新型冠状病毒信息简报

第 45 期（2020 年 5 月 2 日报）

上海科技大学免疫化学研究所

生物医学大数据平台和高通量筛选平台领衔编译制作

联系人：蒋立春 jianglch@shanghaitech.edu.cn

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1. 2020 年 5 月 1 日疫情

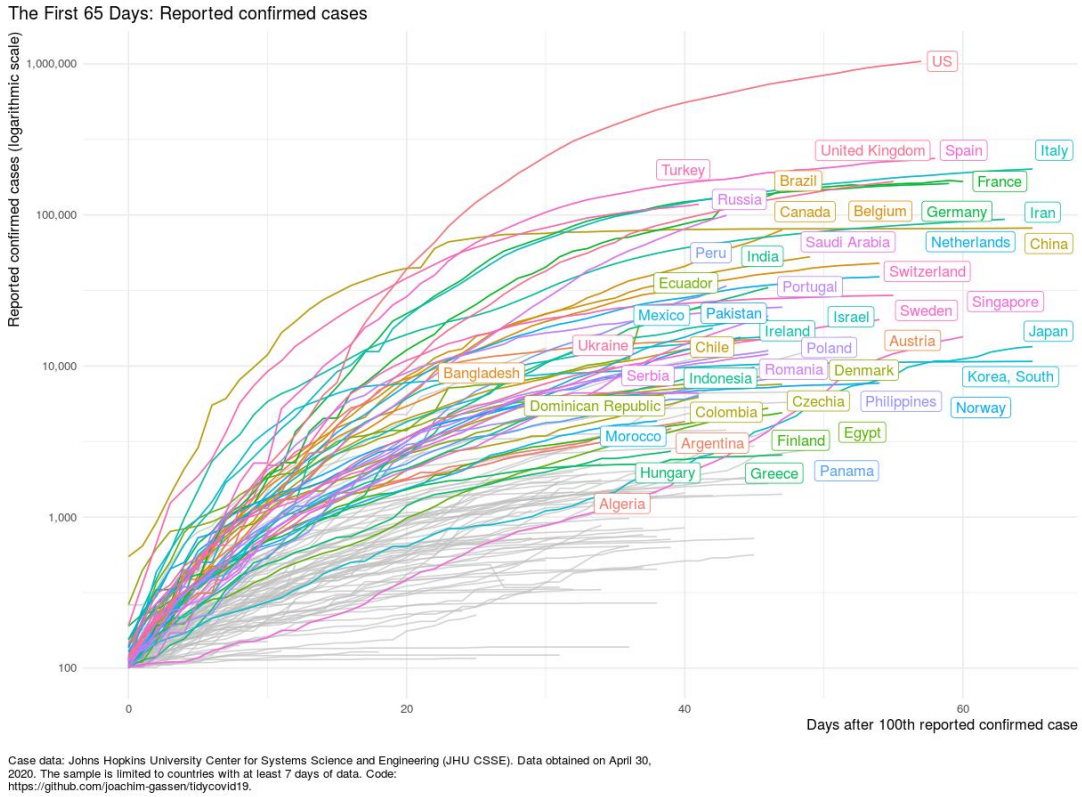
数据来源：WHO

发布时间：2020 年 5 月 1 日北京时间下午 4 点

链接：https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports

根据 WHO 提供的数据，2020 年 5 月 1 日全球累计确诊新型冠状病毒病人 3175207 例，当日新增确诊 84771 例，累计死亡 224172 例，当日新增死亡 6403。

中国累计确诊 84385 例，累计死亡 4643 例，当日新增确诊 12 例，新增死亡 0 例。



重点国家确诊数量曲线（https://jgassen.shinyapps.io/tidycovid19/，数据截止 5 月 1 日北京时间下午 4 点）

全国新型冠状病毒肺炎新增确诊病例分布图（5 月 1 日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

2. 方舱医院医疗废水中存在 SARS-CoV-2 病毒 RNA，医疗废水可能造成的潜在病毒传播，医疗废水消毒的新挑战

Potential spreading risks and disinfection challenges of medical wastewater by the presence of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) viral RNA in septic tanks of fangcang hospital

来源：medrxiv

发布时间：2020-04-29

链接：https://www.medrxiv.org/content/10.1101/2020.04.28.20083832v1

第一作者：Dayi Zhang

通讯作者：Dayi Zhang，Jiuhui Qu

通讯作者单位：清华大学环境系

DOI：

编译者：蒋立春

中文摘要：

SARS-CoV-2 病毒存在于病人的粪便中，越来越多的证据表明生活污水系统在疫情爆发之前就存在 SARS-CoV-2 的病毒 RNA。而怎么处理医疗废水，消杀 SARS-CoV-2 成为了新的问题。用含氯消毒剂来消毒的方法简单易行，被广泛用于消毒。含氯消毒剂处理会生成 600 多种次生反应物，可能会危害生态环境。WHO 以往对集中消毒的推荐是在 PH<8.0 的情况下，用自由氯大于 0.5mg/L 的条件下处理 30 分钟或者以上。COVID-19 疫情爆发以来，我国紧急将医疗废水处理的标准提为自由氯高于 6.5mg/L，处理 1.5 小时以上。在这个研究中，研究者们在 2020 年 2 月 26 日，3 月 1 日和 10 日取样评估了武汉武昌方舱医院化粪池里的 SARS-CoV-2 RNA，意外地发现在 3 月 5 日之前用 800g/m3 次氯酸钠消毒处理后仍然可以发现 SARS-CoV-2 RNA.3 月 5 日之后进一步提高次氯酸钠会完全消除病毒 RNA。如果增加次氯酸钠的剂量，废水里面的 SARS-CoV-2 病毒 RNA 会消失，但是这样操作会导致废水里消毒剂次生反应物浓度过高，会带来不可忽视的生态隐患。

编者注：

文章中讲到 3 月 5 日之后武昌方舱医院提高了氯的浓度，处理后的医疗废水没有病毒 RNA 了。不知道这项措施是否对扩展到了所有定点医院。另外，文章没有讲到如何解决提高的消毒剂浓度带来的次生反应物过多的问题。也许需要更创新的消毒方案？自由氯过多，应该也容易带来参与消杀工作人员的工作安全问题。

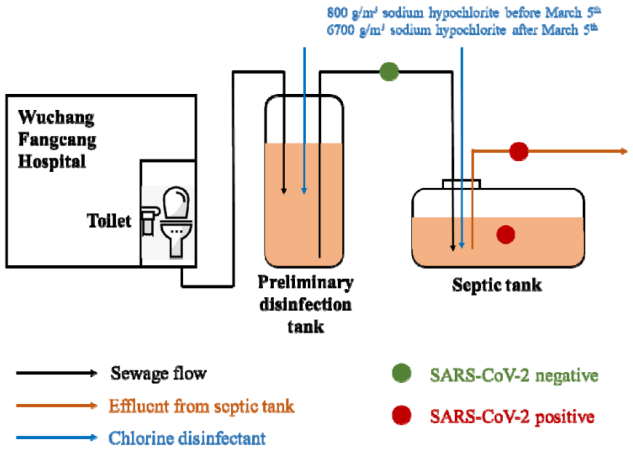


Figure 1. Schematic disinfection process of septic tanks of Wuchang Fangcang Hospital.

Table 1. Ct values of SARS-CoV-2 and free chlorine in the effluents of septic tanks of Wuchang Fangcang Hospital.

Dates	Samples	Positive	Ct		Free chlorine (mg/L)*
			CCDC-ORF1	CDCC-N	
26th February	Influent	0% (0/1)	Negative	Negative	ND
	Effluent	**100% (1/1)**	**32.52**	**31.03**	**ND**
1st March	Influent	0% (0/1)	Negative	Negative	ND
	Effluent	**100% (6/6)**	**Negative-30.15**	**30.69-35.67**	**ND**
10th March	Influent	0% (0/2)	Negative	Negative	ND
	Effluent	**0% (0/2)**	**Negative**	**Negative**	**21-25**

ND: not detectable. *: free chlorine in septic tank 12-hour after sodium hypochlorite addition.

The outbreak of coronavirus infectious disease-2019 (COVID-19) pneumonia raises the concerns of effective deactivation of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in medical wastewater by disinfectants.
In this study, we evaluated the presence of SARS-CoV-2 viral RNA in septic tanks of Wuchang Fangcang Hospital and found their unexpected occurrence after disinfection with sodium hypochlorite. Embedded viruses in faeces particles might be released in septic tanks, behaving as a source of SARS-CoV-2 and potentially contributing to its spread through drainage pipelines.
Current recommended disinfection strategy (free chlorine above 6.5 mg/L after 1.5-hour contact) needs to be reevaluated to completely remove SARS-CoV-2 viral RNA in non-centralized disinfection system and effectively deactivate SARS-CoV-2. The effluents showed negative results for SARS-CoV-2 viral RNA when overdosed with sodium hypochlorite but had high a level of disinfection by-product residuals, possessing significant ecological risks.

3. Poolkeh 找到了在人群里广泛进行 COVID-19 检测的混样策略（以色列，美国和英国为例）

Poolkeh Finds the Optimal Pooling Strategy for a Population-wide COVID-19 Testing (Israel, UK, and US as Test Cases)
来源：medrxiv
发布时间：2020-04-29
链接：https://www.medrxiv.org/content/10.1101/2020.04.25.20079343v1
第一作者：Yossi Eliaz，Mark Danovich，Gregory P. Gasic
通讯作者：Strategic Consulting Amey PLC London, UK；University of Houston
通讯作者单位：休斯顿大学
DOI：
编译者：蒋立春
中文摘要：
SARS-CoV-2 全球大流行改变了世界各国人民的生活方式。决策者需要在数据支持的基础上来制定政策以应对对病毒传播。因为病毒传播呈现指数增长，有可能再次爆发，决策者们需

要频繁快速地制定相关应对政策。在大流行期间准确快速地掌握全球每个人的健康状态可以挽救很多人的生命，也可以帮助大家的生活回到新常态。
研究者们开发了一个数据驱动的工具 poolkeh （https://poolkeh.herokuapp.com/[可惜 host 在 google 上，我们打不开]），让决策者们能更快速通过检测评估病毒在的世界范围内人群里的传播。这个框架可以让各国健康机构找到最优的样品混合方案以最大化扩大 COVID-19 测试能力，从而适应当前各国的疫情需求。

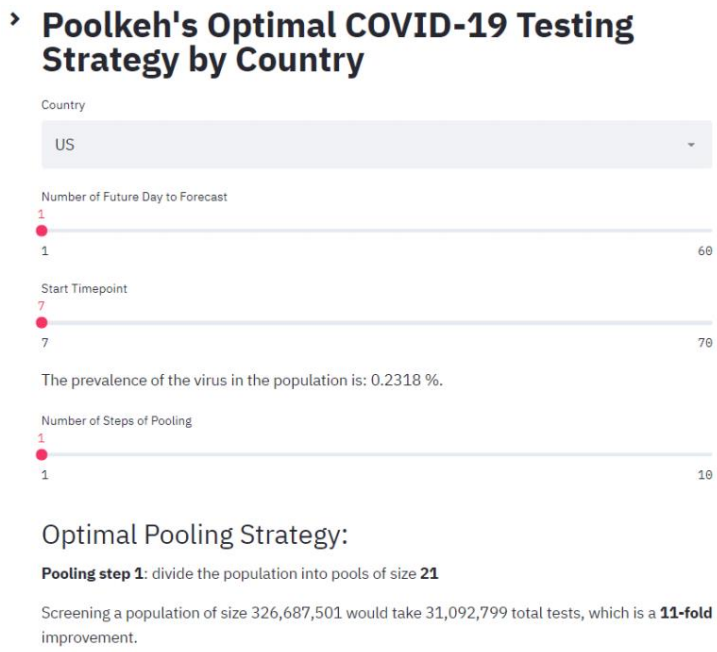


Figure 5: The User-Interface of Poolkeh-COVID-19 pooling optimizer.

Abstract:
The SARS-CoV-2 pandemic has changed the lifestyle of citizens of the world. In order for decision makers to manage the viral spread of COVID-19 both in the intra-national and the international frontiers, it is essential to operate based on data-driven assessments. It's crucial to do so rapidly and frequently, since the nature of the viral spread grows exponentially and can burst worldwide again. A fast and accurate health status of individuals globally during a pandemic can save many lives and bring life back to a new normal. Herein, we present a data-driven tool to allow decision-makers to assess the spread of the virus among the world population. Our framework allows health agencies to maximize the throughput of COVID-19 tests among the world population by finding the best test pooling that fits the current SIR-D status of the nation.

4. 高频率的 SARS-CoV-2 RNAemia（血液 RNA）与重症疾病相关

High frequency of SARS-CoV-2 RNAemia and association with severe disease

来源：medRxiv
发布时间：2020-05-01
链接：https://www.medrxiv.org/content/10.1101/2020.04.26.20080101v1

第一作者：Catherine A. Hogan
通讯作者：Benjamin A. Pinsky
通讯作者单位：斯坦福大学
DOI 或 PUBMED ID：
编译者：宋张悦
中文摘要：

背景：目前已经有报道称在血液中检测到 SARS-CoV-2 RNA，也称为 RNAemia，但其预后意义尚不清楚。本研究旨在确定血浆中 SARS-CoV-2 RNA 的频率及其与 COVID-19 临床严重程度的关系。

方法：在北加州一个单中心三级护理机构进行了一项横断面分析研究，包括通过检测鼻咽拭子样本中的 SARS-CoV-2 RNA 而确诊的 COVID-19 的连续住院患者和门诊患者。研究人员测定了 SARS CoV-2 RNAemia 的患病率及其与临床严重程度变量的相关性，包括需要转入重症监护病房(ICU)、机械通气和 30 天全因死亡率。

结果：收集了来自 85 例患者的配对的鼻咽和血浆样本。总体中位年龄为 55 岁，RNAemia 患者的年龄大于血浆中检测不到 SARS-CoV-2 RNA 的患者(63 vs 50 岁；p = 0.001)。常见的合并基础疾病包括肥胖(37.7%)、高血压(30.6%)和糖尿病(22.4%)。共检出 28/85(32.9%)例 RNAemia 患者，其中 22/28(78.6%)例患者需要住院治疗。RNAemia 在出现重症的患者中被更频繁地检测到，包括需要转入 ICU (32.1% vs 14.0%；(p=0.05)，机械通气(21.4% vs 3.5%；(p=0.01)和 30 天全因死亡率(14.3% vs 0%；p = 0.01)。在 RNAemia 与鼻咽部病毒 RNA 的估计水平之间未发现存在相关性。对 28 名 RNAemia 患者的另外 121 份血浆样本进行了纵向评估，最长可在 10 天的时间内检测到病毒 RNA。

结论：本研究表明，SARS-CoV-2 RNAemia 的比例很高，以及 RNAemia 与临床严重程度之间的相关性，提示血浆病毒检测可作为 COVID-19 的预后指标。

Abstract:

Background: Detection of SARS-CoV-2 RNA in the blood, also known as RNAemia, has been reported, but its prognostic implications are not well understood. This study aimed to determine the frequency of SARS-CoV-2 RNA in plasma and its association with the clinical severity of COVID-19.

Methods: An analytical cross-sectional study was performed in a single-center tertiary care institution in northern California and included consecutive inpatients and outpatients with COVID-19 confirmed by detection of SARS-CoV-2 RNA in nasopharyngeal swab specimens. The prevalence of SARS CoV-2 RNAemia and the strength of its association with clinical severity variables were examined and included the need for transfer to an intensive care unit (ICU), mechanical ventilation and 30-day all-cause mortality.

Results: Paired nasopharyngeal and plasma samples were included from 85 patients. The overall median age was 55 years, and individuals with RNAemia were older than those with undetectable SARS-CoV-2 RNA in plasma (63 vs 50 years; p=0.001). Comorbidities were frequent including obesity (37.7%), hypertension (30.6%) and diabetes mellitus (22.4%). RNAemia was detected in a total of 28/85 (32.9%) individual patients, including 22/28 (78.6%) who required hospital admission. RNAemia was detected more frequently in individuals who developed severe disease including the need for ICU transfer (32.1% vs 14.0%; p=0.05), mechanical ventilation (21.4% vs 3.5%; p=0.01) and 30-day all-cause mortality (14.3% vs 0%;

p=0.01). No association was detected between RNAemia and estimated levels of viral RNA in the nasopharynx. An additional 121 plasma samples from 28 individuals with RNAemia were assessed longitudinally, and RNA was detected for a maximum duration of 10 days.

Conclusion: This study demonstrated a high proportion of SARS-CoV-2 RNAemia, and an association between RNAemia and clinical severity suggesting the potential utility of plasma viral testing as a prognostic indicator for COVID-19.

5. 美国 NIH 发起竞赛，加速 COVID-19 诊断

NIH launches competition to speed COVID-19 diagnostics

来源： Science

发布时间： 2020-04-29

链接： https://www.sciencemag.org/news/2020/04/nih-launches-competition-speed-covid-19-diagnostics#

第一作者： Robert F. Service

通讯作者： Robert F. Service

通讯作者单位：

DOI 或 PUBMED ID：

编译者： 王玮

中文摘要：

美国 NIH 今天宣布了一项 15 亿美元的计划，以加快对导致 COVID-19 病毒的诊断测试的突破。该计划的目标是在夏末之前将美国检测 SARS-CoV-2 的能力提高 100 倍，以赶上流感季节的开始。

NIH 所长 Francis Collins 在与记者的电话会议上说，为了应对全球大流行病，至少在有效的疫苗问世之前，迫切需要改进的检测方法，这些技术对我们恢复正常生活将起到关键作用。这项被称为快速诊断加速（RADx）的工作将使用现有的 NIH 资助的诊断开发中心网络来评估提案。该网络将批准的团队与技术、监管批准、商业化和制造业的专家配对，以加快他们的进展。提案可以使用任何技术来检测感染，并将评估其改进测试性能的可能成功性（如速度、可靠性、准确性和易用性），又比如检测唾液或呼气中的病毒。

NIH 官员在今天的电话会议上说，该院已经接受了相关建议，并预计将批准大约 100 个诊断项目，最多可进行三轮开发。NIH 预计将支持其中一些项目进行全面的商业开发。

匹兹堡大学医学中心的诊断专家 Alan Wells 说，我们有足够的测试平台，问题是供应链被搞砸了，这使得实验室无法获得足够的化学试剂来满负荷运转实验室，期望一项新技术在几个月内从概念到验证并扩大规模是不现实的。我不管你给我多少钱，到 11 月我每周不会有 1000 万次的检查。

美国实验室现在每周进行大约 150 万次冠状病毒检测。目前检测的主流是 RT-PCR 技术，它可以放大病毒的遗传物质，使其更易于检测。但在许多情况下，用于采集样本的鼻拭子无法捕获病毒物质，导致多达 30%的病毒携带者被诊断为没有病毒。将测试转移到测试中心并运行测试也可能需要几天的时间，这意味着最终测试呈阳性的人在等待结果时可能会不知不觉地感染其他人。

一些技术正在开发中，以解决 PCR 的问题。几家公司正试图检测被称为抗原的病毒蛋白。但到目前为止，由于很难找到 SARS-CoV-2 特有的蛋白质靶点，以及在检测少量病毒方面遇到了挑战。另一种正在开发中的方法是使用 CRISPR 来检测 SARS-CoV-2 独有的病毒 RNA 片段。早期的研究表明，这种方法与 RT-PCR 同样精确，但该技术在实际条件下验证测试和扩大生产规模方面面临障碍。

Collins 说，这正是 RADx 可以提供帮助的地方。接受的提案将与项目开发和商业化专家配对，NIH 将提供资金、合作伙伴关系和其他资源，以便在尽可能短的时间内部署成功的测试。国会上周通过的 4840 亿美元的冠状病毒救助计划中包括了这项新计划的资金。如果成功的话，改进的诊断技术将不仅有助于当前的大流行，而且也有助于抗击未来的传染病爆发。

Abstract:
The U.S. National Institutes of Health (NIH) today announced a $1.5 billion initiative to speed breakthroughs in diagnostic tests for the virus that causes COVID-19. The program aims to increase the U.S. capacity for SARS-CoV-2 testing up to 100-fold by late summer, in time for the start of the flu season…

6. 重症新冠肺炎患者中普遍存在维生素 D 缺乏的现象

Vitamin D insufficiency is prevalent in severe COVID-19

来源：medRxiv
发布时间：2020-04-24
链接：https://www.medrxiv.org/content/10.1101/2020.04.24.20075838v1.full.pdf
第一作者：Frank H. Lau
通讯作者：Dr. Frank H. Lau
通讯作者单位：Department of Surgery, Louisiana State University Health Sciences Center New Orleans
DOI 或 PUBMED ID：https://doi.org/10.1101/2020.04.24.20075838
编译者：刘焕珍
中文摘要：
维生素 D 缺乏（VDI）会诱发血栓形成前状态，并对先天性和适应性免疫反应产生不利影响。为了更好地确定 VDI 与新冠肺炎的关系，作者测定了新冠肺炎重症监护病房（ICU）患者中 VDI 的患病率。在研究的 20 例新冠肺炎患者中，有 13 例 ICU 患者。总体而言，ICU 病人和非 ICU 病人之间的差异不显著。但由于受试者数量少的原因，统计分析数据有局限性。ICU 患者入院时乳酸脱氢酶明显更高（441.8 vs. 223.0，p = 0.001）。没有患者被诊断出患有中风，心肌梗塞或肺栓塞。在研究期间有 2 名患者（10％）死亡。在这项研究中，在 ICU 受试者中，作者发现 84.6％(11 例)的新冠肺炎 ICU 患者（13 例）患有 VDI，而 57.1％（4 例）的非 ICU 患者（7 例）患有 VDI，不到 75 岁的 ICU 患者 100％患有 VDI，他们还发现 62.5％的 ICU 患者患有 CAC（冠状动脉钙化），92.3％的 ICU 患者的淋巴细胞减少。根据这些数据，作者假设 VDI 通过 1）促血栓作用和 2）免疫应答紊乱来增强 COVID-19 的严重程度。
Abstract:
Vitamin D insufficiency (VDI) induces a prothrombotic state and adversely impacts both innate and adaptive immune responses. To better define the VDI-COVID-19 link, we determined the prevalence of VDI among our COVID-19 intensive care unit (ICU) patients. Twenty COVID-19 patients were identified; 13 (65.0%) required ICU admission. Overall, few significant differences were identified between ICU and floor patients but statistical analysis was limited by the small number of subjects. Lactate dehydrogenase on admission was significantly higher among ICU patients (441.8 vs. 223.0, p=0.001). No patients were diagnosed with stroke, myocardial infarction, or pulmonary embolus. Two patients (10%) died during the

study period. In this study, among ICU subjects, we found that 84.6% of COVID-19 ICU patients had VDI, vs. 57.1% of floor patients. Strikingly, 100% of ICU patients less than 75 years old had VDI. We also found that 62.5% had CAC, and 92.3% had lymphopenia. Given these data, we hypothesize that VDI enhances COVID-19 severity via 1) its prothrombotic effects and 2) its derangement of the immune response.

7. 意大利 Covid-19 爆发期间的院外心脏骤停

Out-of-Hospital Cardiac Arrest during the Covid-19 Outbreak in Italy

来源：The NEW EANGLAND JOURNAL of MEDICINE
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链接：https://www.nejm.org/doi/full/10.1056/NEJMc2010418?query=featured_home
第一作者：Enrico Baldi
通讯作者：Simone Savastano
通讯作者单位：Fondazione IRCCS Policlinico San Matteo Pavia, Italy
DOI 或 PUBMED ID：10.1056/NEJMc2010418
编译者：张鹏伟
中文摘要：
尽管 Covid-19 可能导致快速呼吸衰竭和心脏并发症，但目前尚不清楚 Covid-19 与院外心脏骤停之间是否存在关联。根据伦巴第心脏骤停登记(Lombardia CARe)，作者比较了 Covid-19 爆发前 40 天（2020 年 2 月 21 日至 3 月 31 日）在 Lodi、Cremona、Pavia 和 Mantua 省发生的院外心脏骤停与 2019 年同期（2 月 21 日至 4 月 1 日）发生的院外心脏骤停。
在 2020 年的研究期间，共报告 9806 例 Covid-19 病例。在此期间，发现 362 例院外心脏骤停，而 2019 年同期发现 229 例（增长 58%）。2020 年和 2019 年患者性别和年龄相似，但 2020 年因病院外心脏骤停发生率高 6.5 个百分点，家庭院外心脏骤停发生率高 7.3 个百分点，而未见证的心脏骤停发生率高出 11.3 个百分点。2020 年急救医疗服务到达时间中位数比 2019 年延长 3 分钟，接受旁观者心肺复苏的患者比例下降 15.6 个百分点。在急诊医疗机构尝试复苏的患者中，2020 年院外心脏骤停发生率比 2019 年高出 14.9 个百分点。
2020 年院外心脏骤停的累积发病率与 Covid-19 的累积发病率密切相关(Spearman rank correlation coefficient, 0.87; 95% confidence interval, 0.83 to 0.91; P<0.001)，在 Covid-19 爆发期间，院外心脏骤停的病例数比 2019 年增加了 133 例。103 例院外心脏骤停患者被怀疑或曾被诊断为 Covid-19（分别为 87 例和 16 例）；这些数字占这些省份 2020 年院外心脏骤停病例增长的 77.4%。
Abstract:
Despite the risk of rapid respiratory failure and cardiac complications due to Covid-19, it is unclear whether there is an association between Covid-19 and out-of-hospital cardiac arrest. Using the Lombardia Cardiac Arrest Registry (Lombardia CARe), we compared out-of-hospital cardiac arrests that occurred in the provinces of Lodi, Cremona, Pavia, and Mantua during the first 40 days of the Covid-19 outbreak (February 21 through March 31, 2020) with those that occurred during the same period in 2019 (February 21 through April 1).
During the study period in 2020, a total of 9806 cases of Covid-19 were reported in the study territory. During this period, 362 cases of out-of-hospital cardiac

arrest were identified, as compared with 229 cases identified during the same period in 2019 (a 58% increase). The sex and age of the patients were similar in the 2020 and 2019 periods, but in 2020, the incidence of out-of-hospital cardiac arrest due to a medical cause was 6.5 percentage points higher, the incidence of out-of-hospital cardiac arrest at home was 7.3 percentage points higher, and the incidence of unwitnessed cardiac arrest was 11.3 percentage points higher. The median arrival time of the emergency medical service was 3 minutes longer in 2020 than in 2019, and the proportion of patients who received cardiopulmonary resuscitation from bystanders was 15.6 percentage points lower. Among patients in whom resuscitation was attempted by the emergency medical service, the incidence of out-of-hospital death was 14.9 percentage points higher in 2020 than in 2019.

The cumulative incidence of out-of-hospital cardiac arrest in 2020 was strongly associated with the cumulative incidence of Covid-19 (Spearman rank correlation coefficient, 0.87; 95% confidence interval, 0.83 to 0.91; P<0.001), and the increase in the number of cases of out-of-hospital cardiac arrest over the number in 2019 (133 additional cases) followed the time course of the Covid-19 outbreak. A total of 103 patients who had out-of-hospital cardiac arrest were suspected to have or had received a diagnosis of Covid-19 (87 and 16 patients, respectively); these numbers account for 77.4% of the increase in cases of out-of-hospital cardiac arrest observed in these provinces in 2020.

8. 建模比较全身与肺氯喹暴露来确定 COVID-19 药物剂量

Modelling of Systemic versus Pulmonary Chloroquine Exposure in Man for COVID-19 Dose Selection

来源：medrxiv

发布时间：2020.04.30

文章链接：https://www.medrxiv.org/content/10.1101/2020.04.24.20078741v1

第一作者：Ghaith Aljayyoussi

通讯作者：Giancarlo A Biagini

通讯作者单位：利物浦热带医学院药物与诊断中心

DOI: https://doi.org/10.1101/2020.04.24.20078741

编译者：张怡

摘要

基于体外对 SARS-CoV-2 的疗效报告，氯喹作为一种潜在的 COVID-19 的预防和治疗的临床候选药物已经引起了广泛的关注。虽然氯喹在疟疾中的药代动力学-药效学(PK-PD)关系已经建立，但在 COVID-19 中关于其剂量-效应关系的信息却很少。

在此，作者通过模拟全身和肺部药物浓度，探讨了 COVID-19 中氯喹的 PK-PD 关系。数据表明，标准的抗疟疾治疗剂量为 3 天 25mg/kg，并不能提供足够的全身性药物暴露来抑制病毒复制。相比之下，使用体内数据或基于人体生理的 PK 模型对肺部氯喹的 PK 预测表明，低至 3 天 3mg/kg/day 的剂量可使暴露量显著高于已报告的抗病毒 EC90，最多可达一周。此外，如果肺部暴露是预防的一个驱动因素，模拟显示，长期每日服用氯喹可能对于预防来说是不必要的。相反，每周 5mg/kg 的剂量将足以实现持续性肺部暴露的治疗活性。

这些发现揭示了氯喹在人体内的高度区域化分布，这可能会显著影响其对 COVID-19 的治疗

潜力。在体循环中，氯喹暴露不足以抑制 SARS-CoV-2 的复制。然而，如果治疗活性是由肺部暴露驱动的，应该有可能将氯喹剂量降低到安全水平。迫切需要随机的对照试验来解决这些突出问题。

Abstract

Chloroquine has attracted intense attention as a potential clinical candidate for prevention and treatment of COVID-19 based on reports of in-vitro efficacy against SARS-CoV-2. While the pharmacokinetic-pharmacodynamic (PK-PD) relationship of Chloroquine is well established for malaria, there is sparse information regarding its dose-effect relationship in the context of COVID-19. Here, we explore the PK-PD relationship of chloroquine for COVID-19 by modelling both achievable systemic and pulmonary drug concentrations. Our data indicate that the standard anti-malarial treatment dose of 25mg/kg over three days does not deliver sufficient systemic drug exposures for the inhibition of viral replication. In contrast, PK predictions of chloroquine in the lungs using in-vivo data or human physiologically based PK models, suggest that doses as low as 3mg/kg/day for 3 days could deliver exposures that are significantly higher than reported antiviral-EC90s for up to a week. Moreover, if pulmonary exposure is a driver for prevention, simulations show that chronic daily dosing of chloroquine may be unnecessary for prophylaxis purposes. Instead, once weekly doses of 5mg/kg would be sufficient to achieve a continuous cover of therapeutically active pulmonary exposures.

These findings reveal a highly compartmentalised distribution of chloroquine in man that may significantly affect its therapeutic potential against COVID-19. The systemic circulation is shown as one site where chloroquine exposure is insufficient to inhibit SARS-CoV-2 replication. However, if therapeutic activity is driven by pulmonary exposure, it should be possible to reduce the chloroquine dose to safe levels. Carefully designed randomized controlled trials are urgently required to address these outstanding issues.

9. 严重 SARS-CoV-2 与中枢神经系统（综述）

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and the Central Nervous System

来源： Trends in Neurosciences

发布时间：2020-04-22

链接：https://www.cell.com/trends/neurosciences/fulltext/S0166-2236(20)30091-6

第一作者：Fernanda G. De Felice

通讯作者：Fernanda G. De Felice

通讯作者单位：里约热内卢大学 Institute of Medical Biochemistry Leopoldo de Meis, Federal

University of Rio de Janeiro, Rio de Janeiro,

DOI 或 PUBMED ID：https://doi.org/10.1016/j.tins.2020.04.004

编译者：孔娟

中文摘要：

新的证据表明 COVID-19 会导致神经并发症。作者简要概述 SARS-CoV-2 感染可能的长期影

响包括神经和神经退行性疾病，SARS-CoV-2 感染和神经系统并发症之间的联系。文中作者提供了关于病毒感染对中枢神经系统影响的大量文献的样本，目的是强调 COVID-19 背景下可能涉及的一些后遗症和机制。

作者首先阐述了冠状病毒、SARS-CoV-2 及其对多器官系统的影响。其次根据已有文献报道阐述了 SARS-CoV-2 可能的神经向性，脑血管疾病是确诊为 COVID-19 并出现严重呼吸并发症的患者的共病之一，很多文献有相关病例报道，作者指出要确定在发生神经系统改变的患者的脑脊液中是否检测到了 SARS-CoV-2，和/或是否存在其他脑脊液改变，针对脑脊液的研究是必要的。

作者阐述了人体 CoV 和其他嗜神经病毒对中枢神经系统的影响，尽管目前还没有研究 SARS-CoV-2 是否以人类大脑或动物模型为目标，但在文献中已经确定，其他病毒以中枢神经系统为目标并引起神经系统改变，包括脑部炎症和脑脊髓炎。例如在多发性硬化患者的人脑组织和脑脊液中发现了 CoV 抗原和核糖核酸。为了更好地理解 SARS-CoV-2 的神经嗜性，并评估其对中枢神经系统的影响是通过直接感染还是通过与炎症/促炎症信号增强相关的继发作用。作者提出了一些待解决问题，同时提出了“SARS-CoV”对中枢神经系统影响的研究路线图，以阐明 SARS-CoV-2 是否以及如何影响中枢神经系统。此外，作者推论由于在神经退行性疾病和其他病毒感染中的发现表明，全身性炎症介质可能通过受损的血脑屏障功能进入中枢神经系统并触发损伤，因此 SARS-CoV-2 感染触发的全身性炎症可能进一步促进神经炎症过程并增加对神经综合征的易感性。

Abstract

Emerging evidence indicates that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the etiologic agent of coronavirus disease 2019 (COVID-19), can cause neurological complications. We provide a brief overview of these recent observations and discuss some of their possible implications. In particular, given the global dimension of the current pandemic, we highlight the need to consider the possible long-term impact of COVID-19, potentially including neurological and neurodegenerative disorders.

10. SARS-CoV-2 选择性地模拟人 ENaC 的可切割肽，以便战略性劫持宿主蛋白水解机器

SARS-CoV-2 selectively mimics a cleavable peptide of human ENaC in a strategic hijack of host proteolytic machinery

来源：bioRxiv

发布时间：2020-04-30

链接：https://www.biorxiv.org/content/10.1101/2020.04.29.069476v1

第一作者：Praveen Anand

通讯作者：AJ Venkatakrishnan、Venky Soundararajan

通讯作者单位：nference, inc, One Main Street, East Arcade, Cambridge, MA 02142, USA

DOI 或 PUBMED ID：Preprint

编译者：张丽双

中文摘要：

宿主蛋白的分子模拟是病毒逃避免疫监视和利用宿主细胞系统采取的一种进化策略。作者报道，SARS-CoV-2 已经进化出一个独特的且在以往冠状病毒序列中没有的 S1/S2 裂解位点（RRARSVAS），它能够模拟人类上皮钠通道 α-亚单位（ENaC-α）上一条序列完全相同的

FURIN 可裂解肽。已知 ENaC-α 裂解位点的基因截短突变可导致患者醛固酮失调，突出了模拟 SARS-CoV-2 肽的功能重要性。来自 65 项研究的单细胞 RNA-seq 显示，在与 COVID-19 病理生理学相关的心血管-肾-肺等细胞类型中，ENaC-α 和病毒的公认受体 ACE2 的表达存在显著重叠。对 178 种人类蛋白酶的氨基酸裂解特征的细胞指纹进行三角剖分，推测病毒可能将组织特异性蛋白降解途径纳入到 SARS-CoV-2 生命周期中。作者推测，SARS-CoV-2 演变成全球冠状病毒大流行的部分原因可能是它对人 ENaC 的靶向模拟和相关宿主蛋白水解酶网络的劫持。

Abstract:
Molecular mimicry of host proteins is an evolutionary strategy adopted by viruses to evade immune surveillance and exploit host cell systems. We report that SARS-CoV-2 has evolved a unique S1/S2 cleavage site (RRARSVAS), absent in any previous coronavirus sequenced, that results in mimicry of an identical FURIN-cleavable peptide on the human epithelial sodium channel α-subunit (ENaC-α). Genetic truncation at this ENaC-α cleavage site causes aldosterone dysregulation in patients, highlighting the functional importance of the mimicked SARS-CoV-2 peptide. Single cell RNA-seq from 65 studies shows significant overlap between the expression of ENaC-α and ACE2, the putative receptor for the virus, in cell types linked to the cardiovascular-renal-pulmonary pathophysiology of COVID-19. Triangulating this cellular fingerprint with amino acid cleavage signatures of 178 human proteases shows the potential for tissue-specific proteolytic degeneracy wired into the SARS-CoV-2 lifecycle. We extrapolate that the evolution of SARS-CoV-2 into a global coronavirus pandemic may be in part due to its targeted mimicry of human ENaC and hijack of the associated host proteolytic network.

11. 在一家大规模的大学医院中验证 N95 过滤口罩的净化方法

英文标题（请覆盖）Validation of N95 filtering facepiece respirator decontamination methods available at a large university hospital

来源：medRxiv
发布时间：2020-04-30
链接：https://www.medrxiv.org/content/10.1101/2020.04.28.20084038v1
第一作者：Krista R. Wigginton
通讯作者：Nancy G. Love[1], Keith S. Kaye[2]
通讯作者单位：1 Department of Civil & Environmental Engineering, University of Michigan, Ann Arbor, MI, USA; 2 Division of Infectious Diseases, Department of Internal Medicine, University of Michigan Health System, Ann Arbor, MI, USA
DOI 或 PUBMED ID：
编译者：宋珂
中文摘要：
重要性：过滤面罩呼吸器（FFR），包括 N95 口罩，是医院中预防感染的重要物资。由于目前 N95 严重短缺，许多医疗保健系统都在探索重复利用 N95 口罩的净化方法。但在真实的医院环境中，这些方法的有效性却缺乏研究数据支持。特别是在已发表的研究中，尚未发现口罩对多种病原体，如：病毒，细菌和真菌，或某单一病原体的过滤效果的评估和全面研究。

目的：作者开展了全面的研究工作。在根据医院的需求和限制而确定的实验条件下，评估了不同的 N95 FFR 的净化方法，以及其对口罩完整性的影响，和对多种微生物的灭活效果。
方法：我们对全新的 3M™ 1860 N95 口罩测试了多种净化方法。包括使用工业清洗设备，在干燥（相对湿度<10%），潮湿（相对湿度在 62-66%）和热（80-82 ℃）的不同条件下，进行循环干燥。或使用环氧乙烷（EtO），脉冲氙气 UV（UV-PX），过氧化氢等离子气体（HPGP）和过氧化氢蒸汽（VHP）进行消毒。对口罩样品进行处理后，分析了不同处理方法对生物指示剂，包括：四种病毒（MS2, phi6, influenza A virus, murine hepatitis virus），三种细菌（*Escherichia coli, Staphylococcus aureus, Geobacillus stearothermophilus*）和 *Aspergillus niger* 的灭活效果。并评估了不同培养基的影响。同时，对净化后的口罩进行了过滤完整性和适用性的评估。
结果：VHP 处理对所有测试的生物指示剂的失活效果≥2 $\log_{10}$。经过 UV-PX + 温湿的联合处理后，除 *G. stearothermohphilus* 外，所有生物指示剂的失活效果≥2 $\log_{10}$。经过 2 次（UV-PX + <10％相对湿度加热）或 10 次（VHP）循环处理后，口罩仍保持了 95%以上的过滤效率，同时也保持了适当的贴合度。UV-PX + 干燥加热无法灭活所有生物指示剂。尽管 HPGP 方法对清除病毒非常有效，但经过 3 次循环处理后，过滤效率会下降。EtO 处理还会引起潜在的毒性风险。作者同时发现，存放病毒的培养基（PBS 缓冲液或 DMEM）也会影响 UV-PX，加热或过氧化氢处理对病毒的灭活效果。
结论和适用性：利用湿热或 VHP 处理，可以达到高水平的生物指示剂灭活效果，而且这些处理方法不会显著影响口罩的过滤效果或贴合性。医院具备多种可扩展处理方法，可以安全地处理并重复利用 N95 口罩。除了针对当前的 Covid-19 疫情，本文中进行了广泛的微生物和条件测试，这些结果对未来可能出现的流行病情况也具有指导意义。

Abstract:
Importance: Filtering facepiece respirators, including N95 masks, are a critical component of infection prevention in hospitals. Due to unprecedented shortages in N95 respirators, many healthcare systems have explored reprocessing of N95 respirators. Data supporting these approaches are lacking in real hospital settings. In particular, published studies have not yet reported an evaluation of multiple viruses, bacteria, and fungi along with respirator filtration and fit in a single, full-scale study.
Objective: We initiated a full-scale study to evaluate different N95 FFR decontamination strategies and their impact on respirator integrity and inactivating multiple microorganisms, with experimental conditions informed by the needs and constraints of the hospital.
Methods: We explored several reprocessing methods using new 3MTM 1860 N95 respirators, including dry (<10% relative humidity) and moist (62-66% relative humidity) heat (80-82 ℃) in the drying cycle of industrial instrument washers, ethylene oxide (EtO), pulsed xenon UV (UV-PX), hydrogen peroxide gas plasma (HPGP), and vaporous hydrogen peroxide (VHP). Respirator samples were treated and analyzed for biological indicator inactivation using four viruses (MS2, phi6, influenza A virus, murine hepatitis virus), three bacteria (Escherichia coli, Staphylococcus aureus, Geobacillus stearothermophilus), and the fungus Aspergillus niger. The impact of different application media was also evaluated. In parallel, decontaminated respirators were evaluated for filtration integrity

and fit.

Results: VHP resulted in ≥2 log_{10} inactivation of all tested biological indicators. The combination of UV-PX + moist heat resulted in ≥2 log_{10} inactivation of all biological indicators except G. stearothermohphilus. Greater than 95% filtration efficiency was maintained following 2 (UV-PX + <10% relative humidity heat) or 10 (VHP) cycles of treatment, and proper fit was also preserved. UV-PX + dry heat was insufficient to inactivate all biological indicators. Although very effective at virus decontamination, HPGP resulted in decreased filtration efficiency after 3 cycles, and EtO treatment raised potential toxicity concerns. The observed inactivation of viruses with UV-PX, heat, and hydrogen peroxide treatments varied as a function of which culture media (PBS buffer or DMEM) they were deposited in.

Conclusions and Relevance: High levels of biological indicator inactivation were achieved following treatment with either moist heat or VHP. These same treatments did not significantly impact mask filtration or fit. Hospitals have a variety of scalable options to safely reprocess N95 masks. Beyond value in the current Covid-19 pandemic, the broad group of microorganisms and conditions tested make these results relevant in potential future pandemic scenarios.

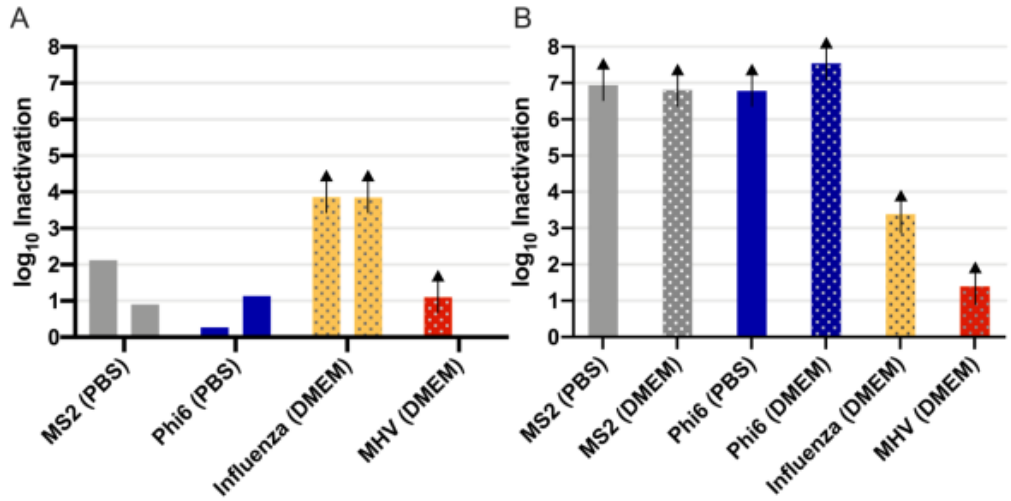

Figure 1. Virus removal from pulsed xenon UV followed by 82 °C heat for 30 mins. (A) Heat treatment with low relative humidity (~8% RH) and (B) heat treatment with moderate humidity (62-66% RH at 80 °C). Each bar represents the average of replicate experiments conducted on a single day (n = 2-3). Arrows identify samples that exceeded assay detection limits after treatment. Viruses were deposited on the coupons in either PBS or DMEM culture medium.

12. FDA 向瑞德西韦发放紧急使用授权用于 COVID-19 的治疗

FDA Issues Emergency Use Authorization for Potential COVID-19 Treatment

来源：FDA

发布时间：2020-05-01

链接：https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-issues-emergency-use-authorization-potential-covid-19-treatment

5 月 1 日，美国 FDA 给瑞德西韦发放了紧急使用授权，用于疑似或者确诊 COVID-19 重症的

的成人以及儿童住院病患。
紧急使用授权不同于 FDA 批准，当特定情况不再存在后将会失效。

编者注：
4 月 30 日简报我们报道了三条关于瑞德西韦治疗 COVID-19 的临床试验结果。虽然不能说是神药，中国的临床试验因为入组标准严格没有能够按照计划完成病人招募。该药在三项研究中，都证明可以算短住院时间，有一定效果。

13. Moderna 和 Lonza 公司达成了关于大规模额生产 COVID-19 疫苗的交易

Moderna and Lonza Enter Large-Scale Manufacturing Deal for Potential COVID-19 Vaccine
来源：biospace
链接：https://www.biospace.com/article/moderna-partners-with-swiss-company-lonza-to-manufacture-covid-19-vaccine/
发布时间：2020-05-01
生物技术公司 Moderna 研发的 COVID-19mRNA 疫苗 mRNA-1273 于 3 月 16 日开始临床试验接种第一个志愿者，在 4 月 23 日在西雅图开始第二轮的健康志愿者接种。一个中期试验预计会在第二季度开始。Moderna 公司和瑞士巴塞尔的 Lonza 公司达成一项大规模额生产 COVID-19 疫苗的交易。这项合作最多可以一年生产 10 剂 50ug/剂的 mRNA-1273 疫苗。达成的交易也包括将来其他疫苗的生产。