## Doctors, Do no Harm?

The AMA and Wisconsin Physicians Association have objected to court-ordered use of Ivermectin for COVID-19. Yup, a doctor in Wisconsin proscribed Ivermectin to a COVID patient who was not responding to other treatments. The patient got court approval for the treatment. Now the AMA together with WPA are arguing, on appeal, against the use of Ivermectin as a treatment.

## FACTUAL BACKGROUND

Ivermectin tablets were approved by the FDA in 1996 for reducing malaria transmission and to treat people with intestinal strongyloidiasis and onchocerciasis, two conditions caused by parasitic worms. In addition, some topical forms of Ivermectin are approved to treat external parasites like head lice and for skin conditions such as rosacea. Ivermectin has been in use worldwide for over 25 years with. Reported side effects include fever, pruritus, and skin rash, but no deaths reported. Ivermectin has been approved for "off label use", which allows a doctor to proscribe for other uses then the approved one. Just like aspirin in the 1950's.

The FDA (and World health Organization for Malaria) used worldwide research when they approved Ivermectin as a broad spectrum anti-parasitic agent, citing several authorities:

One major study (Gonzalez Cangas et al., 2008) has shown Ivermectin to have anti-viral activity against a broad range of viruses (Gotz et al., 2016; Lundberg et al., 2013; Tay et al., 2013; Wagstaff et al., 2012) in vitro. Originally identified as an inhibitor of interaction between the human immunodeficiency virus-1 (HIV-1) integrase protein (IN) and the importin (IMP)  $\alpha/61$  heterodimer responsible for IN nuclear import (Wagstaff et al., 2011), Ivermectin has since been confirmed to inhibit IN nuclear import and HIV-1 replication (Wagstaff et al., 2012). Other actions of ivermectin have been reported (Mastrangelo et al., 2012), but ivermectin has been shown to inhibit nuclear import of host (e.g. (Kosyna et al., 2015; van der Watt et al., 2016)) and viral proteins, including simian virus SV40 large tumour antigen (T-ag) and dengue virus (DENV) nonstructural protein 5 (Wagstaff et al., 2012, Wagstaff et al., 2011). Importantly, it has been demonstrated to limit infection by RNA viruses such as DENV 1-4 (Tay et al., 2013), West Nile Virus (Yang et al., 2020), Venezuelan equine encephalitis virus (VEEV) (Lundberg et al., 2013) and influenza (Gotz et al., 2016), with this broad spectrum activity believed to be due to the reliance by many different RNA viruses on IMP $\alpha/61$ during infection (Caly et al., 2012; Jans et al., 2019). Ivermectin has similarly been shown to be effective against the <u>DNA virus pseudorabies virus</u> (PRV) both in vitro and in vivo, with ivermectin treatment shown to increase survival in PRV-infected mice (<u>Lv et al.</u>, <u>2018</u>). Efficacy was not observed for ivermectin against <u>Zika virus</u> (ZIKV) in mice, but the authors acknowledged that study limitations justified re-evaluation of ivermectin's anti-ZIKV activity (<u>Ketkar et al., 2019</u>). Finally, Ivermectin was the focus of a phase III clinical trial in Thailand in 2014–2017, against DENV infection, in which a single daily oral dose was observed to be safe and resulted in a significant reduction in serum levels of viral <u>NS1 protein</u>, but no change in <u>viremia</u> or clinical benefit was observed (see below) (<u>Yamasmith et al., 2018</u>).

The case before the courts concerns a terminal ill COVID-19 patient who is not responding to other typical treatments. The doctor in question proscribed Ivermectin but the hospital refused. The patient family got a court order for the hospital to administer the drug. The AMA, Wisconsin Physicians Association and hospital have appealed that order in opposition saying Ivermectin is unsafe to administer to COVID-19 patients. A position exact opposed to the FDA, World Health and a multitude of studies. In real life, India continues to provide Ivermectin to its general population free of charge. They have great success combating early symptom of COVID-19.

So again, why would anyone oppose the use without proof or factual findings? Could it be because Ivermectin was recommended by President Trump? A President's view who the AMA and WPA have open contempt and hostility towards. A small group of people filled with so much hate they are willing to forsake their Hippocratic Oath of "Do no harm".

Sadly, the patient has now died. He was never given the Ivermectin.

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