

Covid-19

Does steam Inhalation inactivate the SARS-CoV-2 Virus?

In the heat of the Coronavirus pandemic, many treatments have been and continue to be tried even as vaccines development is underway; including steam inhalation. Researchers hypothesized that steam inhalation could reduce or block the replication of the virus in the upper airway by denaturing its external protein structure. A small trial of ten SARS-CoV-2 infected participants was conducted. Participants' airway mucosae were exposed to humidified steam through inhalation for at least 20 minutes. The primary outcome was a reduction of viral shedding after four days. Cycles of steam inhalation were found beneficial in halting SARS-CoV-2 virus infection in the upper airway mucosae during the initial stages of infection. The researchers, however, noted that these findings would need confirmation in a larger controlled trial.

la Marca G, Barp J, Frenos S, Mugelli A, Galli L, Calistri E, Biasucci G, De Masi S, Guerrini R. Thermal inactivation of SARS COVID-2 virus: Are steam inhalations a potential treatment? *Life Sci.* 2021 Jan 15;265:118801. doi: 10.1016/j.lfs.2020.118801. Epub 2020 Nov 21. PMID: 33232690; PMCID: PMC7680040.

Protection against reinfection with SARS-CoV-2

The extent of protection conferred by SARS-CoV-2 infection against reinfection is unknown. A large population-level study was conducted in Denmark to assess this. During the country's second surge of SARS-CoV-2 infection, researchers compared infection rates among those who had tested PCR-positive with who tested PCR negative during the first surge. Of the 525,339 eligible for follow-up in the second surge, 11068 (2.11%) had tested positive during the first surge: of these, 72 (0.65%) tested positive again during the second surge compared with 16819 (3.27%) who tested negative during the first surge. Protection against repeat infection was 80.5%, though it was much lower in older patients (47.1%). No difference in protection by sex or time since the infection was observed. These findings will inform vaccination program implementation.

Hansen CH, Michlmayr D, Gubbels SM, Mølbak K, Ethelberg S. Assessment of protection against reinfection with SARS-CoV-2 among 4 million PCR-tested individuals in Denmark in 2020: a

population-level observational study. *Lancet.* 2021 Mar 27;397(10280):1204-1212. doi: 10.1016/S0140-6736(21)00575-4. Epub 2021 Mar 17. PMID: 33743221; PMCID: PMC7969130.

Single high dose Vitamin D3 supplementation in moderate to severe COVID-19

The efficacy of Vitamin D3 in COVID-19 has been unclear. Through a multicenter trial in Brazil, the effect of a single high dose of Vitamin D3 compared to placebo on the duration of hospital stay as well as other outcome parameters in patients with moderate to severe COVID-19 was evaluated. Of the 237 participants included in the primary analysis, there was no significant difference in length of stay, in-hospital mortality, admission to the intensive care unit, or need for mechanical ventilation between the two groups. The findings didn't support the use of high dose Vitamin D3 for treatment of moderate to severe COVID-19.

Murai IH, Fernandes AL, Sales LP, et al. Effect of a Single High Dose of Vitamin D3 on Hospital Length of Stay in Patients With Moderate to Severe COVID-19: A Randomized Clinical Trial. *JAMA.* 2021 Mar 16;325(11):1053-1060. doi: 10.1001/jama.2020.26848. PMID: 33595634; PMCID: PMC7890452.

Dexamethasone in Hospitalised Patients with COVID-19

COVID-19 is associated with diffuse lung damage. Dexamethasone may modulate inflammation-mediated lung injury and thereby reduce progression to respiratory failure and death. A large trial to evaluate the efficacy of dexamethasone in hospitalised COVID-19 patients was conducted; patients were assigned to receive dexamethasone (2104 patients), or usual care alone (4321 patients), the primary outcome being 28-day mortality. At analysis, the difference in mortality between groups varied according to the level of respiratory support that the patients were receiving at the time of randomization. The study found that the use of dexamethasone resulted in lower 28-day mortality among those who were receiving either invasive mechanical ventilation or oxygen alone at randomization but not among those receiving no respiratory support.

RECOVERY Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in Hospitalized Patients with Covid-19. *N Engl J Med.* 2021 Feb 25;384(8):693-704. doi: 10.1056/NEJMoa2021436. Epub 2020 Jul 17. PMID: 32678530; PMCID: PMC7383595.

Early plasma therapy to prevent progression of COVID-19 in older adults

Therapies to halt the progression of early COVID-19 remain elusive. Convalescent plasma administered to hospitalized patients has been unsuccessful, maybe because antibodies should be administered earlier in the course of treatment. In a clinical trial, 160 older adult patients were randomized to receive convalescent plasma with high IgG titers against SARS-CoV-2 within 72 hours after the onset of mild COVID-19 symptoms or a placebo. The primary end-point was severe respiratory disease. Severe respiratory disease developed in fewer patients that received convalescent plasma (16%) as compared to 31% who received placebo, with a relative risk reduction of 48%. The researchers concluded that early administration of high-titer convalescent plasma against SARS-CoV-2 to mildly ill infected older adults reduced the progression of COVID-19.

Libster R, Pérez Marc G, et al. Early High-Titer Plasma Therapy to Prevent Severe COVID-19 in Older Adults. *N Engl J Med.* 2021 Feb 18;384(7):610-618. doi: 10.1056/NEJMoa2033700. Epub 2021 Jan 6. PMID: 33406353; PMCID: PMC7793608.

Chest computed tomography findings in asymptomatic patients with COVID-19.

There is paucity of literature on the damage to the respiratory system among asymptomatic patients with coronavirus disease (COVID-19). Researchers at a University teaching hospital in South Korea evaluated the findings of chest computed tomography (CT) and radiography in patients with COVID-19 who had no symptoms. They retrospectively analysed chest CT and radiographic findings of asymptomatic patients who had been admitted with a confirmed diagnosis of COVID-19. They found that all patients (100%) had ground-glass opacity (GGO) on chest CT. The GGO lesions were predominantly distributed peripherally and posteriorly in all the patients. In 90% (9/10) of the patients, the GGO lesions were combined with reticular opacity. Air bronchograms were observed in 8 patients (80%). The lung lesions were dominant on the right side in all patients. They concluded that there was a need to expand the indications of COVID-19 testing to cater for asymptomatic cases.

Chang MC, Lee W, Hur J, Park D. Chest Computed Tomography Findings in Asymptomatic Patients

with COVID-19. *Respiration*. 2020;99(9):748-754. doi: 10.1159/000509334. Epub 2020 Sep 7. PMID: 32894853; PMCID: PMC7573893.

General

Short or long antibiotic therapy for diabetic foot osteomyelitis: Any difference in outcomes?

The optimal duration of antibiotic therapy for diabetic foot osteomyelitis (DFO) post-debridement remains unclear. In a recent randomized non-inferiority pilot trial with 93 participants, researchers compared outcomes and adverse effects in patients receiving either a short (3-weeks) or a long (6-weeks) course of systemic antibiotic therapy in DFO post-debridement. Remission occurred in 37 (84%) of the patients in the 3-weeks arm compared to 36 (73%) in the 6-week arm. This difference was not statistically significant. The incidence of adverse events was also similar in the two groups. The researchers concluded that a 3-week course of systemic antibiotic therapy post-debridement gave similar results as a 6-week course.

Gariani K, Pham TT, et al. Three versus six weeks of antibiotic therapy for diabetic foot osteomyelitis: A prospective, randomized, non-inferiority pilot trial. *Clin Infect Dis*. 2020 Nov 26;ciaa1758. doi: 10.1093/cid/ciaa1758. Epub ahead of print. PMID: 33242083.

Once-weekly Semaglutide in adults with overweight or obesity

Despite obesity being of major public health importance, few pharmacological options exist. Researchers sought to confirm if once-weekly Semaglutide as an adjunct to lifestyle intervention could achieve weight loss. 1961 adults with a body-mass index of 30 or greater without diabetes were assigned to treatment with subcutaneous Semaglutide or placebo for 68 weeks. The endpoints were percentage change in body weight and weight reduction of at least 5%. The findings were significant: a greater change in body weight was seen in the semaglutide group as compared to the placebo (-14.9% Vs. -2.4%) and more patients achieved at least 5% weight reduction (86.4% Vs. 31.5%).

Once-weekly semaglutide was associated with a sustained, clinically relevant reduction in body weight in patients with overweight or obesity.

Wilding JPH, Batterham RL, et al. Once-Weekly Semaglutide in Adults with Overweight or Obesity. *N Engl J Med*. 2021 Mar 18;384(11):989. doi: 10.1056/NEJMoa2032183. Epub 2021 Feb 10. PMID: 33567185.

Subclinical atherosclerosis is associated with poor cardiovascular health

Cardiovascular diseases are a rising burden in sub-Saharan Africa (SSA). Using the cardiovascular health index (CVHI): a tool for monitoring cardiovascular health, a team of researchers sought to expand the evidence for its use in under-studied populations in SSA, by determining its association with common carotid intima-media thickness (CIMT). A multi-centric cross-sectional study involving 9011 participants was conducted, results of which were significant of an inverse association between CVHI and common CIMT. Smoking, physical activity, and hyperglycemia were related to CIMT in women only, while blood pressure and obesity were related to CIMT in both women and men. This study confirmed CVHI as a strong marker of subclinical atherosclerosis and primary prevention should target physical activity, smoking, obesity, hypertension, and hyperglycemia.

Nonterah, E.A., Crowther, N.J., Oduro, A. et al. Poor cardiovascular health is associated with subclinical atherosclerosis in apparently healthy sub-Saharan African populations: an H3Africa AWI-Gen study. *BMC Med* 19, 30 (2021). <https://doi.org/10.1186/s12916-021-01909-6>

Regional differences in health worker behaviours regarding influenza vaccination

The World Health Organization vaccination targets for seasonal influenza for patients over 65 years old are not always met. In the 2013/2014, vaccination rates in Germany ranged between 14 and 65%. Researchers compared attitudes, personal characteristics and vaccination behaviors of general practitioners (GPs) in regions with high and low vaccination rates in Germany. They sent a questionnaire to 1594 GPs practicing in 16 districts with the highest and the lowest vaccination rates in Western and Eastern Germany. GPs ranked their attitudes towards vaccination in general and vaccination against influenza as mostly 'very positive' (80%, n = 352 and 65%, n = 288, respectively). GPs who practiced in regions with low vaccination rates reported their attitudes more negatively than those from regions with high vaccination rates. The strongest predictors of vaccination behavior belonged to external influences and information resources. The researchers concluded that "The results of this study suggest

a correlation between GPs' attitudes and regional vaccination rates. Beneath GPs' individual attitudes, the regional attitude patterns of patients, colleagues and medical assistants surrounding those GPs seem decisive and should be integrated into future campaigns to increase vaccination rates at a regional level".

Arlt J, Flaegel K, Goetz K, Steinhäuser J. Regional differences in general practitioners' behaviours regarding influenza vaccination: a cross-sectional study. *BMC Health Serv Res*. 2021 Mar 4;21(1):197. doi: 10.1186/s12913-021-06177-x. PMID: 33663449; PMCID: PMC7934451.

Impact of multiple cardiovascular medications on mortality after an ischemic stroke or transient ischemic attack

Although patients with stroke receive multiple cardiovascular medications, data on an optimum combination of these remains lacking. Data of 52,619 patients aged 45 and above with an incident stroke event were analyzed. Compared with patients prescribed monotherapy only, the hazard ratios (HRs) of mortality were 0.82 for 2 medications, 0.65 for 3 medications, 0.61 for 4 medications, 0.60 for 5 medications, and 0.66 for more than 6 medications. Patients with any four classes of anti-platelet agents, lipid-regulating medications, angiotensin-converting enzyme inhibitor/angiotensin receptor blockers, beta-blockers, diuretics, and calcium channel blockers had the lowest risk of mortality (HR 0.51), versus any one class. The conclusion was that combination therapy of four or five cardiovascular medications may be optimal to improve long-term survival post-stroke.

Ma TT, Wong ICK, et al. Impact of multiple cardiovascular medications on mortality after an incidence of ischemic stroke or transient ischemic attack. *BMC Med*. 2021 Feb 3;19(1):24. doi: 10.1186/s12916-021-01900-1. PMID: 33530992; PMCID: PMC7856718.

Dexamethasone in Chronic Subdural Hematoma

Chronic Subdural Hematoma (SDH) is a common neurological disorder in elderly patients. Dexamethasone is usually used in this patient group but its effect on outcomes hasn't been well studied. Researchers conducted a large trial involving 748 patients with symptomatic SDH, assigned to receive a 2-week tapering course of oral dexamethasone or placebo. The primary outcome was a score of 0 to 3, representing a favorable outcome on the modified Rankin scale at 6 months after randomization. Find-

ings showed fewer favorable outcomes in the dexamethasone group (83.9%) compared to the placebo (90.3%) at 6 months. Fewer repeat operations were however noted in the dexamethasone group (1.7%) as compared to the placebo (7.1%).

Hutchinson PJ, Edlmann E, et al. Trial of Dexamethasone for Chronic Subdural Hematoma. *N Engl J Med.* 2020 Dec 31;383(27):2616-2627. doi: 10.1056/NEJMoa2020473. Epub 2020 Dec 16. PMID: 33326713.

A randomised trial of Albumin Infusions in hospitalised patients with cirrhosis

Preliminary studies support albumin in patients with decompensated cirrhosis, but large studies to confirm this has been lacking. A large trial involving 777 patients was conducted, patients randomly assigned to receive either albumin infusions for up to 14 days or until discharge, whichever came first, or standard care. The primary endpoint was a composite of a new infection, kidney dysfunction, or death between days 3 and 15 after the initiation of treatment. The percentage of patients with a primary end-point event did not differ significantly between the albumin group (29.7%) and the standard-care group (30.2%). More adverse events occurred in the albumin group than the standard-care group. In conclusion, albumin infusions weren't found more beneficial than standard care.

China L, Freemantle N, et al. A Randomized Trial of Albumin Infusions in Hospitalized Patients with Cirrhosis. *N Engl J Med.* 2021 Mar 4;384(9):808-817. doi: 10.1056/NEJMoa2022166. PMID: 33657293.

HIV Vaccine (ALVAC-HIV and Bivalent Subtype C gp120–MF59) Efficacy Updates

The development of an HIV vaccine has continued to be a challenge. A recently concluded vaccine trial in South Africa is a case in point. 5404 adults without HIV were assigned to receive the vaccine (ALVAC–gp120 regimen) or placebo. The primary efficacy outcome was the occurrence of HIV-1 infection from randomization to 24 months. Prespecified criteria for non-efficacy were met on an interim analysis and further vaccinations were subsequently halted. The incidence of adverse events was similar in the vaccine and placebo groups. During the 24-month follow-up, HIV-1 infection was diagnosed in 138 participants in the vaccine group and 133 in the placebo group. In conclusion, the vaccine didn't prevent HIV-1

infection despite previous evidence of immunogenicity.

Gray GE, Bekker LG, et al. Vaccine Efficacy of ALVAC-HIV and Bivalent Subtype C gp120-MF59 in Adults. *N Engl J Med.* 2021 Mar 25;384(12):1089-1100. doi: 10.1056/NEJMoa2031499. PMID: 33761206; PMCID: PMC7888373.

MCH

Levonorgestrel vs. Copper intrauterine devices for emergency contraception

Emergency contraception is an essential component of family planning. A variety of methods to reduce the risk of unintended pregnancy exist including oral contraceptive pills as well as Intrauterine devices (IUDs). Only copper-IUDs are currently being used by clinicians in emergency contraception because data on the efficacy of the Levonorgestrel-IUDs are lacking. A large trial involving 355 participants from six clinics in Utah was conducted to compare the two IUDs. Participants were randomly assigned to receive a Levonorgestrel 52-mg IUD or a copper T380A IUD. The primary outcome was pregnancy at 1 month after IUD insertion. The Levonorgestrel-IUD was found to be non-inferior to the copper IUD for emergency contraception.

Levonorgestrel vs. Copper Intrauterine Devices for Emergency Contraception. *N Engl. J. Med* 2021 Jan 28;384(4):335- 344, DK Turok, A Gero, RG Simmons, JE Kaiser, GJ Stoddard, CD Sexsmith, LM Gawron, JN Sanders

Effects of maternal folic acid supplementation throughout pregnancy on neurocognitive development in the child

Maternal folic acid (FA) supplementation is known to prevent neural tube defects. It's been uncertain whether continuing FA after the first trimester is beneficial. Researchers evaluated the effect of FA supplementation throughout pregnancy on cognitive performance and brain function in 11-year-old children of mothers who had participated in a trial; one group received FA Supplementation throughout pregnancy while another received a placebo from the 14th gestational week. Both cognitive performance and neuronal function were assessed. Children of mothers randomized to FA, compared with placebo scored significantly higher in two processing Speed tests and had more efficient semantic processing of language.

In conclusion, continued FA supplementation beyond the first trimester can benefit the neurocognitive development of the child.

Caffrey A, McNulty H, Rollins M, et al. Effects of maternal folic acid supplementation during the second and third trimesters of pregnancy on neurocognitive development in the child: an 11-year follow-up from a randomised controlled trial. *BMC Med.* 2021 Mar 10;19(1):73. doi: 10.1186/s12916-021-01914-9. PMID: 33750355; PMCID: PMC7945668.

Higher or lower Hemoglobin Transfusion Thresholds for Pre-term Infants

Preliminary data suggest that higher hemoglobin transfusion thresholds for preterm infants with anemia may reduce the risk of cognitive delay. A total of 1824 infants participated in a large multicenter trial in which pre-term babies were randomly assigned within 48 hours after delivery to receive red-cell transfusions at higher or lower hemoglobin thresholds until 36 weeks of postmenstrual age or discharge, whichever came first. The primary outcome was a composite of death or neurodevelopmental impairment at 2 years of age. There was no significant difference in the outcomes between the two groups. It was hence concluded that a higher hemoglobin threshold for red-cell transfusion did not improve survival without neurodevelopmental impairment at 2 years.

Kirpalani H, Bell EF, Hintz SR, Tan S, Schmidt B, Chaudhary AS, Johnson KJ, Crawford MM, Newman JE, Vohr BR, Carlo WA, D'Angio CT, Kennedy KA, Ohls RK, Poindexter BB, Schibler K, Whyte RK, Widness JA, Zupancic JAF, Wyckoff MH, Truog WE, Walsh MC, Chock VY, Laptook AR, Sokol GM, Yoder BA, Patel RM, Cotten CM, Carmen MF, Devaskar U, Chawla S, Seabrook R, Higgins RD, Das A; Eunice Kennedy Shriver NICHD Neonatal Research Network. Higher or Lower Hemoglobin Transfusion Thresholds for Preterm Infants. *N Engl J Med.* 2020 Dec 31;383(27):2639-2651. doi: 10.1056/NEJMoa2020248. PMID: 33382931.

Maternal Body Mass Index is positively associated with human milk fat

Maternal obesity is a common public health concern and a risk factor for childhood obesity. Evidence on the influence of maternal body mass index (BMI) on human-milk nutrient composition is limited and inconclusive. In a recent meta-analysis that included 69 studies, researchers studied the relation between maternal BMI and human-milk energy, fat, and/or total protein. They assessed human-milk energy (kcal/L), fat (g/L), and total protein (g/L) from mothers 1 to 6 months postpartum. They

found a positive association between maternal BMI and human-milk fat but no significant association between maternal BMI and human-milk energy or total protein. The certainty of evidence, however, was low for human-milk energy and very low for fat and protein. In conclusion the researchers recommended future studies to confirm the relation between maternal BMI and variations in human milk energy, fat, and protein content and the implications for child growth and development

Daniel AI, Shama S, et. al. Maternal BMI is positively associated with human milk fat: a systematic review and meta-regression analysis. *Am J Clin Nutr.* 2021 Apr 6;113(4):1009-1022. doi: 10.1093/ajcn/nqaa410. PMID: 33675341.

Vaginal transmission of cancer from mothers with cervical cancer to infants

Transmission of maternal cancer to their offspring is possible, albeit extremely rare. It occurs in about 1 infant in 500,000 mothers with cancer even though 1 in 1000 live births includes a mother with cancer. Researchers in Japan recently reported two cases of pediatric lung cancer (in 23-month-old and 6-year-old boys) that resulted from mother-to-infant transmission of uterine cervical tumors. The diagnosis was made incidentally during routine

next-generation sequencing of paired samples of tumor and normal tissue. Some lesions in the 23-month-old child spontaneously regressed and slow growth of the tumor mass was observed in the second child, suggesting the existence of alloimmune responses against the transmitted tumors. Immune inhibitor therapy with Nivolumab was administered to the 23-month-old child and all remaining tumors regressed. The researchers concluded that next-generation sequencing of paired samples of tumor and normal tissue may play a major role in diagnosing cancer that is transmitted from mothers to infants.

Arakawa A, Ichikawa H, Kubo T, et al. Vaginal transmission of cancer from mothers with cervical cancer to infants. *N Engl J Med.* 2021;384(1):42-50. doi:10.1056/NEJ-Moa2030391

COVID-19 vaccine acceptance among pregnant women and mothers of young children: a multinational survey

Data on COVID-19 vaccination distribution and uptake is still insufficient and estimates of global vaccine acceptance among pregnant women and mothers of young children are unknown. Researchers administered an online survey and assessed acceptance

of COVID-19 vaccination among pregnant women and mothers of children younger than 18-years-old, plus potential predictors for acceptability. 17,871 survey responses were received from 16 countries (14 with a high incidence and 2 with low incidence) between October 28 and November 18, 2020. Assuming a 90% COVID-19 vaccine efficacy, 52.0% of pregnant women and 73.4% of non-pregnant women indicated an intention to get vaccinated. 69.2% of women, both pregnant and non-pregnant, indicated an intention to have their children vaccinated. Vaccine acceptance varied by country. Confidence in vaccine safety or effectiveness, worrying about COVID-19, belief in the importance of vaccines to their own country, compliance to mask guidelines, trust of public health agencies/health science, as well as attitudes towards routine vaccines were the strongest predictors of vaccine acceptance. The researchers concluded that “Vaccination campaigns for women and children should be specific for each country in order to attain the largest impact”.

Skjette M, Ngirbabul M, et. al. COVID-19 vaccine acceptance among pregnant women and mothers of young children: results of a survey in 16 countries. *Eur J Epidemiol.* 2021 Feb;36(2):197-211. doi: 10.1007/s10654-021-00728-6. Epub 2021 Mar 1. PMID: 33649879; PMCID: PMC7920402.



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