Coronavirus

Natural Health Research Review

By Ronald Steriti, ND, PhD

Covid-19

- This course describes Coronavirus 2019 and natural therapies based on published research.
- It is brief and written for the primary care physician in a private practice setting, which is often where people seek answers and preventive therapies.

Coronaviruses

- Coronaviruses are enveloped positive-stranded RNA viruses.
- People are frequently infected with four human coronaviruses: 229E, NL63, OC43, and HKU1
- They typically cause an upper respiratory tract infection with of symptoms the common cold.

- Habibzadeh, P and EK Stoneman (2020), 'The Novel Coronavirus: A Bird's Eye View.', *Int J Occup Environ Med*, 11 (2), 65-71. PubMed: 32020915

Appearance

- At the time this article was written, COVID-19 had just appeared in the United States.
- Many are scared and some are wondering if it is really that bad.

Severity

- According to Bill Gates recent article in *The New England Journal of Medicine*, we face an immediate crisis.
- Coronavirus disease 2019 (COVID-19-19) can kill healthy adults in addition to elderly people with existing health problems.

- Gates, B (2020), 'Responding to Covid-19 - A Once-in-a-Century Pandemic', *N Engl J Med*, PubMed: 32109012

Fatality Rate

- Its fatality rate (about 1%) is between the 1957 influenza pandemic and the 1918 influenza pandemic.
- Covid-19 has already caused 10 times as many cases as SARS in a quarter of the time.
- Covid-19 spreads very quickly.

- Gates, B (2020), 'Responding to Covid-19 - A Once-in-a-Century Pandemic', *N Engl J Med*, PubMed: 32109012

A Global Emergency

- The World Health Organization declared it a global emergency. (Sohrabi et al., 2020)

- Sohrabi, C, et al. (2020), 'World Health Organization declares Global Emergency: A review of the 2019 Novel Coronavirus (COVID-19).', *Int J Surg*, PubMed: 32112977

Symptoms

- The symptoms of COVID-19 are mild and include:
  - fever,
  - dry cough and
  - shortness of breath.
- People may be sick for 1 to 14 days before developing symptoms.

Transmission

- The novel virus is spread through respiratory droplets when patients cough, talk loudly or sneeze.
- Close contact is a source of transmission
  - contact with the mouth, nose or eye conjunctiva through contaminated hand

- Chen, ZM, et al. (2020), 'Diagnosis and treatment recommendations for pediatric respiratory infection caused by the 2019 novel coronavirus.', *World J Pediatr*, PubMed: 32026148

Prior Outbreaks

- Several coronavirus outbreaks have occurred.
  - 2003 SARS Severe Acute Respiratory Syndrome
  - 2012 MERS Middle East Respiratory Syndrome
  - 2015 MERS in South Korea
  - 2018 MERS
  - 2019 Covid-19

In-Home Isolation

- In-home isolation with health care monitoring is appropriate for those with mild symptoms.
- Schedule regular phone calls to assess symptoms (every day is optimal) and, if necessary, order specific diagnostic tests.

- Jin, YH, et al. (2020), 'A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version).', *Mil Med Res*, 7 (1), 4. PubMed: 32029004
- Habibzadeh, P and EK Stoneman (2020), 'The Novel Coronavirus: A Bird's Eye View.', *Int J Occup Environ Med*, 11 (2), 65-71. PubMed: 32020915

Key Signs

- Two key signs of severe illness are:
  - Continued fever (higher than 38°C, 100.4˚F)
  - Difficulty breathing.
- Increased respiration rates above 70/minute (children ≤ 1 year) or 50/minute (> 1 year) indicate severe illness.
- Those are about double normal: 12-20 for adults, and 30-60 for children ≤ 1 year.
- Liu, W, et al. (2020), 'Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease.', *Chin Med J (Engl)*, PubMed: 32118640

Lung Signs

- Patients in severe condition may have:
  - shortness of breath,
  - moist rales in lungs,
  - weakened breath sounds,
  - dullness in percussion, and
  - increased or decreased tactile speech tremor, etc.

- Jin, YH, et al. (2020), 'A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version).', *Mil Med Res*, 7 (1), 4. PubMed: 32029004

Progression

- Most COVID-19 cases spontaneously resolve.
- However, some progress to fatal complications.
- These include organ failure, septic shock, pulmonary edema, severe pneumonia, and acute respiratory distress syndrome (ARDS).

- Sohrabi, C, et al. (2020), 'World Health Organization declares Global Emergency: A review of the 2019 Novel Coronavirus (COVID-19).', *Int J Surg*, PubMed: 32112977

Comorbidities

- The most prevalent comorbidities are
  - Hypertension (17 ± 7, 95% CI 14-22%)
  - Diabetes (8 ± 6, 95% CI 6-11%)
  - Cardiovascular diseases (5 ± 4, 95% CI 4-7%)
  - Respiratory system disease (2 ± 0, 95% CI 1-3%).

- Yang, J, et al. (2020), 'Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis.', *Int J Infect Dis*, PubMed: 32173574

Cytokine Storm

- Severe illness from coronavirus is associated with
  - rapid virus replication,
  - massive inflammatory cell infiltration and
  - elevated pro-inflammatory cytokine/chemokine responses
- This results in acute lung injury and acute respiratory distress syndrome (ARDS).

- Channappanavar, R and S Perlman (2017), 'Pathogenic human coronavirus infections: causes and consequences of cytokine storm and immunopathology.', *Semin Immunopathol*, 39 (5), 529-39. PubMed: 28466096

Conventional Labs

- Conventional lab tests are for the common cold and influenza, and include a swab test of the nose or throat, nasal or tracheal aspirate.
- The general idea is to rule out common infections, such as influenza or pneumonia

- https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html

Diagnostic Panel

- According to the CDC, key clinical features indicating the 2019-nCoV diagnostic panel include:
  - fever with severe acute lower respiratory illness (e.g., pneumonia or acute respiratory distress syndrome) requiring hospitalization
  - without alternative explanatory diagnosis (such as influenza).
- This changes quickly as tests became available.
- https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html

CBC

- In early stages, leukocytes are decreased or normal, with decreased lymphocyte count or increased or normal monocytes.
- High attention should be paid on the situation where the absolute value of lymphocyte is less than 0.8 x 10^9/L, or the numbers of CD4 and CD8 T cells are significantly decreased, which generally recommend rechecking the blood routine changes after 3 days.

- Jin, YH, et al. (2020), 'A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version).', *Mil Med Res*, 7 (1), 4. PubMed: 32029004

CBC

- White blood cell count is usually normal or reduced, with decreased lymphocyte count; progressive lymphocytopenia in severe cases.
- CRP is normal or increased.
- Procalcitonin (PCT) is normal in most cases. PCT > 0.5 ng/mL indicates the co-infection with bacteria.
- Elevated liver enzymes, muscle enzymes and myoglobin, and increased D-dimer may be seen in severe cases.
- Chen, ZM, et al. (2020), 'Diagnosis and treatment recommendations for pediatric respiratory infection caused by the 2019 novel coronavirus.', *World J Pediatr*, PubMed: 32026148

Monitoring

- Routine monitoring includes:
  - CRP for inflammation
  - Procalcitonin (PCT) for bacterial sepsis
  - Organ function: liver enzymes, bilirubin, myocardial enzymes, creatinine, urea nitrogen, urine volume, etc.
  - Coagulation function
  - Arterial blood gas analysis
  - Chest imaging

Jin, YH, et al. (2020), 'A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version).', *Mil Med Res*, 7 (1), 4. PubMed: 32029004

Chest Imaging

- The imaging features of Coronavirus are highly non-specific and are typically bilateral with sub-pleural and peripheral distribution.
- Findings range from ground-glass opacities in milder forms to consolidations in more severe forms.

- Kooraki, S, et al. (2020), 'Coronavirus (COVID-19) Outbreak: What the Department of Radiology Should Know.', *J Am Coll Radiol*, PubMed: 32092296

Chest Xray or CT

- A portable X-ray may be recommended to limit patient transport and transmission.
- CT scans may monitor disease progression.

- Yoon, SH, et al. (2020), 'Chest Radiographic and CT Findings of the 2019 Novel Coronavirus Disease (COVID-19): Analysis of Nine Patients Treated in Korea.', *Korean J Radiol*, PubMed: 32100485

Conventional Treatment

- According to the CDC, no vaccine or specific treatment for COVID-19 is available.
- Care is supportive.

- https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html

Treatment of Fever

- Ibuprofen may be recommended when the temperature is higher than 38.5°C (101.3˚F).
- A temperature below 38 °C (100.4 ˚F) is acceptable.
- Much lower body temperatures may not conducive to antiviral treatment. (Jin et al., 2020) (Foxman et al., 2015)

- Foxman, EF, et al. (2015), 'Temperature-dependent innate defense against the common cold virus limits viral replication at warm temperature in mouse airway cells.', *Proc Natl Acad Sci U S A*, 112 (3), 827-32. PubMed: 25561542

Antibacterial Drugs

- Antibacterial drugs against pneumonia are often recommended.
  - Amoxicillin,
  - Azithromycin
  - Fluoroquinolones

- Jin, YH, et al. (2020), 'A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version).', *Mil Med Res*, 7 (1), 4. PubMed: 32029004

Antivirals

- Antiviral medications may also be recommended.
  - Oseltamivir (Tamiflu)
- Oseltamivir is a competitive neuraminidase inhibitor, the enzyme that cleaves the sialic acid.
- It prevents new viral particles from being released

- Wang, BX and EN Fish (2019), 'Global virus outbreaks: Interferons as 1st responders.', *Semin Immunol*, 43 101300. PubMed: 31771760
- Arabi, YM, R Fowler, and FG Hayden (2020), 'Critical care management of adults with community-acquired severe respiratory viral infection.', *Intensive Care Med*, 46 (2), 315-28. PubMed: 32040667

Oseltamivir

- Side effects include:
  - Nausea and vomiting and and gastrointestinal upset are the most common side effects
  - Gastrointestinal events were mild and transient and were less likely when oseltamivir was taken with food.
  - Headaches

Jefferson, T, et al. (2014), 'Oseltamivir for influenza in adults and children: systematic review of clinical study reports and summary of regulatory comments.', *BMJ*, 348 g2545. PubMed: 24811411

McClellan, K and CM Perry (2001), 'Oseltamivir: a review of its use in influenza.', *Drugs*, 61 (2), 263-83. PubMed: 11270942

Guaifenesin

- Guaifenesin thins mucus, which makes it easier to cough up the mucus and clear the airways.

- LaForce, C, DA Gentile, and DP Skoner (2008), 'A randomized, double-blind, parallel-group, multicenter, placebo-controlled study of the safety and efficacy of extended-release guaifenesin/pseudoephedrine hydrochloride for symptom relief as an adjunctive therapy to antibiotic treatment of acute respiratory infections.', *Postgrad Med*, 120 (2), 53-59. PubMed: 18654069

Indomethacin

- Indomethacin (Indocin) is a non-steroidal anti-inflammatory drug (NSAID)
- A study found that indomethacin is a potent inhibitor of coronavirus replication in vitro
- With both anti-inflammatory and antiviral activity, indomethacin could be beneficial in SARS therapy.

- Amici, C, et al. (2006), 'Indomethacin has a potent antiviral activity against SARS coronavirus.', *Antivir Ther*, 11 (8), 1021-30. PubMed: 17302372

ACE Inhibitors

- ACE2 has been identified as a functional receptor for coronaviruses
- ACE2 is involved in heart function, hypertension and diabetes mellitus.
- ACE inhibitors or angiotensin-receptor blockers in patients with COVID-19 should be carefully considered.

- Zheng, YY, et al. (2020), 'COVID-19 and the cardiovascular system.', *Nat Rev Cardiol*, PubMed: 32139904

Natural Therapies

- There is very little research on natural therapies for coronavirus.
- There are several natural therapies studied for the common cold or influenza that may be beneficial.

Roxas, M and J Jurenka (2007), 'Colds and influenza: a review of diagnosis and conventional, botanical, and nutritional considerations.', *Altern Med Rev*, 12 (1), 25-48. PubMed: 17397266

Mousa, HA (2017), 'Prevention and Treatment of Influenza, Influenza-Like Illness, and Common Cold by Herbal, Complementary, and Natural Therapies.', *J Evid Based Complementary Altern Med*, 22 (1), 166-74. PubMed: 27055821

Vitamin C

- “In the absence of a specific treatment for SARS coronavirus, the possibility that vitamin C may show non-specific effects on severe viral respiratory tract infections should be considered.”

- Hemilä, H (2003), ‘Vitamin C and SARS coronavirus.’, *J Antimicrob Chemother*, 52 (6), 1049-50. PubMed: 14613951

Vitamin C & Colds

- There are many studies on the efficacy of vitamin C for the common cold.
- Most studies find that vitamin C reduces the incidence and severity.

- Hemilä, H and E Chalker (2013), 'Vitamin C for preventing and treating the common cold.', *Cochrane Database Syst Rev*, (1), CD000980. PubMed: 23440782

Ascorbate

- A study showed that chick embryo tracheal organ cultures showed increased resistance to infection by a coronavirus after exposure to ascorbate.

- Atherton, JG, CC Kratzing, and A Fisher (1978), 'The effect of ascorbic acid on infection chick-embryo ciliated tracheal organ cultures by coronavirus.', *Arch Virol*, 56 (3), 195-99. PubMed: 205194

Vitamin C IV

- A clinical trial at the Zhongnan Hospital of Wuhan University, China is examining the use of vitamin C infusion for the treatment of severe 2019 new coronavirus infected pneumonia.
- Vitamin C 24 grams will be infused in the experimental group per day for 7 days with an infusion pump at a speed of 7ml/h.
- Estimated study completion date is September 30, 2020.
- https://clinicaltrials.gov/ct2/show/NCT04264533

Vitamin C in Sepsis

- Kuhn, SO, et al. (2018), 'Vitamin C in sepsis.', *Curr Opin Anaesthesiol*, 31 (1), 55-60. PubMed: 29176375

Ascorbic Acid IV

- Twenty-four patients with severe sepsis in the medical intensive care unit were randomized 1:1:1 to receive intravenous infusions every six hours for four days of ascorbic acid, or Placebo (5% dextrose/water, n = 8).
- Low Ascorbic Acid (50 mg/kg/24 h, n = 8), or
- High Ascorbic Acid (200 mg/kg/24 h, n = 8)

Fowler, AA, et al. (2014), 'Phase I safety trial of intravenous ascorbic acid in patients with severe sepsis.', *J Transl Med*, 12 32. PubMed: 24484547

Ascorbic Acid Levels

- Mean plasma ascorbic acid levels at entry for the entire cohort were 17.9 ± 2.4 μM (normal range 50-70 μM).
- Ascorbic acid infusion rapidly and significantly increased plasma ascorbic acid levels.
- No adverse safety events were observed in ascorbic acid-infused patients.

Improvements

- Patients receiving ascorbic acid exhibited prompt reductions in Sequential Organ Failure Assessment (SOFA) scores while placebo patients exhibited no such reduction.
- Ascorbic acid significantly reduced the pro-inflammatory biomarkers C-reactive protein and procalcitonin.
- Unlike placebo patients, thrombomodulin in ascorbic acid infused patients exhibited no significant rise, suggesting attenuation of vascular endothelial injury.

Results

- Intravenous ascorbic acid infusion was safe and well tolerated in this study and may positively impact the extent of multiple organ failure and biomarkers of inflammation and endothelial injury.

- Fowler, AA, et al. (2014), 'Phase I safety trial of intravenous ascorbic acid in patients with severe sepsis.', *J Transl Med*, 12 32. PubMed: 24484547

Antioxidants

- A study investigated the effect of intravenous antioxidant therapy on antioxidant status, lipid peroxidation, hemodynamics and nitrite in patients with septic shock.

- Galley, HF, et al. (1997), 'The effects of intravenous antioxidants in patients with septic shock.', Free Radic Biol Med, 23 (5), 768-74. PubMed: 9296454

Protocol

- Thirty patients randomly received either 5% dextrose or antioxidants intravenously:
  - N-Acetylcysteine 150 mg/kg for 30 min then 20 mg/kg/h plus bolus doses of 1 g ascorbic acid and 400 mg alpha-tocopherol.

Oxidative Response

- Basal vitamin C was low and redox-reactive iron was elevated in all patients.
- In the 16 patients receiving antioxidants, vitamin C increased ($p = .0002$) but total antioxidant capacity was unaffected.
- Lipid peroxides were elevated in all patients but did not increase further in the patients receiving antioxidants.
- Plasma total nitrite also increased ($p = .007$) in the antioxidant group.

Cardiac Response

- Heart rate increased in patients receiving antioxidants at 60 min ($p = .018$) and 120 min ($p = .004$).
- Cardiac index also increased at 60 min ($p = .007$) and 120 min ($p = .05$).
- Systemic vascular resistance index decreased at 120 min in the antioxidant treated patients ($p = .003$).

Adjunct

- Antioxidants may be a useful adjunct to conventional approaches in the management of septic shock.

- Galley, HF, et al. (1997), 'The effects of intravenous antioxidants in patients with septic shock.', Free Radic Biol Med, 23 (5), 768-74. PubMed: 9296454

Laurel Oil

- Laurus nobilis (bay laurel) is an evergreen tree.
- Whole bay leaves are used as a cooking spice.
- An infusion is used in folk medicine as a stomachic and carminative for the treatment of gastric diseases.

- Dall'Acqua, S, et al. (2009), 'Phytochemical composition and antioxidant activity of Laurus nobilis L. leaf infusion.', *J Med Food*, 12 (4), 869-76. PubMed: 19735189

Laurel Berry Oil

- Laurel nobilis (sweet laurel) berry oil has strong antiviral activity of against SARS coronavirus
- IC50 value is 120 mg/ml. IC50 is the concentration required to inhibit 50% of virus growth.
- The main constituents are
  - beta-ocimene (21.83%),
  - 1,8-cineole (9.43%),
  - alpha-pinene (3.67%), and
  - beta-pinene (2.14%).

- Loizzo, MR, et al. (2008), 'Phytochemical analysis and in vitro antiviral activities of the essential oils of seven Lebanon species.', *Chem Biodivers*, 5 (3), 461-70. PubMed: 18357554

Laurel against IBV

- 1,8-Cineole, α-pinene and (-)-β-pinene have activity against infectious bronchitis virus (IBV)
- IBV is the prototype species of the family Coronaviridae.

- Yang, Z, et al. (2010), 'Anti-infectious bronchitis virus (IBV) activity of 1,8-cineole: effect on nucleocapsid (N) protein.', *J Biomol Struct Dyn*, 28 (3), 323-30. PubMed: 20919748
- Yang, Z, et al. (2011), 'Comparative anti-infectious bronchitis virus (IBV) activity of (-)-pinene: effect on nucleocapsid (N) protein.', *Molecules*, 16 (2), 1044-54. PubMed: 21350392

Laurel Leaf Oil

- Laurel leaf oil typically used as a therapeutic
- It contains 1,8-Cineole (31.9%), sabinene (12.2%), linalool (10.2%), α-pinene (5.8%) and β-pinene (1.4%). (Caputo et al., 2017)
- Tunisian laurel leaves essential oil contained 1,8-cineole (46.8%), α-pinene (6.1%) and β-pinene (2.5%).

- Caputo, L, et al. (2017), 'Laurus nobilis: Composition of Essential Oil and Its Biological Activities.', *Molecules*, 22 (6), PubMed: 28587201
- Dhifi, W, et al. (2018), 'Phytochemical composition and antioxidant activity of Tunisian Laurus nobilis.', *Pak J Pharm Sci*, 31 (6), 2397-402. PubMed: 30473510

Leaf or Berry Oil

- Laurel leaf oil is designed for therapeutic use as an essential oil
- Laurel berry oil less expensive and is typically for topical use or a carrier oil

Essential Oils

- Studies show essential oils possess a wide-spectrum of antibacterial, antifungal and anti-viral activity.
- Several essential oils have antiviral activities against many RNA and DNA viruses, including
  - HSV-1 and HSV-2, dengue virus type 2,
  - influenza virusadeno virus type 3, poliovirus,
  - Junin virus, and coxsackievirus B1

Tariq, S, et al. (2019), 'A comprehensive review of the antibacterial, antifungal and antiviral potential of essential oils and their chemical constituents against drug-resistant microbial pathogens.', *Microb Pathog*, 134 103580. PubMed: 31195112

Licorice

- Glycyrrhizin, its amides and conjugates (components of licorice) have antiviral activity against SARS-coronavirus.
- Glycyrrhizin increases blood pressure

- Fiore, C, et al. (2008), 'Antiviral effects of Glycyrrhiza species.', *Phytother Res*, 22 (2), 141-48. PubMed: 17886224
- Hoever, G, et al. (2005), 'Antiviral activity of glycyrrhizic acid derivatives against SARS-coronavirus.', *J Med Chem*, 48 (4), 1256-59. PubMed: 15715493
- Cinatl, J, et al. (2003), 'Glycyrrhizin, an active component of liquorice roots, and replication of SARS-associated coronavirus.', *Lancet*, 361 (9374), 2045-46. PubMed: 12814717

Resveratrol

- Resveratrol, a natural compound found in grape seeds and skin and in red wine,
- Resveratrol was found to be potent against MERS coronavirus infection in Vero E6 cells.
- The expression of nucleocapsid protein, essential for MERS replication, was decreased after resveratrol treatment

- Lin, SC, et al. (2017), 'Effective inhibition of MERS-CoV infection by resveratrol.', *BMC Infect Dis*, 17 (1), 144. PubMed: 28193191

Elderberry

- Sambucus FormosanaNakai, a species of elderberry, showed strong activity against human coronavirus NL63.
- Caffeic acid may be the vital component.

- Weng, JR, et al. (2019), 'Antiviral activity of Sambucus FormosanaNakai ethanol extract and related phenolic acid constituents against human coronavirus NL63.', *Virus Res*, 273 197767. PubMed: 31560964

Elderberry Review

- A meta-analysis examined the effects of elderberry.
- The analysis included 180 participants
- Elderberry substantially reduced upper respiratory symptoms.

- Hawkins, J, et al. (2019), 'Black elderberry (Sambucus nigra) supplementation effectively treats upper respiratory symptoms: A meta-analysis of randomized, controlled clinical trials.', *Complement Ther Med*, 42 361-65. PubMed: 30670267

Chaga Mushroom

- A study tested bioactive compounds foranti-SARS activity.
- Betulonic acid (found in Chaga mushrooms) had an IC50 > 100

- Wen, CC, et al. (2007), 'Specific plant terpenoids and lignoids possess potent antiviral activities against severe acute respiratory syndrome coronavirus.', *J Med Chem*, 50 (17), 4087-95. PubMed: 17663539

Turmeric

- The same study also found that curcumin (from Turmeric, Curcuma longa) had an IC50 of 40

Wen, CC, et al. (2007), 'Specific plant terpenoids and lignoids possess potent antiviral activities against severe acute respiratory syndrome coronavirus.', *J Med Chem*, 50 (17), 4087-95. PubMed: 17663539

Flavonoids

- Herbacetin, rhoifolin and pectolinarin were found to block the enzymatic activity of SARS-Coronavirus 3C-like protease (3CLpro).

- Jo, S, et al. (2020), 'Inhibition of SARS-CoV 3CL protease by flavonoids.', *J Enzyme Inhib Med Chem*, 35 (1), 145-51. PubMed: 31724441

Rhoifolin

- Rhoifolin is found in:
  - Bitter orange, bergamot,
  - grapefruit, lemon, tomatoes, artichoke,
  - bananas and grapes.

- Refaat, J, SY Desoukey, and MA Ramadan (2015), 'Rhoifolin: A review of sources and biological activities', *Int J Pharmacognosy*, 2 (3), 102-9.

Herbacetin

- Herbacetin is found in
  - Flaxseed and
  - Rhodiola rosea.

- Péter Zomborszki, Z, et al. (2019), 'Rhodiosin and Herbacetin in Rhodiola rosea Preparations: Additional Markers for Quality Control?', *Pharm Biol*, 57 (1), 295-305. PubMed: 31356124
- Struijs, K, et al. (2007), 'The flavonoid herbacetin diglucoside as a constituent of the lignan macromolecule from flaxseed hulls.', *Phytochemistry*, 68 (8), 1227-35. PubMed: 17141814

Quercetin

- A study found that quercetin selectively inhibited the duplex DNA-unwinding activity in micromolar range (IC50 = 8.1 μM) in a model of SARS

- Lee, C, et al. (2009), 'Investigation of the pharmacophore space of Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) NTPase/helicase by dihydroxychromone derivatives.', *Bioorg Med Chem Lett*, 19 (16), 4538-41. PubMed: 19625187

Alpha-Lipoic Acid

- A study found that glucose-6-phosphate dehydrogenase (G6PD) deficiency enhanced human coronavirus 229E infection in mice.
- Viral gene expression and viral particle production were correlated with increased oxidant production,
- They were attenuated by antioxidants, such as alpha-lipoic acid.

- Wu, YH, et al. (2008), 'Glucose-6-phosphate dehydrogenase deficiency enhances human coronavirus 229E infection.', *J Infect Dis*, 197 (6), 812-16. PubMed: 18269318

Rhubarb

- Emodin (isolated from Rheum Palmatum, rhubarb) blocks the SARS coronavirus spike protein and angiotensin-converting enzyme 2 interaction.
- Emodin may be considered as a potential lead therapeutic agent in the treatment of SARS.

- Ho, TY, et al. (2007), 'Emodin blocks the SARS coronavirus spike protein and angiotensin-converting enzyme 2 interaction.', *Antiviral Res*, 74 (2), 92-101. PubMed: 16730806
- Kuba, K, et al. (2006), 'Lessons from SARS: control of acute lung failure by the SARS receptor ACE2.', *J Mol Med (Berl)*, 84 (10), 814-20. PubMed: 16988814

Vitamin D

- Vitamin D alleviates lipopolysaccharide-induced acute lung injury via regulation of the renin-angiotensin system.
- The mechanism was by modulating the renin-angiotensin system cascade.

- Xu, J, et al. (2017), 'Vitamin D alleviates lipopolysaccharide-induced acute lung injury via regulation of the renin-angiotensin system.', *Mol Med Rep*, 16 (5), 7432-38. PubMed: 28944831

Black Tea

- Crude theaflavin was extracted from black tea and assayed for activity against coronavirus
- EC50 was 34.7 micrograms/ml.

- Clark, KJ, et al. (1998), 'An in vitro study of theaflavins extracted from black tea to neutralize bovine rotavirus and bovine coronavirus infections.', *Vet Microbiol*, 63 (2-4), 147-57. PubMed: 9850995

Charcoal and Clay

- Adsorbent agents including charcoal, clay, and clay minerals have excellent capability of adsorbing coronavirus.
- Percent adsorptions was 99.99% for coronavirus.

- Clark, KJ, et al. (1998), 'In vitro studies on the use of clay, clay minerals and charcoal to adsorb bovine rotavirus and bovine coronavirus.', *Vet Microbiol*, 63 (2-4), 137-46. PubMed: 9850994

Rosaceae

- The extracts of Rosa nutkana and Amelanchier alnifolia, both members of the Rosaceae, were very active against an enteric coronavirus.

- McCutcheon, AR, et al. (1995), 'Antiviral screening of British Columbian medicinal plants.', *J Ethnopharmacol*, 49 (2), 101-10. PubMed: 8847882

Echinacea

- A randomized, double-blind, double-dummy, multicenter, controlled clinical trial compared a new echinacea formulation with the neuraminidase inhibitor oseltamivir, the gold standard treatment for influenza.

- Rauš, K, et al. (2015), 'Effect of an Echinacea-Based Hot Drink Versus Oseltamivir in Influenza Treatment: A Randomized, Double-Blind, Double-Dummy, Multicenter, Noninferiority Clinical Trial.', *Curr Ther Res Clin Exp*, 77 66-72. PubMed: 26265958

Participants

- 473 patients with early influenza symptoms (≤48 hours) were recruited in primary care in the Czech Republic
- They were randomized to either 5 days of oseltamivir followed by 5 days of placebo, or
- 10 days of an Echinacea purpurea and Elderberry formula: Echinaforce Hotdrink (A. Vogel Bioforce AG, Roggwil, Switzerland).

Recovery

- Recovery from illness was comparable in the 2 treatment groups after treatment with Echinaforce Hotdrink and oseltamivir, respectively
  - 1.5% versus 4.1% after 1 day,
  - 50.2% versus 48.8% after 5 days, and
  - 90.1% versus 84.8% after 10 days .
- Non-inferiority was demonstrated for each day and overall

Self-Care

- Echinaforce Hotdrink is as effective as oseltamivir in the early treatment of clinically diagnosed and virologically confirmed influenza virus infections with a reduced risk of complications and adverse events.
- It may be an attractive treatment option, particularly suitable for self-care.

Zinc Review

- Thirteen placebo-controlled comparisons examined zinc lozenges on common cold
- 5 used less than 75 mg and found no effect.
- 3 used zinc acetate daily over 75 mg with a 42% reduction in the duration of colds (95% CI: 35% to 48%).
- Five trials used other zinc salts daily over 75 mg, with a 20% reduction in the duration of colds (95% CI: 12% to 28%).

- Hemilä, H (2011), 'Zinc lozenges may shorten the duration of colds: a systematic review.', *Open Respir Med J*, 5 51-58. PubMed: 21769305

Ginseng

- Panax quinquefolium (North American ginseng) has been shown in controlled trials to reduce the incidence, duration, and severity of colds and flu in both ill and healthy individuals.

- Vohra, S, et al. (2008), 'Safety and tolerability of North American ginseng extract in the treatment of pediatric upper respiratory tract infection: a phase II randomized, controlled trial of 2 dosing schedules.', *Pediatrics*, 122 (2), e402-10. PubMed: 18676527

- Kaneko, H and K Nakanishi (2004), 'Proof of the mysterious efficacy of ginseng: basic and clinical trials: clinical effects of medical ginseng, korean red ginseng: specifically, its anti-stress action for prevention of disease.', *J Pharmacol Sci*, 95 (2), 158-62. PubMed: 15215639

Prevention

- Coronaviruses can persist on inanimate surfaces like metal, glass or plastic for up to 9 days.

- Rabenau, HF, et al. (2005), 'Stability and inactivation of SARS coronavirus.', *Med Microbiol Immunol*, 194 (1-2), 1-6. PubMed: 15118911

Disinfectants

- A few studies tested disinfectants against coronavirus.

- Kampf, G, et al. (2020), 'Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents.', *J Hosp Infect*, 104 (3), 246-51. PubMed: 32035997
- Dellanno, C, Q Vega, and D Boesenberg (2009), 'The antiviral action of common household disinfectants and antiseptics against murine hepatitis virus, a potential surrogate for SARS coronavirus.', *Am J Infect Control*, 37 (8), 649-52. PubMed: 19692148
- Geller, C, M Varbanov, and RE Duval (2012), 'Human coronaviruses: insights into environmental resistance and its influence on the development of new antiseptic strategies.', *Viruses*, 4 (11), 3044-68. PubMed: 23202515
- Rabenau, HF, et al. (2005), 'Efficacy of various disinfectants against SARS coronavirus.', *J Hosp Infect*, 61 (2), 107-11. PubMed: 15923059

Disinfectant List

- Clorox bleach (sodium hypochlorite)
- Hydrogen peroxide 0.5%
- Povidone iodine
- Lysol disinfectant spray (ethanol)
- Dettol brown liquid (PCMX)
- Clean & Smooth Antibacterial Soap (Triclosan)
- Pine-Sol (pine oil)
- Wine vinegar (acid concentration 6%)

Alcohol-Free

- Disinfectant hand rubs tested include:
  - Sterillium, Sterillium Rub and Sterillium Gel (alcohol-based)
- Surface disinfectants include
  - Mikrobac
  - Kohrsolin
  - Dismozon
- Instrument disinfectants include
  - Korsolex

WHO Disinfectants

- The World Health Organization (WHO) recommends two alcohol-based disinfectant formulations.
- Formula I contains: ethanol 80%, glycerol 1.45% and hydrogen peroxide (H2O2) 0.125%.
- Formula II contains: isopropyl alcohol 75%, glycerol 1.45%, hydrogen peroxide 0.125%.

WHO Effectiveness

- Both WHO formulas were found effective against Middle East respiratory syndrome coronavirus (MERS) and severe acute respiratory syndrome coronavirus (SARS).

- Siddharta, A, et al. (2017), 'Virucidal Activity of World Health Organization-Recommended Formulations Against Enveloped Viruses, Including Zika, Ebola, and Emerging Coronaviruses.', *J Infect Dis*, 215 (6), 902-6. PubMed: 28453839

Hydrogen Peroxide

- Hydrogen peroxide 3% concentration inactivated all the viruses under study within 1-30 min.
- Coronavirus and influenza viruses were found to be most sensitive.
- Hydrogen peroxide is a convenient means for virus inactivation.

- Mentel', R, et al. (1977), '[Virus inactivation by hydrogen peroxide].', *Vopr Virusol*, (6), 731-33. PubMed: 203115

Soap

- Soap has a very long history as an antiseptic and disinfectant.

- Symes, JO (1899), 'The Antiseptic and Disinfectant Properties of Soap.', *Bristol Med Chir J (1883)*, 17 (65), 193-97. PubMed: 28897108

Soap versus Virus

- Unfortunately, soap has not been studied for its antiviral effects against coronavirus.
- There are a few studies on other viruses.
- Soap and water was found to be better than alcohol-based hand rub.

- Tuladhar, E, et al. (2015), 'Reducing viral contamination from finger pads: handwashing is more effective than alcohol-based hand disinfectants.', *J Hosp Infect*, 90 (3), 226-34. PubMed: 25936671

Norwalk Virus

- Antibacterial liquid soap treatment (0.67 to 1.20 log(10) reduction) and water rinse only (0.58 to 1.58 log(10) reduction) were effective.
- The alcohol-based hand sanitizer was relatively ineffective.

- Liu, P, et al. (2010), 'Effectiveness of liquid soap and hand sanitizer against Norwalk virus on contaminated hands.', *Appl Environ Microbiol*, 76 (2), 394-99. PubMed: 19933337

Rhinovirus

- Single treatment with ethanol hand rub is ineffective against human rhinovirus
- Hand washing with soap and water removes the virus efficiently.

- Savolainen-Kopra, C, et al. (2012), 'Single treatment with ethanol hand rub is ineffective against human rhinovirus--hand washing with soap and water removes the virus efficiently.', *J Med Virol*, 84 (3), 543-47. PubMed: 22246844

Influenza A

- Hand hygiene with soap and water or alcohol-based hand rub is highly effective in reducing influenza A virus on human hands.
- Soap and water is the most effective intervention.

- Grayson, ML, et al. (2009), 'Efficacy of soap and water and alcohol-based hand-rub preparations against live H1N1 influenza virus on the hands of human volunteers.', *Clin Infect Dis*, 48 (3), 285-91. PubMed: 19115974

Hand Washing

- Although it may have been over-stated, washing your hands is an extremely effective preventive measure
- Regular soap, which is still available in stores, is very effective against viruses.

Conclusion

- Coronavirus 2019 has quickly become a global crisis and medical doctors and natural health practitioners are responding.
- This article presented published research on both conventional and natural therapies that may be beneficial.