

Ivermectin for Covid-19

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Discussion of scholar papers published until June 20, 2020, on Ivermectin, and of news that we can find about its use for Covid-19. A list of clinical trials is also given. For what concerns scholar papers, we report among them a preprint posted on 10 June in MedRxiv, which concludes that Ivermectin was associated with lower mortality during treatment of Covid-19. From news, we consider in particular the case of Iquitos, capital city of the Loreto Region in Peru, where, by May 25, Covid-19 cases and deaths had dropped notably.

Torino, June 20, 2020 - Version 5 ¹- 10.5281/zenodo.3902051

In [1], an article which is discussing the drugs used in Italy for the treatment of Covid-19, we mentioned the Ivermectin. In [1], published on 9 May 2020, we reported the news "Novità positive su Remdesivir e altri farmaci COVID-19/Farmaci", dated 7 May and written by Ernesto Carafoli and Enrico Bucci, archived <http://archive.is/YdIqh>. There it is told that "L'ultimo farmaco giunto sulla scena del Covid-19 che vale la pena di citare è l'Ivermectina: un antiparassitario noto per la sua attività antivirale a largo spettro usato anche in terapia umana per affezioni dermatologiche. Un interessante studio australiano ha dimostrato che la sua aggiunta a cellule infettate con SARS_CoV-2 riduce in 48 ore il livello dell'RNA infettante di 5000 volte. Tuttavia, bisogna considerare alcune obiezioni che sono state sollevate, prima di essere sicuri che abbia senso iniziare dei trial su questo composto, come peraltro sembra si voglia fare in Francia". That is, the latest drug that arrived on the Covid-19 scene, and which is worth mentioning, is Ivermectin. This drug is a pesticide known for its broad-spectrum antiviral activity and also used in human therapy for dermatological diseases. An interesting Australian study has shown that its addition to SARS_CoV-2 infected cells reduces the level of infectious RNA in 48 hours by 5000 times. However, it is necessary to consider some objections that have been raised, before being sure that it makes sense to start trials on this compound, as it seems to want to do in France.

Let us see the scholar papers published until now on Ivermectin and the news that we can find about its use for Covid-19. For what concerns scholar papers, we also report a preprint posted on 10 June in MedRxiv which concludes that Ivermectin was associated with lower mortality during treatment of COVID-19. From news, we consider in particular the case of Iquitos, Peru. In this city, by May 25, Covid-19 cases and deaths had dropped notably.

Nobel Prize

Before discussing literature and news, let us remember the extraordinary history of the drug.

Ivermectin is a drug derived from avermectin. Actually, avermectin is a series of drugs and pesticides used to treat parasitic worms and insect pests. Its molecules are naturally occurring, being generated as fermentation products by *Streptomyces avermitilis*, a soil actinomycete. Half of the

¹ Version 1 10.5281/zenodo.3893751 Jun 14, 2020; Version 2 10.5281/zenodo.3894839 Jun 14, 2020; Version 3 10.5281/zenodo.3900122 Jun 18, 2020; Version 4 10.5281/zenodo.3900336 Jun 18, 2020

2015 Nobel Prize in Physiology or Medicine was awarded to William C. Campbell and Satoshi Ōmura, for discovering ivermectin, the derivatives of which have drastically lowered the incidence of river blindness and lymphatic filariasis. The other half of the prize was awarded to Tu Youyou for her discoveries concerning a novel therapy against Malaria. <http://archive.is/JMRhi>

Scholar literature

In the above-mentioned article written by Carafoli and Bucci, it is told of an interesting Australian study concerning the drug. This study is published in [2].

Ref. 2 is the origin of researches, trials and use of Ivermectin. The authors - Caly, L., Druce, J., Catton, M., Jans, D. & Wagstaff, K. - tell that this drug, an FDA-approved anti-parasitic, which has previously shown to have broad-spectrum anti-viral activity in vitro, "is an inhibitor of the causative virus (SARS-CoV-2), with a single addition to Vero-hSLAM cells 2 h post infection with SARS-CoV-2 able to effect ~5000-fold reduction in viral RNA at 48 h. **Ivermectin therefore warrants further investigation for possible benefits in humans**".

However, some objections exist. We can find them given in [3]. In the abstract it is told that "Caly, Druce [2] reported that ivermectin inhibited SARS-CoV-2 in vitro for up to 48 h using ivermectin at 5 μ M. The concentration resulting in 50% inhibition (IC₅₀, 2 μ M) was >35x higher than the maximum plasma concentration (C_{max}) after oral administration of the approved dose of ivermectin when given fasted". Authors of [3] conclude that "The likelihood of a successful clinical trial using the approved dose of ivermectin is low. Combination therapy should be evaluated in vitro. Re-purposing drugs for use in COVID-19 treatment is an ideal strategy but is only feasible when product safety has been established and experiments of re-purposed drugs are conducted at clinically relevant concentrations".

In [4], abstract tells that "Ivermectin plays a role in several biological mechanisms, therefore it could serve as a potential candidate in the treatment of a wide range of viruses including COVID-19 as well as other types of positive-sense single-stranded RNA viruses. In vivo studies of animal models revealed a broad range of antiviral effects of ivermectin, however, clinical trials are necessary to appraise the potential efficacy of ivermectin in clinical setting".

In [5], it is told that "potential drugs like hydroxychloroquine, ivermectin and azithromycin have been tested by diverse group of researchers worldwide for their potential against novel coronavirus". The authors of [5] are proposing a report derived from the major researches about the above-mentioned drugs. "Hydroxychloroquine and ivermectin were known to act by creating the acidic environment and inhibiting the importin (IMP α / β 1) mediated viral import. Azithromycin was found to act similar to the hydroxychloroquine as an acidotropic lipophilic weak base. All the three categories of drugs seemed to potentially act against novel coronavirus infection. However, their efficacies need to be studied in detail individually and in combination in-vivo in order to combat COVID-19 infection".

Ref.5 illustrates the action of Ivermectin, as we can also find in Ref.2.. "SARS-CoV-2 (causative agent of COVID-19) is a single stranded RNA virus (positive sense) which is closely related to SARS coronavirus (SARS-CoV). Recent study on ivermectin against SARS-CoV-2 under in vitro conditions revealed that it can inhibit the viral replication. The single treatment of this drug was able to reduce the virus up to 5000-fold in culture within 48h. However, no further reduction was reported with further increase in time period i.e up to 72h. Moreover, no toxicity was seen with the drug at any point of time" [2]. "Mechanism by which ivermectin responded against the CoV-19 virus is not known and was believed to be working similarly as it acted on other viruses. It was known to inhibit the nuclear import of viral and host proteins. Integrase protein of viruses and the importin (IMP) α / β 1 heterodimer was responsible for IN nuclear import which further increases the infection. As most of the RNA viruses are dependent upon IMP α / β 1 during infection, Ivermectin acts on it and inhibits the import with the increase in antiviral response" [2,6].

In Ref.7 the authors report, as [2] and [5], that the "antiviral potential of ivermectin against various viruses is mediated via the targeting of the following: importin α/β -mediated nuclear transport of HIV-1 integrase and NS5 polymerase; NS3 helicase; nuclear import of UL42; and nuclear localization signal-mediated nuclear import of Cap. As SARS-CoV-2 is an RNA virus, the antiviral activity of ivermectin may be mediated through the inhibition of importin α/β -mediated nuclear transport of viral proteins. The clinical efficacy and utility of ivermectin in SARS-CoV-2-infected patients are unpredictable at this stage, as we are dealing with a completely novel virus".

In [7], it is told that it "has also been hypothesized that combination therapy using hydroxychloroquine and ivermectin may exert a synergistic inhibitory effect on SARS-CoV-2. In this combination, hydroxychloroquine acts by inhibiting the entry of SARS-CoV-2 into the host cells, whereas ivermectin further enhances the antiviral activity by inhibiting viral replication" [8].

In [9], we find an article proposing "an alternative mechanism of action for this drug [Ivermectin] that makes it capable of having an antiviral action, also against the novel coronavirus, in addition to the processes already reported in literature".

In [10], the dosage of Ivermectin is considered. "Caly et al. report a 5,000-fold reduction in SARS-CoV-2 RNA levels, compared with those in controls, after infected Vero/hSLAM cells were incubated for 48 hours with 5 μ M ivermectin. ... Pharmacokinetic studies in healthy volunteers have suggested that single doses up to 120 mg of ivermectin can be safe and well tolerated. However, even with this dose," which is quite greater than those approved by the US FDA we are "one order of magnitude lower than effective in vitro concentrations against SARS-CoV-2. These findings may seem to discourage follow-up clinical trials with ivermectin. However, some in vivo effect may be possible even if efficacious in vitro concentrations are physiologically unattainable. ... Until we have a better understanding of ivermectin's antiviral mode of action and of appropriate in vitro systems for testing, we caution against using findings in Vero cells as more than a qualitative indicator of potential efficacy". The authors continue telling that they "believe the recent findings regarding ivermectin warrant rapidly implemented controlled clinical trials to assess its efficacy against SARS-CoV-2. These trials may open a new field of research on the potential use of avermectin antiparasitic drugs, including compounds with an improved pharmacokinetic profile, as antivirals". The authors are pointing out some points, that need to be considered "before testing ivermectin in severe disease". Three of the authors of [10] are involved in trial [11].

Ref. 12 is a systematic review of the antiviral effects of Ivermectin. "Several studies reported antiviral effects of ivermectin on RNA viruses such as Zika, dengue, yellow fever, West Nile, ... Furthermore, there are some studies showing antiviral effects of ivermectin against DNA viruses". Playing a role in several biological mechanisms, Ivermectin "could serve as a potential candidate in the treatment of a wide range of viruses including COVID-19 as well as other types of positive-sense single-stranded RNA viruses. In vivo studies of animal models revealed a broad range of antiviral effects of ivermectin, however, clinical trials are necessary to appraise the potential efficacy of ivermectin in clinical setting".

In [13], we find told that "There are many common observations between COVID-19 and dengue. Elevated levels of ferritin, interleukin-6 (IL-6), vascular endothelial growth factor (VEGF), D-dimer, coagulopathy, urticaria and ARDS are reported in both diseases. There are many indicators that mast cell degranulation and histamine release may have a major role in COVID-19 and dengue severity. Mast cell stabilizers, antihistamines, Vitamin C, HCQ, azithromycin, ivermectin may address different aspects of this cascade and thus reduce disease severity. Disease mechanisms and immunopathology must be understood. Focusing on anti-viral action of drugs alone could be counter productive. For example, CQ had no effect on viraemia but decreased cases of DHF".

In [14], "the in vitro antiviral activity end-points are analyzed from the pharmacokinetic perspective. The available pharmacokinetic data from clinically relevant and excessive dosing studies indicate that the SARS-CoV-2 inhibitory concentrations are not likely to be attainable in humans".

In [15], it is told that "Concerning the treatment outcome, adverse effect, and safety, IvermectinDoxycycline combination is a better alternative to Hydroxychloroquine-Azithromycin therapy in the case of mild to moderate degree of COVID19 patients. Though, both the treatment regimens were found to be effective in this study".

In [16], the results are the following. "The search of the databases led to the retrieval of 25 articles. After the different phases of the selection process, eight articles were included in the present review for the extraction of relevant data. The results suggest that ivermectin inhibits the viral replication of SARS-CoV-2 through the action of the hypoxia-inducible factor (HIF-1 α) and consequent destabilization of importin α/β 1 proteins. Conclusions tell that "Ivermectin inhibits the viral replication of SARS-CoV-2. Laboratory and clinical studies are needed to provide more evidence in terms of the best posology and possible associations with other drugs for combatting COVID-19".

Let us conclude this section with a report on the use of Ivermectin in Covid-19 patients [17]. It is a preprint posted on 10 June in MedRxiv.

In [17], the authors conclude that "Ivermectin was associated with lower mortality during treatment of COVID-19, especially in patients who required higher inspired oxygen or ventilatory support. These findings should be further evaluated with randomized controlled trials". Objective of [17]: "To determine whether Ivermectin is associated with lower mortality rate in patients hospitalized with COVID-19". Design and Setting are: "Retrospective cohort study of consecutive patients hospitalized at four Broward Health hospitals in South Florida with confirmed SARS-CoV-2. Enrollment dates were March 15, 2020 through May 11, 2020. Follow up data for all outcomes was May 19, 2020. Participants: 280 patients with confirmed SARS-CoV-2 infection (mean age 59.6 years [standard deviation 17.9], 45.4% female), of whom 173 were treated with ivermectin and 107 were usual care were reviewed".

Clinical trials

On June 20, 2020, we can find 27 clinical trials reported by ClinicalTrials.gov , at the following link <https://clinicaltrials.gov/ct2/results?cond=COVID&term=ivermectin+&cntry=&state=&city=&dist=>

For other trials about drugs for Covid-19, see [18].

In the following list, the date is that when the trial was first posted on ClinicalTrials.gov .

- 1) 13 April 2020 - Efficacy of Ivermectin as Add on Therapy in COVID19 Patients - Drug: Ivermectin (IVM) - Locations: General Directorate of Medical City, Bagdad, Baghdad, Iraq - <https://ClinicalTrials.gov/show/NCT04343092>
- 2) 4 May 2020 - Max Ivermectin - COVID 19 Study Versus Standard of Care Treatment for COVID 19 Cases. A Pilot Study - Drug: Ivermectin - Locations: Max Super Speciality hospital, Saket (A unit of Devki Devi Foundation), New Delhi, Delhi, India - <https://ClinicalTrials.gov/show/NCT04373824>
- 3) 19 May 2020 - Efficacy of Ivermectin in COVID-19 - Drug: Ivermectin 6 MG Oral Tablet (2 tablets) - Locations: Combined Military Hospital Lahore, Lahore, Punjab, Pakistan - <https://ClinicalTrials.gov/show/NCT04392713>
- 4) 27 May 2020 - Ivermectin and Doxycycline in COVID-19 Treatment - Drug: Ivermectin, Doxycycline, Chloroquine - Locations: Sherief Abd-Elsalam, Tanta, Egypt - <https://ClinicalTrials.gov/show/NCT04403555>
- 5) 9 June 2020 - Prophylactic Ivermectin in COVID-19 Contacts - Drug: Ivermectin Tablets - Locations: Zagazig University, Zagazig, Sharkia, Egypt - <https://ClinicalTrials.gov/show/NCT04422561>

- 6) 11 June 2020 - Ivermectin In Treatment of COVID 19 Patients - Drug: Ivermectin - Locations: isolation and referral hospitals for COVID 19 patients, Cairo, Egypt - <https://ClinicalTrials.gov/show/NCT04425707>
- 7) 17 April 2020 - The Efficacy of Ivermectin and Nitazoxanide in COVID-19 Treatment - Drug: Chloroquine, Nitazoxanide, Ivermectin - Locations: Tanta University, Tanta, Egypt - <https://ClinicalTrials.gov/show/NCT04351347>
- 8) 22 May 2020 - Ivermectin-Azithromycin-Cholecalciferol (IvAzCol) Combination Therapy for COVID-19 - Drug: Ivermectin, Azithromycin, Cholecalciferol - Locations: Outpatient treatment, Mexico City, Mexico - <https://ClinicalTrials.gov/show/NCT04399746>
- 9) 11 May 2020 - Ivermectin Effect on SARS-CoV-2 Replication in Patients With COVID-19 - Drug: IVERMECTIN (IVER P®) arm will receive IVM 600 µg / kg once daily plus standard care. CONTROL arm will receive standard care. - Locations: Centro de Educación Médica e Investigaciones Clínicas "Norberto Quirno" CEMIC, Buenos Aires, Ciudad De Buenos Aires, Argentina - <https://ClinicalTrials.gov/show/NCT04381884>
- 10) 5 May 2020 - Trial to Promote Recovery From COVID-19 With Ivermectin or Endocrine Therapy - Drug: Bicalutamide 150 Mg Oral Tablet|Drug: Ivermectin 3Mg Tab - Locations: Johns Hopkins Hospital, Baltimore, Maryland, United States - <https://ClinicalTrials.gov/show/NCT04374279>
- 11) 24 April 2020 - Ivermectin and Nitazoxanide Combination Therapy for COVID-19 - Combination Product: Ivermectin plus Nitazoxanide, Other: Standard Care - <https://ClinicalTrials.gov/show/NCT04360356>
- 12) 18 May 2020 - New Antiviral Drugs for Treatment of COVID-19 - Drug: Treatment group: will receive a combination of Nitazoxanide, Ribavirin and Ivermectin for a duration of seven days - Locations: Mansoura University, Mansoura, Select A State Or Province, Egypt - <https://ClinicalTrials.gov/show/NCT04392427>
- 13) 16 June 2020 - A Comparative Study on Ivermectin and Hydroxychloroquine on the COVID19 Patients in Bangladesh - Drug: Ivermectin + Doxycycline | Drug: Hydroxychloroquine + Azithromycin - Locations: Chakoria Upazilla Health Complex, Cox's Bazar, Bangladesh - <https://ClinicalTrials.gov/show/NCT04434144>
- 14) 12 June 2020 - Ivermectin vs. Placebo for the Treatment of Patients With Mild to Moderate COVID-19 - Drug: Ivermectin Oral Product - Locations: Sheba Medical Center, Ramat-Gan, Israel - <https://ClinicalTrials.gov/show/NCT04429711>
- 15) 18 May 2020 - Hydroxychloroquine and Ivermectin for the Treatment of COVID-19 Infection - Drug: Hydroxychloroquine, Ivermectin, Placebo - Locations: Jose Manuel Arreola Guerra, Aguascalientes, Mexico - <https://ClinicalTrials.gov/show/NCT04391127>
- 16) 28 May 2020 - Efficacy of Ivermectin in Adult Patients With Early Stages of COVID-19 - Drug: Ivermectin Oral Product, Placebo - <https://ClinicalTrials.gov/show/NCT04405843>
- 17) 29 May 2020 - Efficacy and Safety of Ivermectin and Doxycycline in Combination or IVE Alone in Patients With COVID-19 Infection. - Drug: Ivermectin + Doxycycline + Placebo, Ivermectin + Placebo, Placebo - <https://ClinicalTrials.gov/show/NCT04407130>
- 18) 15 May 2020 - Sars-CoV-2/COVID-19 Ivermectin Navarra-ISGlobal Trial - Drug: Ivermectin, Placebo - Clinica Universidad de Navarra, Pamplona, Navarra, Spain - <https://ClinicalTrials.gov/show/NCT04390022>
- 19) 17 June 2020 - Ivermectin vs Combined Hydroxychloroquine and Antiretroviral Drugs (ART) Among Asymptomatic COVID-19 - Drug: Ivermectin Pill, Combined ART/hydroxychloroquine - Locations: Siriraj Hospital, Bangkok Noi, Bangkok, Thailand - <https://ClinicalTrials.gov/show/NCT04435587>

- 20) 29 May 2020 - Efficacy, Safety and Tolerability of Ivermectin in Subjects Infected With SARS-CoV-2 With or Without Symptoms - Drug: Ivermectin, Placebo - <https://ClinicalTrials.gov/show/NCT04407507>
- 21) 11 May 2020 - Novel Regimens in COVID-19 Treatment - Drug: Nitazoxanide, Ivermectin, Chloroquine, Azithromycin - <https://ClinicalTrials.gov/show/NCT04382846>
- 22) 11 June 2020 - IVERMECTIN Aspirin Dexametasone and Enoxaparin as Treatment of Covid 19 - Drug: Ivermectin 5 MG/ML - Locations: Hospital Eurnekian, Buenos Aires, Argentina - <https://ClinicalTrials.gov/show/NCT04425863>
- 23) 11 June 2020 - USEFULNESS of Topic Ivermectin and Carrageenan to Prevent Contagion of Covid 19 - Device: iota carrageenan, Ivermectin - Locations: Hospital Eurnekian, Buenos Aires, Argentina - <https://ClinicalTrials.gov/show/NCT04425850>
- 24) 5 May 2020 - Novel Agents for Treatment of High-risk COVID-19 Positive Patients - Drug: Hydroxychloroquine|Drug: Hydroxychloroquine and Azithromycin, Hydroxychloroquine and Ivermectin, Camostat Mesilate - Locations: University of Kentucky Markey Cancer Center, Lexington, Kentucky, United States - <https://ClinicalTrials.gov/show/NCT04374019>
- 25) 14 June 2020 - A Real-life Experience on Treatment of Patients With COVID 19 - Drug: Chloroquine, Favipiravir, Nitazoxanide, Ivermectin, Niclosamide, Other drugs - Locations: Tanta university hospital, Tanta, Egypt - <https://ClinicalTrials.gov/show/NCT04345419>
- 26) 16 June 2020 - A Study to Compare the Efficacy and Safety of Different Doses of Ivermectin for COVID-19 - Drug: Ivermectin, Other: Standard treatment for COVID-19 - Locations: Hospital Univeristário da Universidade Federal de São Carlos (HU-UFSCar), São Carlos, São Paulo, Brazil - <https://ClinicalTrials.gov/show/NCT04431466>
- 27) 19 June 2020 - COVidIVERmectin: Ivermectin for Treatment of Covid-19 - Drug: Ivermectin - Other: Placebo - Locations: IRCCS Sacro Cuore Don Calabria hospital, Negrar, Verona, Italy, Policlinico S. Orsola, Bologna, Italy, Ospedale Luigi Sacco, Milan, Italy, Ospedale di Rovereto, Rovereto, Italy, Ospedale Amedeo di Savoia, Turin, Italy, Hospital Clinic/ISGlobal, Barcelona, Spain, Hospital La Paz-Carlos III, Madrid, Spain - <https://ClinicalTrials.gov/show/NCT04438850>

News

<https://worldhealth.net/news/> Anti Aging News-May 25, 2020 - Bangladesh Medical Team Claims Ivermectin With Doxycycline Clears COVID-19 - Archived <http://archive.is/wh6uE>

"A Bangladeshi medical team is claiming that their research on the combination of two widely used and common drugs has yielded positive results in clearing COVID-19 patients with acute symptoms of the disease. "We have got astounding results. Out of 60 COVID-19 patients, all recovered as the combination of the two drugs were applied", said Professor Dr Md Tarek Alam, the head of medicine department at private Bangladesh Medical College Hospital (BMCH). According to Alam who is a reputed clinician in Bangladesh the antiprotozoal medicine **Ivermectin** in combination with one dose of the antibiotic **Doxycycline** yielded the results of COVID-19 patients being cleared as being negative from the disease".

UNB NEWS DHAKA PUBLISH- JUNE 06, 2020, 06:21 PM UNB NEWS - UPDATE- JUNE 07, 2020, 10:35 AM - Covid-19: BMCH physician reports 'amazing results' using **ivermectin**, **Doxycycline**. It is not the patients who decide the medication, says Dr Tarek Alam - Archived <http://archive.is/A2rc2>

"Physicians from Bangladesh Medical College Hospital (BMCH), led by Dr Tarek Alam, claimed that a combination of the anti-parasitic drug '**ivermectin**' with antibiotic '**Doxycycline**' yielded

amazing results against Covid-19".

<https://www.thedailystar.net/> 12:00 AM, June 14, 2020 / LAST MODIFIED: 08:43 AM, June 14, 2020 - Use of **Ivermectin**: Hope held out, caution called for - Archived <http://archive.is/Hup01>

"Physicians at a Dhaka hospital claimed they have observed "cumulative efficacy" of **ivermectin** in Covid-19 patients while using the drug in combination with **doxycycline**. They said although they were yet to be certain about the exact efficacy of the drug combination, they would seek permission from Bangladesh Medical and Research Council (BMRC) for a clinical trial to know further about its effectiveness."

<https://www.trialsitenews.com/university-of-naples-federico-ii-physicians-hypothesize-why-not-try-hydroxychloroquine-ivermectin-in-combo-against-covid-19/> May 3, 2020- Archived <http://archive.is/yFsuG> "University of Naples Federico II Physicians Hypothesize: Why Not Try **Hydroxychloroquine & Ivermectin** in Combo Against COVID-19?"

"Two researchers/physicians out of the University of Naples Federico II—one of the oldest universities in the world—introduce the use of two drugs classically used by dermatologists for the investigational use in fighting SARS-CoV-2, the virus behind the COVID-19 pandemic. The two doctors hypothesize that the use of **Hydroxychloroquine** (HCQ) and **Ivermectin** may evidence a consequential and synergistic action if administered simultaneously both for chemoprophylaxis and treatment of COVID-19". Physicians are Dr. Angela Patri and Dr. Gabriella Fabbrocini.

<https://www.stampareggiiana.it> - 8 Aprile 2020 - Una novità importante è che oggi al San Raffaele inizia anche la sperimentazione di un nuovo farmaco, l'**IVERMECTINA**. Archived <http://archive.is/tqnX7>

"Il suo utilizzo [Ivermectina] è stato approvato in via sperimentale dall'AIFA, l'ente Italiano del farmaco". Dopo la nuncio della sua efficacia in vitro, "Adesso si ricerca la conferma clinica, si tratta di un farmaco da tempo usato contro la scabbia, i vermi ed altre malattie prodotte da parassiti la cui specifica modalità di azione è stata chiarita. Aumenta la concentrazione di cloro all'interno delle cellule che hanno specifici recettori, Covid 19 compreso. Questo fatto determina la paralisi e poi la morte del virus. Ora resta la rapida sperimentazione clinica autorizzata in Italia essendo uno dei paesi più colpiti".

<https://www.newsmax.com/us/> - Breakthrough Drug: **Ivermectin** Shows 'Astounding' Results Against Coronavirus - By David A. Patten | Friday, 22 May 2020 11:16 PM - Archived <http://archive.is/uqrxr>

"Doctors have administered the drug ivermectin in several simultaneous trials in several countries sometimes in combination with other common medications. Physicians who participated in the study report that patients' viral loads began declining almost immediately after they began administering ivermectin, a widely available prescription drug approved to combat parasites, scabies and head lice. ... Emergency medical physician Dr. Peter H. Hibberd, M.D., of Palm Beach County, Florida, told Newsmax Friday evening in an exclusive interview that he's optimistic the drug will prove to be an important therapeutic advance, although he expects more trials will be needed before it wins FDA approval for use as a COVID-19 medication. He noted it has impressed doctors in clinical trials on multiple continents. In some cases, doctors reported just one dose of ivermectin markedly improved a patient's condition. U. S. patients received a single oral dose, and some of them received a booster dose seven days later. The FDA-approved dose for parasitic infections was used. ... On Thursday, a team of U.S. doctors led by Dr. Jean-Jacques Rajter at the Broward Health Medical Center in Fort Lauderdale, Florida, submitted findings to an institutional review board. According to a medical source familiar with the study, some 250 coronavirus patients were involved in the Broward trial. The results were dramatic, with "statistically significant improvement in mortality," according to the source".

About the trial, see <https://www.trialsitenews.com/broward-county-doctor-using-ivermectin-off-label-combo-on-covid-19-patients-it-is-working-secures-county-health-protocol-approval/> Archived

<http://archive.is/IQSts> (See Ref.17).

<https://www.jpost.com/>- Israeli researcher: Antiparasitic drug could 'cure' coronavirus - JUNE 15, 2020 - Archived <http://archive.is/HADqB>

"Prof. Eli Schwartz launched a clinical trial of the drug **Ivermectin**, a broad-spectrum antiparasitic agent that has also been shown to fight viruses. A tropical disease expert is testing a drug used to fight parasites in third-world countries that he said could help reduce the length of infection for people who catch coronavirus, enabling them to go back to work and life in as little as a few days. ... "At the onset of this virus, everyone was talking about the anti-malaria drug," he said, referring to hydroxychloroquine, which was first touted by US President Donald Trump, but has since been linked to increased risk of death in coronavirus patients, among other health risks. "We decided to look more widely for other medications and considered a few drugs that might have antiviral activity," he said; Ivermectin was selected".

<https://www.trialsitenews.com/> - In Pursuit of Real-World **Ivermectin** Stories: Tales from Pathanamthitta JUN 17, 2020 - <http://archive.is/iWQu6>

<https://www.trialsitenews.com/> - 100-Year-Old Discharged from Mumbai's Rajawadi Hospital after Successful Ivermectin Treatment - UN 18, 2020- <http://archive.is/hkuON> - "Now apparently commonly in use in India, the medics at Rajawadi Hospital report that **Ivermectin** was the drug that actually worked, leading to the recent discharge of 100 year old Mr. Mali. It was to the thrill of all the staff to see this patient heal rapidly".

<https://www.the-scientist.com/> - 16 June 2020 - Surgisphere Sows Confusion About Another Unproven COVID-19 Drug - "The company behind a now-discredited study on hydroxychloroquine also posted a report that has been cited by Latin American governments recommending ivermectin as a possible coronavirus treatment. Clinicians there say the effects have been extremely damaging". <http://archive.is/G6JM6> .

This article is telling "One of the most influential studies on ivermectin's effect in COVID-19 patients was a large observational study that used a database owned by Surgisphere, a now-discredited Illinois-based company founded by vascular surgeon Sapan Desai. That study, published on the preprint server SSRN in early April and updated a couple weeks later, reported a strong positive association between ivermectin treatment and COVID-19 patient survival, and has been cited in white papers and reports by Latin American health researchers and governments as evidence of the drug's efficacy". The paper in SSRN is no more available. About it, see please the discussion by Carlos Javier Chaccour (he is running a clinical trial about ivermectin). <http://archive.is/d0VOd>

www.the-scientist.com/ is highlighting in the web page the following: "With ivermectin firmly entrenched in political and public minds as a weapon against the pandemic, the question of evidence is now of secondary importance for some members of the medical and scientific communities". Even if mitigated by a "some members", this is a serious accusation against these communities. Let us observe that the sentence of the-scientist concerning ivermectin, that is "firmly entrenched in political and public minds as a weapon against the pandemic", could have been applied to hydroxychloroquine too, the "Trump's 'miracle' drug", as defined in The Guardian, <http://archive.is/ToTiv> . About this drug, "Praised by presidents", see "Three big studies dim hopes that hydroxychloroquine can treat or prevent COVID-19", Jun 9, 2020, in Science, <http://archive.is/oVg7I>

<https://cnnespanol.cnn.com/> - **Ivermectina**, el arma sin validación científica que se usa en Bolivia para tratar covid-19 - Por Gloria Carrasco, CNN Publicado a las 16:23 ET (20:23 GMT) 29 mayo, 2020 Archived <http://archive.is/17R1Y>

"Bolivia incluyó a la ivermectina dentro de la lista de medicamentos esenciales para que pueda ser usada en el tratamiento de pacientes con covid-19. En el departamento de Beni, en el norte del país, hay una campaña para distribuir gratuitamente este medicamento entre los pobladores del municipio

de Trinidad".

<https://cnnespanol.cnn.com/> - 17:17 ET(21:17 GMT) 10 Junio, 2020 - Perú da impulso a **hidroxicloroquina** e **ivermectina** como tratamiento para covid-19 - Por Kiarinna Parisi Archived <http://archive.is/w8KLw> - Bolivia autoriza el uso de ivermectina contra covid-19 3:53

"El Ministerio de Salud de Perú (Minsa) dio impulso como tratamiento para el nuevo coronavirus a dos medicamentos que carecen de autorización por parte de autoridades sanitarias o de consenso científico sobre su eficacia y seguridad para pacientes de covid-19. ... Por su parte, la ivermectina es un agente antiparasitario de amplio espectro, aprobado por la Administración de Medicinas y Alimentos de Estados Unidos para ciertos usos en humanos y animales, aunque la prevención o tratamiento contra el coronavirus no es uno de ellos. A principios de mayo, dicha autoridad desaconsejó su uso asociado al covid-19 tras afirmar que se necesitaban más estudios al respecto".

12/6/2020 <https://www.eleconomistaamerica.pe/> "El hospital de San Juan de Lurigancho empezó a elaborar **ivermectina** para cubrir la demanda existente de este medicamento por parte de pacientes afectados por la COVID-19, que llegan al nosocomio que pertenece a la Dirección de Redes Integradas de Salud (Diris) Lima Centro, informó el Ministerio de Salud". Archived <http://archive.is/hak3F>

<https://exitosanoticias.pe/> - 13/6/2020 Dr. Fernández: "Si más peruanos tomaran **ivermectina**, habría menos casos de COVID-19" - Usar la Ivermectina es como ponerte un chaleco antibalas contra la enfermedad. En el Perú, más de 1 millón de personas la consumen, y nadie se ha muerto", indicó. Archived <http://archive.is/fusra>

¿Qué hace la Ivermectina en el cuerpo? "Evita que el virus se multiplique en las células. Por eso, la **Ivermectina** y la **Hidroxicloroquina** trabajan muy bien en casos iniciales o cuando recién comienza la enfermedad".

<https://www.marca.com/claro-mx/> - 11/6/2020 - **Hidroxicloroquina** e **ivermectina**: ¿por qué llevan la delantera contra el coronavirus? "Por su parte, Marcelo Navajas, Ministro de Salud de Bolivia, emitió un permiso para la aplicación de la Ivermectina en los humanos para tratar el Covid-19 en dicho país, aunque aclaran que su uso contra el coronavirus no está avalado por la Organización Mundial de la Salud." web.archive.org/web/20200614112908/https://www.marca.com/claro-mx/trending/2020/06/11/5ee18c6d268e3eaf4b8b45a9.html

<https://www.connuestroperu.com/> - Miscelánea 12 Junio 2020 - La Libertad producirá 150 mil dosis de ivermectina para luchar contra el coronavirus - El Gobierno Regional de La Libertad producirá 150 mil dosis de **ivermectina** para combatir el coronavirus COVID-19 en los pacientes leves. Archived <http://archive.is/BKf8q>

<https://www.connuestroperu.com/> - An interview with Dr. Antonio Camargo, 02 Junio 2020 - Archived <http://archive.is/Cy8Wc> . "Usted contrajo la enfermedad y se curó con **ivermectina**, ¿podría narrarnos su experiencia? Me infecté en mis actividades laborales, atendiendo pacientes oncológicos. Un paciente que buscó ayuda y estuvo buen tiempo en nuestro centro contagió a dos trabajadoras y la trabajadora de limpieza me infectó. El diagnóstico de mi infección fue realizado el 8 o 9 de mayo. Tenía una carga viral terriblemente alta, como para hacer una especie de patrón de vigilancia. Tengo un laboratorio de biología molecular y recuerdo que el biólogo me dijo que mi carga viral era muy alta. Hasta ese momento no sentía nada, sólo una resequedad en la garganta, sin tos ni malestar general ni fiebre, pero sabía que se venía un "tsunami" sobre mí. Allí decidí probar en mí lo que estaba probando en otros pacientes. De inmediato tomé 60mg por día de **ivermectina**, **acompañando con hidroxicloroquina**: 200 mg por la mañana y 200mg por la noche, más 200mg de **sales de zinc** por día, que son dosis altas. Ese fue el tratamiento coronicida. A las 48 horas me realicé un control con PCR, test molecular para controlar mi carga viral y no había carga viral en mi faringe, no había virus".

In this interview, Dr. Camargo is reporting his experience and the use of ivermectin, hydroxychloroquine and zinc.

The case of Iquitos (Peru)

<https://www.connuestroperu.com/> - 13/6/2020 "El verdadero Comando COVID-19 de Iquitos: médicos independientes lograron contener el azote del coronavirus, no el Minsa ni Essalud" - Archived <http://archive.vn/ePtmg>

"Desde fines de abril a mayo las escenas diarias en los hospitales de Iquitos eran de avalancha de infectados con el coronavirus COVID-19, que sobrepasaron su capacidad y muchos pacientes no podían ser atendidos, mientras que otros hasta morían en los exteriores. ... Es gracias a los médicos independientes que Iquitos superó el desastre que causó la pandemia, que ahora está controlada, pues de no contener a muchísimos pacientes en sus domicilios con estos tratamientos exitosos, todos ellos habrían muerto". Interview by Con Nuestro Perú with Dr. Sergio Bardon, "uno de los médicos independientes que participaron en esta lucha y fueron el verdadero Comando COVID-19 en Iquitos".

Question: "Desde abril y mayo hay un número creciente de médicos que usan exitosamente ivermectina, habiendo una cura. ¿A qué atribuye que internacionalmente no se difunda ello y se prefiera a fármacos que tienen menor efecto? Answer; "Con respecto a la **ivermectina** lo que se ha visto es que ha bajado en muchísimos pacientes la carga viral, es decir, la cantidad de virus que una persona tiene en el cuerpo, y por lo tanto, va a mejorar su cuadro clínico y disminuir drásticamente las posibilidades de que la persona se complique la infección viral".

Dr. Bardon tells also: "Lo cierto es que somos muchos los médicos que estamos usando ivermectina con muchísimo éxito. Por supuesto, estos medicamentos tienen mayor éxito cuanto antes se recetan y cuanto menos síntomas tiene el paciente, porque cuando llega a una fase de complicación aguda, con una disnea importante, allí ya empiezan a actuar muchas otras cosas que no son necesariamente la carga viral, porque es la respuesta inflamatoria que tiene cada paciente. Entonces la ivermectina ya no tiene mucho sentido, por eso es importante no solamente darla sino darla a tiempo ... Efectivamente, el éxito que he tenido con ivermectina es mucho. En general, a partir del tercero o cuarto día ya en la gran mayoría de los pacientes no se han visto síntomas ni signos de COVID-19, y con respecto a la negativización de la prueba, se obtiene también rápidamente a partir de una semana".

Then, in Iquitos the ivermectin was used. Iquitos is the capital city of Peru's Maynas Province and Loreto Region. It is the largest metropolis in the Peruvian Amazon, east of the Andes, and it is the ninth most populous city of Peru.

In [19], it was told that the health system in this town was subjected to a very high stress for Covid-19. "The first COVID-19 case in the Peruvian Amazon, detected on March 17, seemed to be a one-off — a tour guide who apparently caught it from foreign visitors. Within weeks, however, Carlos Calampa [Regional Health Director] saw patients overflowing into the corridors of the Loreto Regional Hospital in Iquitos, where he was director". After describing the situation in the town and Peru, the article [19] ends telling "By May 25, COVID-19 cases and deaths had dropped in Iquitos but were rising in remote areas accessible only by river or light plane, Calampa said. He is reinforcing staff and coordinating with the military to deliver medicine, oxygen, and other supplies to health centres on the Marañón, Corrientes, and Tigre rivers, where much of the population is Indigenous".

It seems that something happened before May 25. And in fact, in the article of June 8, 2020, entitled "Effective formula knocks out Covid-19 in the Peruvian Amazon", by Juan J Chamie <https://medium.com/@juanjchamie/effective-formula-knocks-out-covid-19-in-the-peruvian-amazon-150565e9b6c6> archived <http://archive.is/pI5x6>, we find the proper question "How did they get through it so quickly?". "The numbers don't lie. While the coastal departments (Sí Covid) haven't stopped the growing number of reported deaths, the main departments in the jungle region (Ex-Covid), for example in Loreto and Ucayali, broke the trend and within three weeks drastically lowered the rise in mortality rates. Although they still need more time to reach normal values, the

trend indicates that they'll manage it very soon". - And then: How did they get through it so quickly? - Author of the article in Medium tells that the "drop in deaths in the region is attributed to the general use of a medication, and that without even having scientific evidence, according to local residents, it has saved many lives". The drug is Ivermectin.

"In mid-April, a group of volunteers initiated a campaign in the department of Ucayali to deliver ivermectin to residents. They openly acknowledged that they were using veterinarian ivermectin and confirmed positive results, as well. ... Similarly, in the city of Iquitos ... an independent group of volunteer doctors initiated a public campaign plus free vaccinations with ivermectin".

Here news in <http://www.perulactea.com/> on 16/05/2020 - "En Iquitos vienen aplicando Ivermectina de uso veterinario con buenos resultados frente a Covid19". Archived <http://archive.is/yx24r>

"La dosificación que se está utilizando es 1ml x 2 días. Una botella de 1000 ml Ivermecticina al 1% de uso en ganadería, se consigue en 130 soles en las veterinarias. En pocas palabras con 130 soles se pueden inyectar a 500 personas. Se afirma que ya atendieron más de 2000 personas con este tratamiento, quedando claro que la Ivermectina está dando resultados favorables para pacientes covid 19 en etapas 1 y 2. ... Desde el día martes 12 de mayo se esta aplicando la inyección de IVERMECTINA a personas con síntomas leves de Covid 19, la atención será totalmente GRATUITA". The article tells that the dosage of the drug that is being used is 1ml x 2 days. A bottle of 1000 ml Ivermectin at 1% of use in livestock, is available in 130 soles in veterinary medicine. In short, with 130 soles², 500 people can be injected. It is stated that more than 2000 people have already been treated with this treatment, making it clear that Ivermectin is giving favorable results for covid 19 patients in stages 1 and 2. Since Tuesday, May 12, the Ivermectin injection is being applied to people with mild symptoms of Covid 19, the care will be totally for free.

A drug for humans

About the concerns of using a drug mainly involved in veterinary use, an answer is the following. "La Ivermectina fue creada para el tratamiento de humanos" - El médico trujillano Gustavo Elera ha frenado en seco al coronavirus en unos mil 200 pacientes en Chanchamayo con este fármaco, muy empleado en medicina veterinaria". <http://www.laindustria.pe/nota/16073-la-ivermectina-fue-creada-para-el-tratamiento-de-humanos> Archived <http://archive.is/beTgM>

"Desde abril a la fecha, el médico Gustavo Elera Arévalo, trujillano él, ha tratado con excelentes resultados a mil 200 pacientes, todos en su momento afectados por el coronavirus, en La Merced, Chanchamayo, Junín".

In this article, the reporter asks Dr. Elera about the difference between Ivermectin for human and veterinary use. Question: "En el mercado encontramos la Ivermectina para uso humano y animal. La de uso humano ha escaseado y las pocas que se encuentran, tienen un costo muy elevado. Así las cosas, ¿se puede emplear la veterinaria?" Answer: "Claro. No es tóxica. Nosotros hemos utilizado la de uso veterinario para el penal de La Merced (Chanchamayo), para la Policía Nacional, para todos los pacientes que estamos viendo sin ningún problema y la vamos a utilizar en el barrido que haremos en algunos otros sectores del mismo Chanchamayo. La diferencia entre la Ivermectina de uso humano y la de uso veterinario es que la de uso humano es Ivermectina más agua y Sorbitol, que es un saborizante que la vuelve dulce, y la de uso veterinario es Ivermectina más agua y punto".

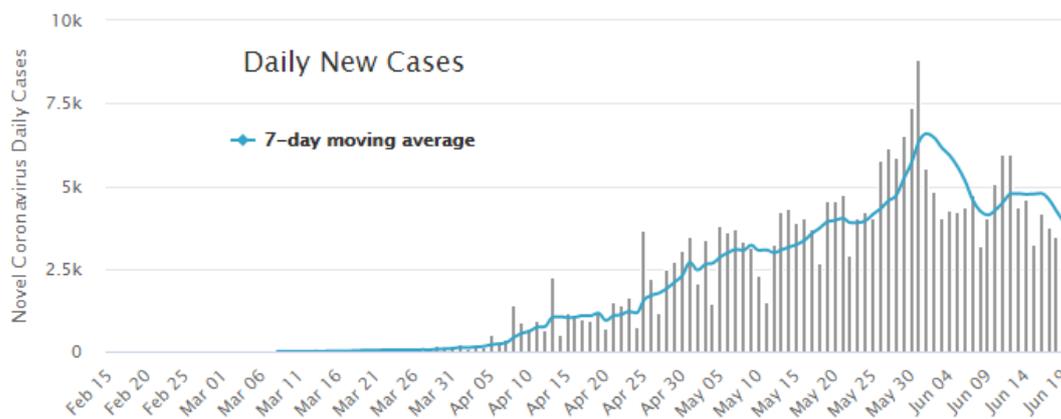
In the market we find Ivermectin for human and veterinary use. The formulations for human use are in short supply and at a very high cost. "So, can you use veterinary medicine?" Elera's answer: "Sure. It is not toxic. We have used the one for veterinary use for the ... The difference between Ivermectin for human use and that for veterinary use is the following. The formulation for human use is Ivermectin plus water and Sorbitol, which is a flavouring that makes it sweet. The formulation for veterinary use is Ivermectin plus water, plain and simple."

2 1 Sol equals 0.26 Euro

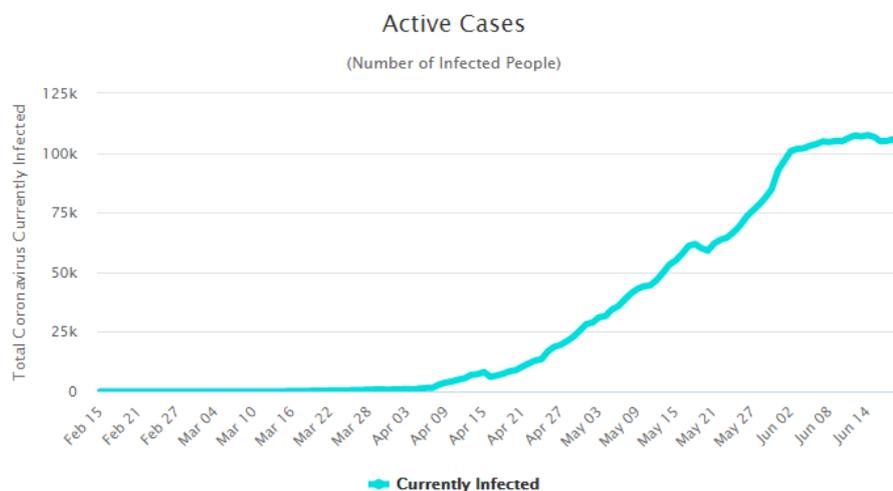
Of course, it is necessary to check the formulations, and avoid self-medication (the use of drugs needs medical supervision). At this is clear because of different concentrations. "El médico veterinario Eleazar Vargas señaló que la ivermectina que viene siendo usada para humanos difiere en concentración del empleado para animales". 18 Junio, 2020 - <http://archive.is/1qN3N>

Data

As we can appreciate in the news from Peru - and South-America, in general - a large use of ivermectin is and will be made for Covid-19. It is therefore clear that an effectiveness of the drug can be easily evidenced by the numbers about new and active cases in the country.



Courtesy: <https://www.worldometers.info/coronavirus/country/peru>



Courtesy: <https://www.worldometers.info/coronavirus/country/peru>

The plot given above is showing the number of active cases in Peru. In the next weeks, it is reasonable to imagine that the curve will decrease. The behaviour of the decrease will be influenced by any effectiveness of the drug.

Acknowledgement

I would like to offer my special thanks to Dr. Rocio Ferrel for her precious support on literature and news concerning Ivermectin.

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