA) for use in treating *any* viral illness and is not authorized for use to treat COVID-19 within the European Union. Self-medication with a concentrated formula intended for horses has led to a bunch of serious hospitalizations.

Ivermectin earned the title of "wonder drug" for the treatment of nematodes and arthropod parasites. Its *in vitro* antiviral characteristics are being studied with chikungunya and yellow fever, and its toxicity to malaria plasmodium and the mosquito are promoting investigation. There are still clinical trials for COVID-19 being performed with ivermectin that may change our understanding.

The problem with using ivermectin as a treatment for COVID-19 is that it is not the intended use; it's not Standard Operating Procedure. Yes, for its intended purpose it is a “wonder drug”. For this un-intended use, *it's a risk*. Until any(?) antiviral properties are understood, we simply don't have good guidance on its efficacy or dosages, and we're seeing harm as a result of misuse. In our line of work, always following SOP keeps us safe on the bench, and straying from SOP leads to trouble; this is an Administrative Control for biosafety. Until large clinical trials can show efficacy and safety, we should stick to the SOP for ivermectin.

Have a great week and be safe,

Bryan

