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羟氯喹：青霉素之后的第二次医学大革命*

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摘要：撰写此手稿是旨在拯救 Covid-19 流行病患者生命的紧迫压力下促成。新冠病毒综合症自 2020 年 2 月以来已夺走了 50 多万美国人的生命，这很可能是由于实际上缺乏正确的治疗方法所致。作者不是专业的病毒学家/流行病学家。凭借中国传统草药的家庭背景，作者拥有丰富的学习经验，在业余时间关注世界上不断改进的生产和专注于该药物的最新方法论相互比较验证。
[叶宁 (Ning Ye). **羟氯喹：青霉素之后的第二次医学大革命.** *Academ Arena* 2021;13(3):71-80]. ISSN1553-992X(print); ISSN2158-771X(online). http://www.sciencepub.net/academia. 9. doi:10.7537/marsaaj130321.09.

关键词： Covid-19; 流行病; 患者; 生命; 新冠病毒综合症; 病毒学; 草药; 生产; 药物; 方法论；验证。

撰写此手稿是旨在拯救 Covid-19 流行病患者生命的紧迫压力下促成。新冠病毒综合症自 2020 年 2 月以来已夺走了 50 多万美国人的生命，这很可能是由于实际上缺乏正确的治疗方法所致。作者不是专业的病毒学家/流行病学家。凭借中国传统草药的家庭背景，作者拥有丰富的学习经验，在业余时间关注世界上不断改进的生产和专注于该药物的最新方法论相互比较验证。并经常和在医学科学领域位居前茅的卓越科学家进行彻夜长谈之后发现了**羟氯喹**的巨大抗病毒作用。美国国立卫生研究院是世界上拥有数量最多的著名顶尖生命科学家的总部。代表着最前沿的生命科学发展巅峰。本作者在那里收益甚丰。自 2020 年 1 月以来，本作者向中国大陆贡献了 5 个 Covid-19 替代疗法，其中包括热柠檬姜茶，以及逆转人体蛋白质缺乏和过度疲劳的方法。作为得到部分接受的方法论指南，其目的仅仅是为了挽救生命于毁灭性的 Covid 大流行。对于大多数 Covid 患者，他都有完全康复的方法论答案。叶先生在 2020 年 2 月上旬就准确预测，中国新冠流行拐点将出现于 2020 年 3 月。并进一步指出所谓拐点是指全国新冠死亡人数减少 95％以上的转折点。这种应该会在三月底之前出现。而钟南山院士认为拐点将是 2020 年 5 月。不幸的是，预测美国的转折点应该在 2020 年 5 月出现失败了。因为唐纳德 • 特朗普总统大胆的**羟氯喹**倡导在 4 月份遭到挫败。随后 FDA 撤销了颁发给**羟氯喹的**临时“临床试验”许可。死亡率随后迅速攀升。全国各地医院的 Covid-19 伤亡人数急剧上升。叶宁为**羟氯喹在**美国纽约南区地方法院（20-3067-RA）寻求 Mandamus 令状而进行的法律斗争并未带来迅速而积极的结果。现在，由于所有非医学方面干扰**羟氯喹**当作治疗过滤性慢病毒流行病的合力在大选后逐渐消失，今天应该是大家一心来专注于这一挽救生命的崇高事业的时候了。

1. HCQ 的发现及其抗病毒作用

氯喹（CQ）是一种 9-氨基喹啉，于 1934 年被发现。羟氯喹（HCQ）是一种具有更强治疗效果的先进 CQ 类型，是基于神谕在中国开始的临床试验中海选出来的一种古老药物，已被使用。与致命的大流行瘟疫作斗争。**羟氯喹**之前，还没有有效的药物来治疗由 Flu 到 Covid-19 甚至 AIDS 这类滤过性慢病毒引起的各种传染病的有效化学配方。已经表明，羟氯喹（HCQ）对流感病毒 SARS-CoV 和 SARS-CoV2 及其变异分枝 Covid-19 病毒感染灵长类动物细胞的滤过性慢病毒具有显效能以此进行有效的治疗。人类首次发现羟氯喹（HCQ）对广谱滤过性慢病毒病毒具有抑制作用和较低/极微弱毒副作用的治疗效果。对病毒性流感和新冠综合症具有极强的抗病毒作用。此外，临床试验证明，每天接受 200-600mg 羟氯喹（HCQ）剂量的每个成员三到五天治疗期间显示出几乎接近 100％的康复结果。对于急性流感患者，小剂量服药一到三次，症状全部消失。

2. HCQ 治疗 Covid-19 的临床评价

严重急性呼吸系统综合症（SARS）及其新类型变异 Covid-19，是由新发现的冠状病毒 SARS-CoV2 引起的。 Covid-19 是一种新兴疾病，全球范围内的努力因非医学并发症（这对人类而言非常不幸）而失败，未能鉴定出冠状病毒科（冠状病毒科的新成员）的病原体冠状病毒，再加上未能找到和鉴定最有效和可用的治疗与医学无关的并发症的药物成为借口。*在 2005 年之前*，确实没有有效的预防或暴露后的治疗方法。

值得注意的是，据报道，每天服用 400-800 毫克羟氯喹治疗 Covid-19 并发症前患者获得 100％的清除率和奇迹结果，所有病毒均被消除。（1）Vladimir Zelenko 博士和其他人使用他的 HCQ-基于鸡尾酒的鸡尾酒已经在临床试验中成功治疗了数百名 Covid-19 患者，他最近预测，从英国传播的 Covid-19 病毒的新变种也在羟氯喹 HCQ 治疗区范围之内。（2）（今年三月初钟南山院士在全国医学科学连线会议宣布磷酸氯奎对治疗早期新冠具有显效。）

此外，在使用羟氯喹 HCQ 治疗 Covid-19 患者的临床试验中，有一些失败或不足的报道。这种零星的故障被用来恶意攻击羟氯喹 HCQ。未公开的原因可能是由于剂量不足或为时已晚。Vladimir Zelenko 博士的不足在于并非在所有 Covid-19 病例中都必须千篇一律的鸡尾酒疗法。对于没有发现细菌感染或炎症的早期 Covid-19 患者，是不需要抗生素更不需要大剂量抗生素的。但是，对于已经历 Covid-19 病毒触发的非病毒性并发症的晚期患者，单纯使用羟氯喹 HCQ 则为时已晚。在后期，该过程需要支持性对症治疗，例如抗生素，抗炎，抗血栓形成/抗凝血和/或降低自身免疫性风暴疗法，也可谨慎地使用后遗症严重的万金油激素疗法。另外，如瑞典的经验所示，抗生素过量也会造成严重后果，因此必须采取预防措施。

3. 羟氯喹 HCQ 极为低毒

改良的羟氯喹 HCQ 配方已被广泛用于治疗人类疾病，例如疟疾，阿米巴病，HIV，狼疮和自身免疫性细胞因子风暴，而没有明显有害的副作用，即使对于孕妇也绝对安全。尽管这种效果似乎比大多数（如果不是全部）FDA 批准的用于治疗癌症患者的化疗药物不知道要安全多少倍。尽管在大多数文明国家的《药物规范》中早就包含了这种化学疗法的指南。但是，最近还是对羟氯喹服用后的安全性和毒副作用做了持续一年之久的双盲临床实验。美国国立卫生研究院相关诊所于 2012 年 3 月至 2013 年 3 月对 103 例狼疮患者进行了一项观察羟氯喹 HCQ 安全性的临床试验。对照组每个成员每日 HCQ 200-400 mg 的剂量，累积总量高达 144000 毫克。没有，重复一遍，羟氯喹 HCQ 服用组中没有任何人遭受任何可见的副作用。（3）太安全了。

羟氯喹 HCQ 的分子“重量”为 434（433.96）单位。体外有效消除显示 10 μ M 氯喹 CQ 或 5 μ M 羟氯喹 HCQ，消除了 100％的广谱过滤慢病毒。在通过数学模型考虑了所有可能的降解率之后，治愈 Covid-19 早期患者或 Flu 患者的平均剂量应为 2.17 mg / kg 体重。对于 Covid-19 中晚期患者，应该增加剂量为为 6.21 mg / kg 体重。因此，每日剂量 200-600mg 口服就足够了。一周剂量将有效地消除几乎所有病毒感染并消除体内病毒。由于羟氯喹 HCQ 表现出极低的毒性，因此如果临床剂量每天增加至 400-800 mg，则在临床试验中短时间（例如，连续处方少于 6 个月）不会产生任何具有统计意义的毒副作用。对于相对超重的患者，前两天口服剂量为 800 毫克，不会引起毒性反应。

4. CQ 氯喹和羟氯喹 HCQ 的感染前和感染后效果

羟氯喹 HCQ 可以全面有效地预防细胞培养中从急性流感到 Covid-19 和 SARS 等滤过性慢病毒的传播。在实验室的体外实验和中国的体内临床试验中，当在过滤慢病毒感染之前或之后用 HCQ 处理细胞时，均观察到了良好的病毒传播抑制作用[1]。

最近，Vincent 等人报道在 Vero E6 细胞中用 0.1 μ MCQ 或 0.05 μ MHCQ 进行预处理可将感染率降低 28％，而将 10 μ M 氯喹 CQ 或 5 μ M 羟氯喹 HCQ 进行预处理可将感染率降低 100％（图 1）.1

该研究还评估了病毒吸附后氯喹 CQ 的即时作用，他们发现在病毒吸附后 3 和 5 小时加入氯喹可以有效地清除感染的病毒（图 2）。1 电子显微镜分析表明，在 5-6 h 内出现了大量的细胞外病毒颗粒 4 这些数据表明，用氯喹 CQ 预处理 Vero E6 细胞使这些细胞难以抵抗 SARS-CoV 感染，感染后给予氯喹 CQ 显示出明显治愈作用。

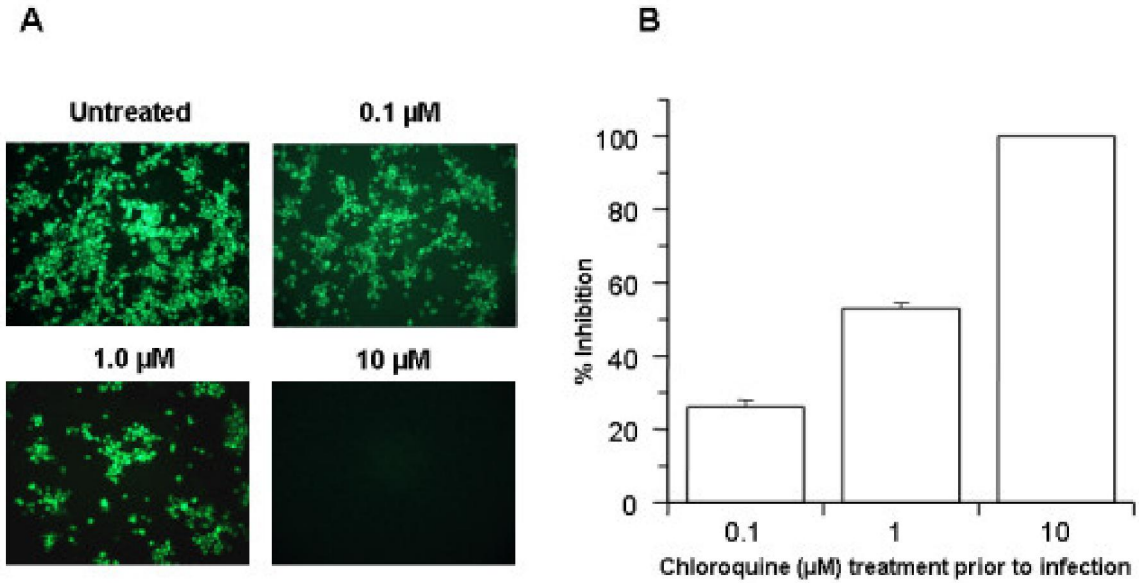

图 1. 10 μ M 氯喹 CQ 或 5 μ M 羟氯喹 HCQ 进行预处理可将感染率降低 100%

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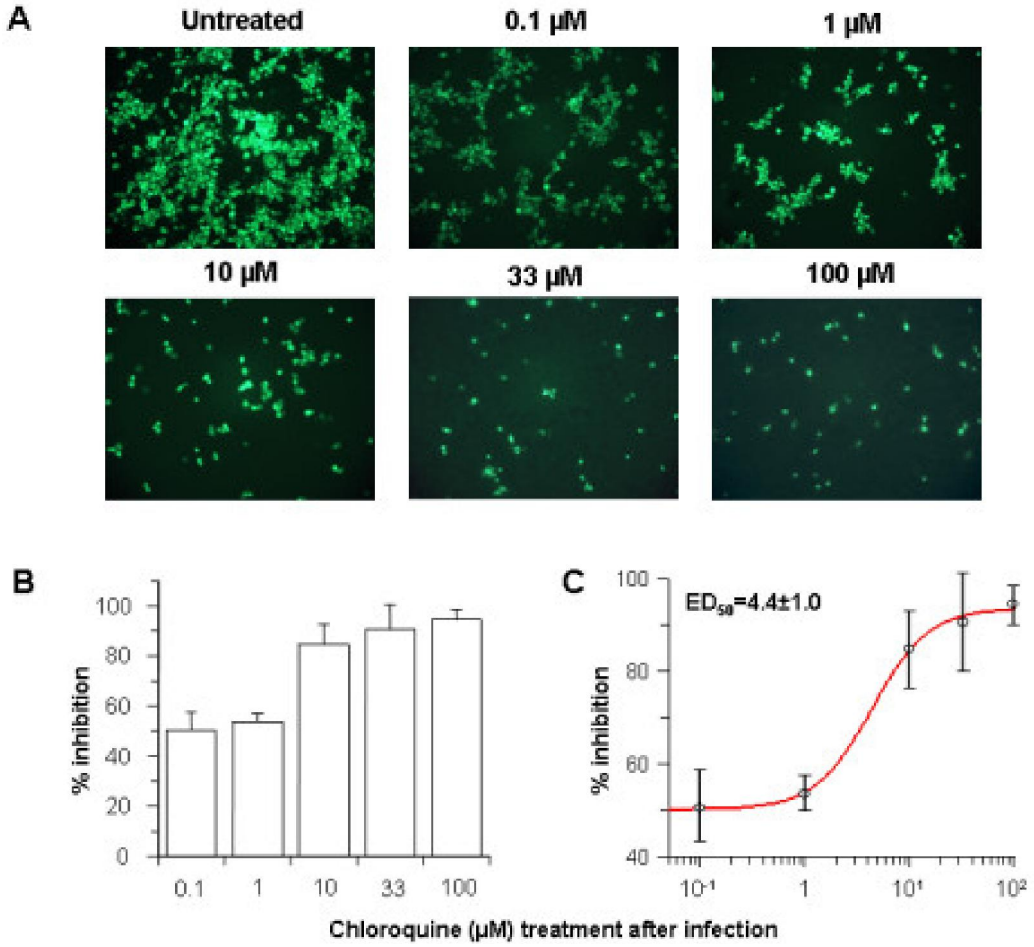

图 2. 定时用氯喹进行感染后治疗。

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4.2 羟氯喹 HCQ 阻止了 *Covid-19 与刺突糖蛋白的结合*

当在细胞外添加氯喹时，氯喹 CQ 的非质子化部分进入细胞，在那里质子化并浓缩在酸性，低 pH 的细胞器中，例如内体，高尔基囊泡和溶酶体。氯喹 CQ 可以多种方式影响病毒感染，抗病毒作用部分取决于病毒利用内体进入的程度。除了羟氯喹 HCQ 的众所周知的功能（例如提高内体 pH 平衡）外，该药物似乎还*干扰了细胞受体血管紧张素转换酶 2（ACE2）的末端糖基化*。这可能会对*病毒-受体的结合产生阻抗等负面影响并消除感染*，并因水泡 pH 值的升高而产生进一步的治疗后果，从而在临床允许的浓度范围内对流感综合症，SARS CoV 和 Covid-19 的感染和传播产生全面和奇迹般的抑制作用。已经被中国各地医院的临床试验证明其显效。（在美国何尝不是呢？）

在人类八十多年的抗病毒药物研究中，生命科学家们长期以来一直致力于阻止病毒剑突糖蛋白（类似于信号输出天线）与宿主细胞的 ACE2 受体之间的连接附着，以消除与细胞受体的病毒结合，从而遏制引发病毒感染。这种研究思路一以贯之，长达八十多年几乎没有进展。以 Covid-19 和 Sars 为例，SARS-CoV 的出芽发生在高尔基体中，并导致包膜刺突糖蛋白掺入到病毒体中。刺突糖蛋白是一种 I 型膜蛋白，可促进病毒附着于细胞受体并引发感染，血管紧张素转换酶 2（ACE2）已被鉴定为这种过滤性慢病毒（包括 SARS-CoV 和 Covid）的功能性细胞受体。Vincent 等人最近发现，刺突蛋白的加工受到弗林蛋白酶样转化酶的影响，并且特定抑制剂对这种裂解的抑制作用消除了细胞病变，并显著降低了病毒效价（图 3）。相反， 羟氯喹 HCQ 的抗病毒作用可能不是由于病毒糖蛋白生物合成和加工过程的改变。（1）与之前的分析一致，（1）他们观察到了较大蛋白质的存在，在这里被称为寡聚物。最近，Song 女士等研究者提供的证据表明这些是 SARS-CoV 穗蛋白的同源三聚体，并已掺入病毒体中。

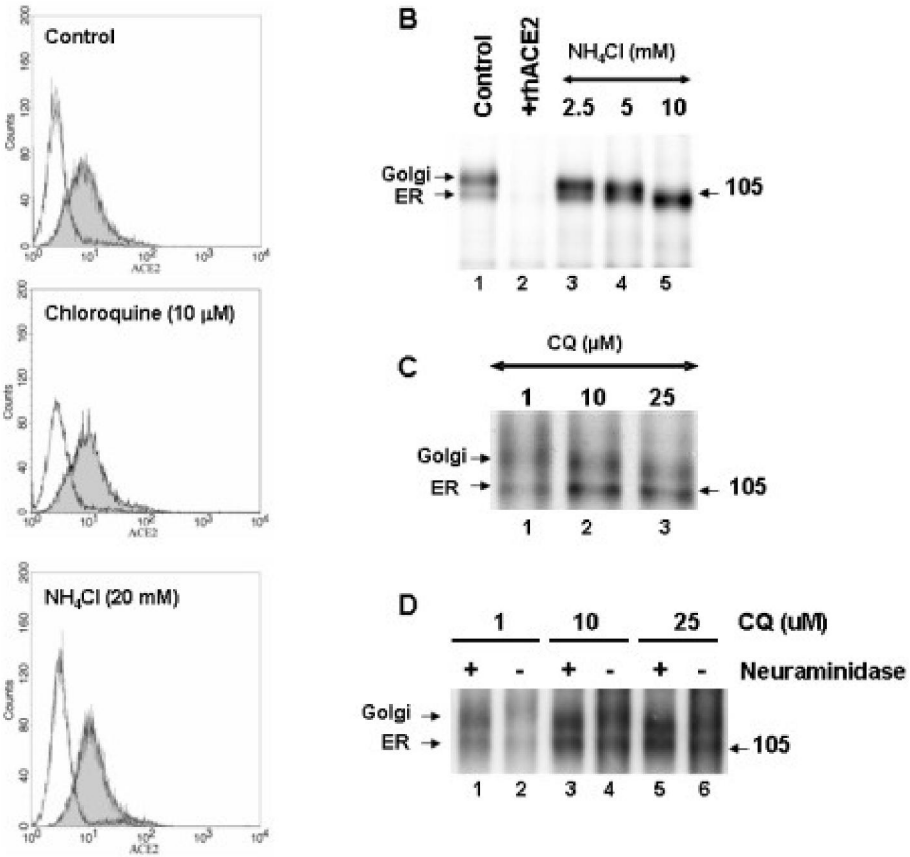

图 3. 溶智剂对 ACE2 在细胞表面表达和生物合成的影响。

羟氯喹 HCQ 在 Covid-19 治疗中的未来临床应用疫苗，特别是 mRNA 类疫苗，属于体内免疫系统增强作用类，其改变人类基因的潜在因素不可忽视，且跟不上病毒突变速度。自行车赶飞弹。疫苗不是直接用来消除病毒的化学杀毒剂杀手，当羟氯喹 HCQ 密度达到 10 MU 时，体外可 100%消除病毒。对于这种代际突变过快的病毒（例如 Covid-19），疫苗的开发速度是否可以与该代际突变相匹配，并且毒性评估可能还不清楚。羟氯喹已被证明是有效的或什至是全效的，在体内没有或几乎没有毒性副作用。今天，我们见证了由羟氯喹 HCQ 领导的具有里程碑意义的转折点，它是一种经过验证的有效的广谱抗病毒剂，几乎没有毒性的副作用，这为 Lord 带来了“Great Grace 好消息”，从而挽救了成千上万的大流行病毒患者的生命。一场开创性的医学革命，就像发现青霉素以消除八十年前的各种致死细菌一样，开始了。新冠综合症对人类的另类贡献巨大,尽管代价惨重！另外，羟氯喹本身具有降低自身免疫性风暴的有益功能。此外，氯喹还具有改善患者的酸碱平衡水平的作用。

羟氯喹 HCQ 是继青霉素之后的第二次医学革命吗？

在 1928 年苏格兰科学家亚历山大·弗莱明（Alexander Fleming）发现青霉素之前，细菌是主要的死亡原因。自 1942 年起，医学界开始使用青霉素来治疗细菌感染，医学界这种漫长的黑暗夜晚已经结束。其中包括抗葡萄球菌青霉素，氨基青霉素和抗假单胞菌青霉素。（5）它们来自青霉素真菌。青霉素的发现是治疗人类疾病的医学领域的一场伟大革命，其中许多疾病在青霉素之前非常致命。因此，为表彰亚历山大·弗莱明（Alexander Fleming）博士，他与牛津大学的科学家霍华德·弗洛里（Howard Florey）博士和恩斯特·鲍里斯·链博士（Ernst Boris Chain）共同获得了诺贝尔生理学或医学奖，后者开发了改良的青霉素配方，广泛用于临床治疗。

在发现青霉素后的大约八十年中，整个医学界在世世代代的共同努力下，在寻找有效的方法来发现，配制和提供任何化学药品方面几乎没有取得什么进展（如果有的话）对抗任何过滤性慢病毒的药物或药物，包括流感，埃博拉病毒，艾滋病，SARS-CoV 和 Covid-19。我们在一次伟大的庆典中亲眼目睹了人类应该如何感恩上帝，这是祂在 1928 年以后的第二次恩典。在这一次瘟疫中尚未被击败的致命敌人正在通过整个过滤慢病毒的爆发，导致严重的致命病毒综合症。从流感，Covid-19 到艾滋病。由于 Covid-19 的严重性以及急性感染，滤过性慢病毒引发的疾病迅速传播的潜力以及缺乏公认的有效且安全的病毒体内抑制剂，因此确定抗大流行病很重要可有效用于治疗和预防潜在慢病毒感染的药物羟氯喹的广泛疗效意义重大。

结合此处提供的数据，显示了与患者治疗相适应的羟氯喹 HCQ 剂量对细胞培养物中的病毒抑制作用，建议立即，完全和永久 FDA 批准羟氯喹 HCQ 用于预防和治疗这种过滤性慢病毒引发的流行病，如急性流感，Covid-19 强烈推荐 SARS 流行患者。

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Hydroxychloroquine: The Second Revolution in Medical Science After Penicillin

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Abstract: This manuscript was written under the urgent pressure of being motivated in saving lives of Covid-19 epidemics which has claimed more than 500,000 American lives since February 2020, most likely due to virtual absence of correct therapy. The author is not a professional virologist/epidemiologist. With family background of Chinese traditional herbal medicine, this author had extensive learning experience interacting in appendices nature with the world's improved ways to produce and concentrate on the drug and prove its antiviral effects following topnotch scientists in medical science mostly in the NIH, the world's most prestigious headquarter compound representing the most cutting-edge life science development.
[Ning Ye**. Hydroxychloroquine: The Second Revolution in Medical Science After Penicillin.** *Academ Arena* 2021;13(3):71-80]. ISSN 1553-992X (print); ISSN 2158-771X (online). http://www.sciencepub.net/academia. 9. doi:10.7537/marsaaj130321.09.

Keywords: live; Covid-19; epidemics; therapy; virology; epidemiology; Chinese traditional herbal medicine; drug; NIH; science

Introduction

This manuscript was written under the urgent pressure of being motivated in saving lives of Covid-19 epidemics which has claimed more than 500,000 American lives since February 2020, most likely due to virtual absence of correct therapy. The author is not a professional virologist/epidemiologist. With family background of Chinese traditional herbal medicine, this author had extensive learning experience interacting in appendices nature with the world's improved ways to produce and concentrate on the drug and prove its antiviral effects following topnotch scientists in medical science mostly in the NIH, the world's most prestigious headquarter compound representing the most cutting-edge life science development. Since January 2020, this author contributed 5 Covid-19 alternative therapy package involving hot-lemon ginger tea to ways to reverse protein deficiency and over-fatigue, to HCQs, in China, as partially accepted methodology guidelines whose mere motive is to save lives from devastating Covid pandemics. The driving cause pushing this author to involve himself in humanitarian crusade in saving lives of Covid-19 patients during starting the darkest period is what he was shocked by what he watched video footage taken in Wuhan, China that many collapsed in the streets and deeply scared people having committed suicide by jumping off from the windows of the high rise apartment buildings. "You don't have to die with this kind of disease as corona virus infected syndrome!" He out-cried. He has the answer to get fully recovery, for the super majority of Covid patients. Mr. Ye accurately forecast in earlier February, 2020 that the turning point with 95%+ death toll reduction throughout China should appear in March 2020, in comparison to Academician Zhong Nanshan's forecasting that the turning point would be in May 2020. Mr. Ye's forecasting that the turning point in the United States should be May 2020 was unfortunately failed because President Donald Trump's courageous advocacy of HCQ was defeated by the establishment in April followed with FDA's revocation of temporary "clinical trial" permit, and further followed with swift climbing up of death tolls of Covid-19 casualty from hospitals throughout the nation. Ning Ye's legal battle for the sake of HCQ seeking for Writ of Mandamus with U.S. District Court for the Southern District of New York (20-3067-RA) did not result in prompt and positive outcome. Now, with all non-medical aspects in interfering the HCQ as the crusade to treating filtering lentivirus epidemics dying down after general election, it is high time to concentrate upon this noble cause in saving lives.

1. The discovery of HCQ and its anti-virus effects

Chloroquine (CQ), a 9-aminoquinoline that was identified in 1934. Hydroxychloroquine (HCQ), the advanced type of CQ with more effective therapeutic, is an ancient drug in the random selection during the clinical trials starting in China, which has

been used in fighting against lethal pandemic. Before, HCQ, there has been no effective drug for the treatment of various infectious diseases caused by lentivirus from Flu to Covid-19, even AIDS. It has been shown that HCQ has effective therapeutic, virus-suppression and lower by effect has strong antiviral effects on filtering lentivirus ranging from flu virus SARS-CoV and SARS-CoV2 and its variation ramification Covid-19 virus infection of primate cells. In addition, clinical trial proves that each member receiving 200-600mg HCQ daily dosage showed 100% recovery result during the three to five-day treatment for acute Flu patients.

2. Clinical evaluation of HCQ in the treatment of Covid-19

Severe acute respiratory syndrome (SARS) and its neo-type variation, Covid-19, is caused by a newly discovered coronavirus SARS-CoV2. Covid-19 is an emerging disease that was first reported in Hubei Province, China, in late 2019. The disease rapidly spread to the entire world with most severe impact upon the United States having claimed six digits Covid-19 related deaths and worldwide efforts have failed for non-medical complications, very unfortunately to humanity, in the identification of the etiological agent coronavirus, a novel member of the family Coronaviridae, coupled with wasteful failure in finding and identification of most effective and available treating drug for complications irrelevant to medical science for its own sake. No effective prophylactic or post-exposure therapy had been available before 2005.[1]

Of note, it has been reported that HCQ administration with daily dosage of 400-800mg HCQ treating Covid-19 pre-complication patients received 100% sweeping and miracle results, all virus were eliminated.[1] Dr. Vladimir Zelenko and others used his HCQ-based cocktails has successfully treated hundreds of Covid-19 patients in clinic trial and he recently predicted that neo-variation of Covid-19 virus spreading from the UK is also within the sphere of HCQ's therapeutic zone.[2]

In addition, there are some reports of failure or inadequacy in the clinical trials of using HCQ to treat Covid-19 patients. Such sporadic failures were used to maliciously attack HCQ. The unrevealed reason is probably due to insufficient or excessive dosage, or too late. Cocktail therapy is not necessarily required in all Covid-19 cases, and large doses of antibiotics are not required for early stage Covid-19 patients without bacterial infection or inflammation. Using HCQ too late, however, for late-stage patients who have experienced non-viral complications triggered by the Covid-19 virus. In the late stages, the process requires supportive symptomatic treatments such as antibiotics, anti-inflammatory, antithrombotic/anticoagulation and/or anti-autoimmune storm. In addition, as the experience in Sweden shows, preventive measures must be taken.

3. Low toxicity of HCQ

The improved formula HCQ has been widely used to treat human diseases such as malaria, amoebiosis, HIV, Lupus and autoimmune cytokine storms, without significant detrimental side effects which appears absolutely safe even to pregnant women. Though such safety by effects, which appears much, much safer than most, if not all, FDA approved chemical agents in chemotherapy treating cancer patients, have long been contained in the Drug Codes in the most civilized nations, however, a one-year long clinical trial to observe HCQ's safety was conducted by NIH related clinic for a control group of 103 Lupus patients from March 2012 to March 2013. Daily dosage of HCQ 200-400 mg for each member of controlled group, the accumulated total quantity was up to 144000 mg. None, repeat, none in the HCQ group suffered any visible side effects.[3]

An HCQ's molecule "weight" is 434 (433.96). An effective elimination *in vitro* shows 10μM CQ or 5 μM HCQ, eliminated broad spectrum filtering lentivirus by 100%. After all possible degrading ratio is taken into account through mathematical models, the average dosage to heal a Covid-19 or Flu patient with HCQ should be 2.17 mg/kg body weight. For mid and later phase Covid-19 patients, 6.21 mg/kg body weight. Therefore, a daily dosage 200-600mg, oral is sufficient, and a weekly dosage will effectively repeal all viral infection with elimination of virus *in vivo*. Due to the fact that HCQ shows extreme low toxicity which does not show any statistical value for short period (*e.g.*, less than 6 months period of continuous prescription) administration in clinical trials, if the clinical dosage be increased up to 400-800 mg daily oral dosage for the first two days to relatively overweight patients, it causes no toxicity response.

4. Preinfection and postinfection effect of CQ and HCQ

HCQ demonstrates full-scale effective in preventing the spread of filtering lentiviral epidemics ranging from acute Flu to Covid-19 and SARS in cell culture. Favorable inhibition of virus spread was observed when the cells were either treated with HCQ prior to or after such filtering lentivirus infection on both *in vitro* experiment in laboratories and *in vivo* clinical trials in China.[1]

Recently, Vincent *et al.*, reported that pretreatment with 0.1μM CQ or 0.05μM HCQ, reduced

infectivity by 28%, and 10μM CQ or 5 μM HCQ, reduced infectivity by 100% in Vero E6 cells (Figure 1).[1] The antiviral effects by CQ immediately after virus adsorption was also evaluated, they found that adding chloroquine 3 and 5 h after virus adsorption effectively removed infected virus (Figure 2).[1] Electron microscopic analysis indicated the appearance of significant amounts of extracellular virus particles 5-6 h after infection.[4] These data demonstrated that pretreatment of Vero E6 cells with CQ rendered these cells refractory to SARS-CoV infection, and that administration of CQ after infection also showed curative effect.

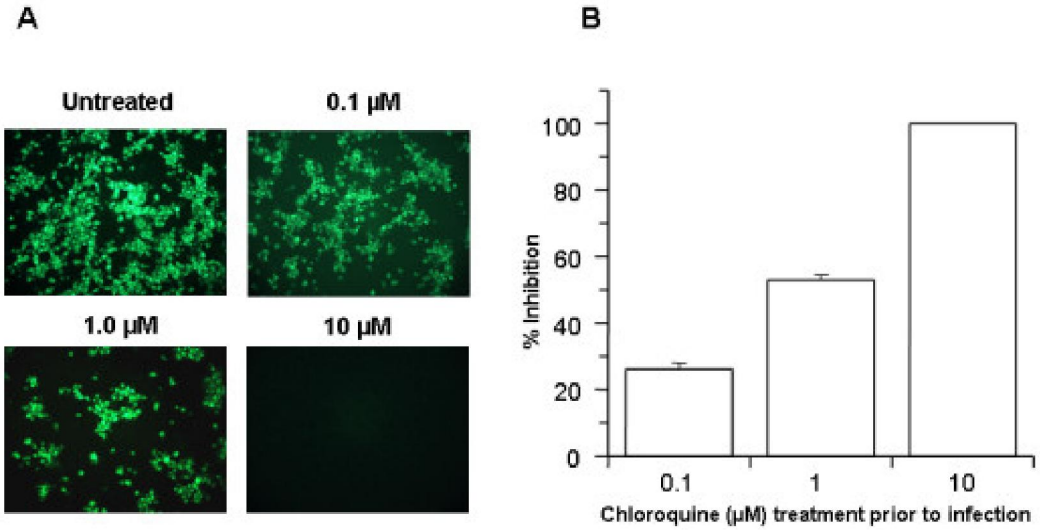

Figure 1. Prophylactic effect of chloroquine.

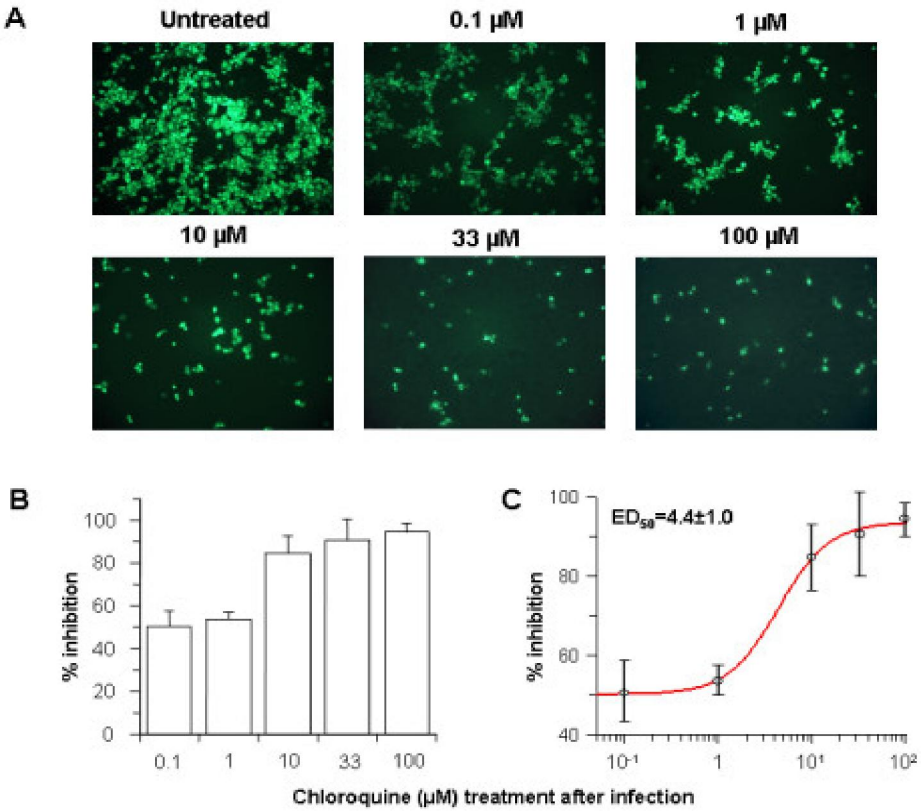

Figure 2. Timed post-infection treatment with chloroquine.

4.2 HCQ prevented the binding of Covid-19 with spike glycoprotein

When added extracellularly, the non-protonated portion of CQ enters the cell, where it becomes protonated and concentrated in acidic, low-pH organelles, such as endosomes, Golgi vesicles, and lysosomes. CQ can affect virus infection in many ways, and the antiviral effect depends in part on the extent to which the virus utilizes endosomes for entry. In addition to the well-known functions of HCQ's such as elevations of endosomal pH balancing, the drug appears to interfere with terminal glycosylation of the cellular receptor, angiotensin-converting enzyme 2 (ACE2). This may negatively influence the virus-receptor binding and abrogate the infection, with further ramifications by the elevation of vesicular pH, resulting in sweeping and miracle inhibition of infection and spread of Flu syndrome, SARS CoV and Covid-19 at clinically admissible concentrations by all clinical trials in hospitals throughout China.

Over eighty years of antiviral drug research, scientists have long focused on blocking the attachment between the viral spike glycoprotein (similar to the signal output antenna) and the host cell's ACE2 receptor, to eliminate viral attachment to the cellular receptor that initiates a viral infection. Taking example of Covid-19 and Sars, budding of the SARS-CoV occurs in the Golgi apparatus and results in the incorporation of the envelope spike glycoprotein into the virion. The spike glycoprotein is a type I membrane protein that facilitates viral attachment to the cellular receptor and initiation of infection, and angiotensin-converting enzyme-2 (ACE2) has been identified as a functional cellular receptor of such filtering lentivirus including SARS-CoV and Covid-19. Vincent *et al.*, have recently shown that the processing of the spike protein was affected by furin-like convertases and that inhibition of this cleavage by a specific inhibitor abrogated cytopathicity and significantly reduced the virus titer (Figure 3).[1] In contrast, the antiviral effect of HCQ is probably not due to alteration of virus glycoprotein biosynthesis and processing. Consistent with this previous analysis,[1] they observed the presence of a larger protein, which is referred to here as oligomers. Recently, Song et al. provided evidence that these are homotrimers of the SARS-CoV spike protein and were incorporated into the virions.

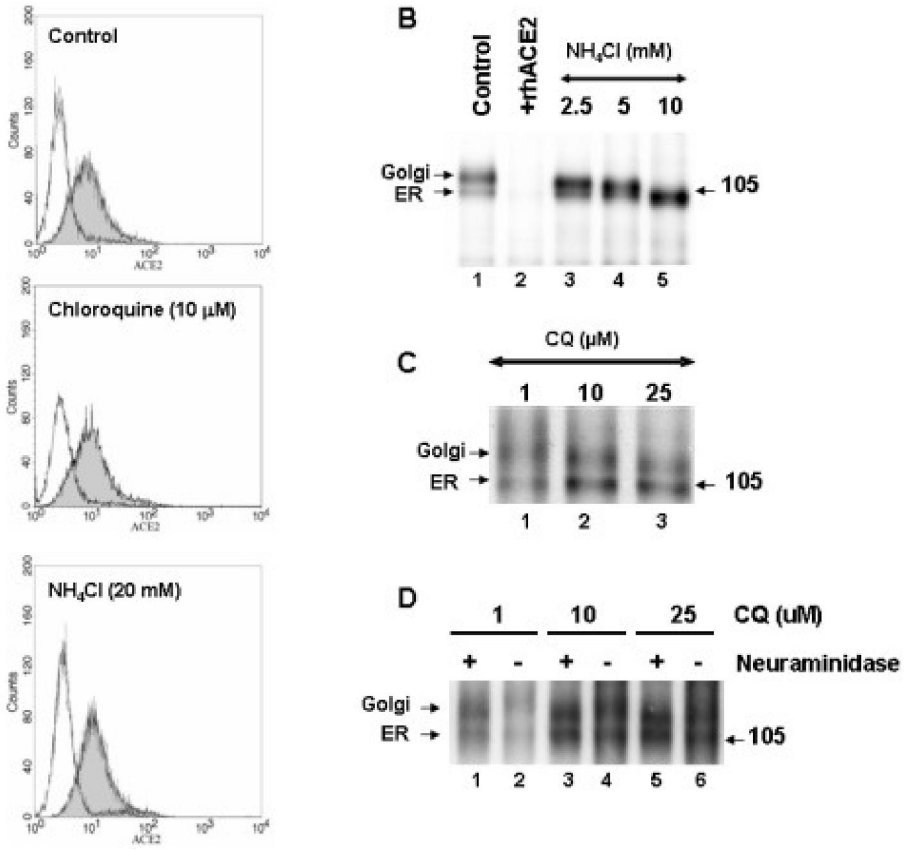

Figure 3. Effect of lysomotropic agents on the cell-surface expression and biosynthesis of ACE2.

Future clinical application of HCQ in the treatment of Covid-19

Vaccines belongs to *in vivo* immune system enhancement, not a chemical agent virus killer that directly eliminates viruses, which was shown 100% elimination of virus *in vitro* when the density of HCQ reached 10MU. For such viruses with too fast intergenerational mutations, such as that of Covid-19, whether the vaccine development speed can match that intergenerational mutation, and the toxicity evaluation may not have been crystal clear. Hydroxychloroquine has proven effective or even full effect with none or insignificantly little toxic side effects *in vivo*. We have witnessed today that a landmark turning point led by the HCQ as a proven effective broad spectrum anti-virus agent with insignificant little by-effect of toxicity has brought the Good News of Great Grace from Lord, in saving millions of pandemic virus patients as a groundbreaking medical science revolution just like discovery of Penicillin to eliminate various lethal bacteria eighty some years before. In addition, chloroquine itself has the beneficial function of degrading autoimmune storms. Moreover, chloroquine also has the effect of improving the pH balancing level of the patients.

Is HCQ the second revolution in medical science after penicillin?

Before Penicillin was discovered in 1928 by Scottish scientist Alexander Fleming, bacteria was the primary cause of death. This long night of darkness in medical science treating human disease has been ended when Penicillin was used to by medicinal society to treat bacteria infections starting 1942. It is making a new era started when there are several enhanced penicillin families which are effective against additional bacteria; these include the antistaphylococcal penicillins, aminopenicillins and the antipseudomonal penicillins.[5] They are derived from Penicillin fungi. Discovery of Penicillin is a great revolution in medical science treating human diseases many of which had been deadly before Penicillin. Consequently, in recognition of Dr. Alexander Fleming, a Nobel Prize in Physiology or Medicine was awarded to him sharing with Dr. Howard Florey and Dr. Ernst Boris Chain, scientists with Oxford University who developed improved penicillins formulas.

During the same period of approximately eight decades after discovery of Penicillin, the entire medical community through out of the world with orchestrated efforts by generations, has made little progress, if any, to find effective way to discover, formulate and made it available any chemical agents or drugs in fighting against any filtering lentivirus, ranging from that of Flu, of Ebola, of AIDS, of SARS-CoV, and of Covid-19. We have witnessed in great celebration that humanity, thanks the God, has encountered her second year of 1928, this time, yet to be defeated lethal enemy is filtering lentivirus probably by its entire family, which causes such crippling or deadly virus triggering human diseases ranging from Flu, Covid-19 to AIDS. Due to the severity of Covid-19 as well as acute Flu infection, the potential for rapid spread of the filtering lentivirus triggered diseases, and the absence of proven effective and safe in vivo inhibitors of the virus, it is important to identify anti-pandemic drug that can effectively be used to both treat and prevent potential lentiviral infections.

Together with data presented here, showing virus inhibition in cell culture by HCQ doses compatible with patient treatment, recommendation of immediate, full and permanent FDA approval of HCQ to be used in prevention and treating such filtering lentivirus triggered epidemic as Acute Flu，Covid-19 and SARS epidemic patients is strongly recommended.

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3/25/2021