



Physician connect

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Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you '**Physician connect**' which contains latest and interesting news in the field of Medicine.

This issue contains

- The origin, transmission on coronavirus disease 2019 (COVID-19) outbreak
- e-Cigarettes Plus Counseling More Effective Than Counseling Alone in Smoking Cessation: E3 Trial
- Inclisiran for the Treatment of Heterozygous Familial Hypercholesterolemia: ORION study

Should you require any specific article or medical information, please feel free to contact us at

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Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Limited

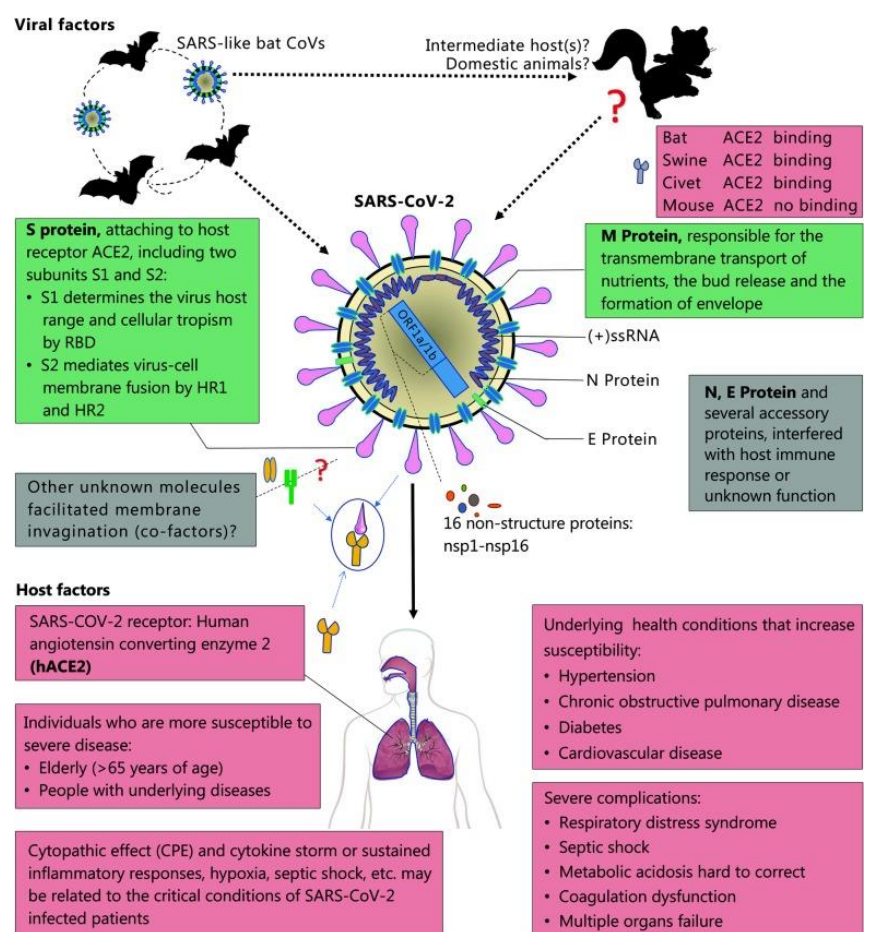
The origin, transmission on coronavirus disease 2019 (COVID-19) outbreak

In December 2019, a cluster of pneumonia cases, caused by a newly identified β -coronavirus, occurred in Wuhan, China. This coronavirus, was initially named as the 2019-novel coronavirus (2019-nCoV) on 12 January 2020 by World Health Organization (WHO). WHO officially named the disease as coronavirus disease 2019 (COVID-19) and Coronavirus Study Group (CSG) of the International Committee proposed to name the new coronavirus as SARS-CoV-2, both issued on 11 February 2020.

Meanwhile, several independent research groups have identified that SARS-CoV-2 belongs to β -coronavirus, with highly identical genome to bat coronavirus, pointing to bat as the natural host. The novel coronavirus uses the same receptor, angiotensin-converting enzyme 2 (ACE2) as that for SARS-CoV, and mainly spreads through the respiratory tract. Importantly,

increasingly evidence showed sustained human-to-human transmission, along with many exported cases across the globe.

The clinical symptoms of COVID-19 patients include fever, cough, fatigue and a small population of patients appeared gastrointestinal infection symptoms. The elderly and people with underlying diseases are susceptible to infection and prone to serious outcomes, which may be associated with acute respiratory distress syndrome (ARDS) and cytokine storm. Currently, there are fewer specific antiviral strategies, but several potent candidates of antivirals and repurposed drugs are under urgent investigation. The supporting treatments, combined with potent



antiviral drugs, such as remdesivir, chloroquine, or lopinavir/ritonavir, have been conducted with definite effect on treat COVID-19 patients, while solid data from more clinical trials are needed. However, questions remain vague and more studies are urgent to explore the transmission and pathogenicity mechanism of the emerging coronavirus. To make clear the evolutionary path from the original host to cross-species transmission so as to potentially limit the transmission to naïve animals or humans. In addition, to uncover the mystery of the molecular mechanism of viral entry and replication, which provides the basis of future research on developing targeted antiviral drugs and vaccines.

Source: Guo YR, et al. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak – an update on the status. *Mil Med Res.* 2020 Mar 13;7(1):11.

e-Cigarettes Plus Counseling More Effective Than Counseling Alone in Smoking Cessation: E3 Trial

In a comparative study, 376 participants (average age, 53 years) were included who had smoked for an average of 35 years and smoked an average of 21 cigarettes a day before the study. All participants were motivated to quit. One-third of the participants received e-cigarettes containing nicotine, one-third received e-cigarettes without nicotine and one-third did not receive an e-cigarette. Over the course of the study, all participants received about 100 minutes of counseling with guidance on quitting smoking. Those receiving e-cigarettes were instructed to vape as much as they felt they needed. Researchers stopped enrollment early (after reaching 77% of target enrollment) due to a disruption in the supply of commercial e-liquid used in the study. The study was underway before reports of vaping-linked lung injuries, and no such lung injuries occurred among study participants.

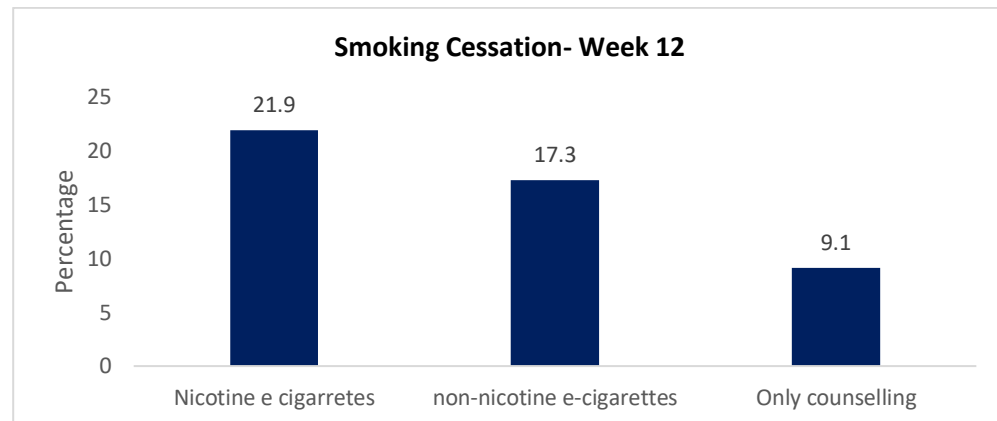
Health effects of e-cigarettes are unknown, and they should not be used for any purpose other than smoking cessation

The results showed that at 12 weeks, 21.9% of participants given nicotine-containing e-cigarettes had quit smoking, 17.3% of participants given non-nicotine e-cigarettes had quit and 9.1% of participants given only counseling had quit. Overall, those using nicotine-containing e-cigarettes were 2.4-times more likely to quit than those who did not vape at all.

Researchers also found that among participants who did not quit smoking, their daily use of cigarettes was cut in half or more by 61% of those vaping with nicotine, 45.7% of those vaping without nicotine and 30.9% of those receiving counseling alone.

Smokers who received smoking cessation counseling and used electronic cigarettes (e-cigarettes) containing nicotine were more than twice as likely to successfully quit smoking compared with those who received counseling but did not use e-cigarettes.

These findings show that nicotine e-cigarettes are effective for smoking cessation in the short term. The study will continue to collect data for one year to assess whether these effects persist over time. Researchers cautioned that the health effects of e-cigarettes are unknown, and they should not be used for any purpose other than smoking cessation.



It is important to note that in this study the participants were chronic smokers, who were highly motivated to discontinue cigarettes in favor of a non-smoking form of nicotine. The dose chosen was determined by the number of cigarettes used. This design acknowledges that nicotine is a drug that is highly addictive and supports the concept that substituting a less harmful type of nicotine such as gum, patch or e-cigarette, offers one mechanism by which to help smokers quit.

Source: Eisenberg MJ et al. E3 Trial: E-Cigarettes Plus Counseling More Effective Than Counseling Alone in Smoking Cessation. ACC 2020.

Inclisiran for the Treatment of Heterozygous Familial Hypercholesterolemia: ORION study

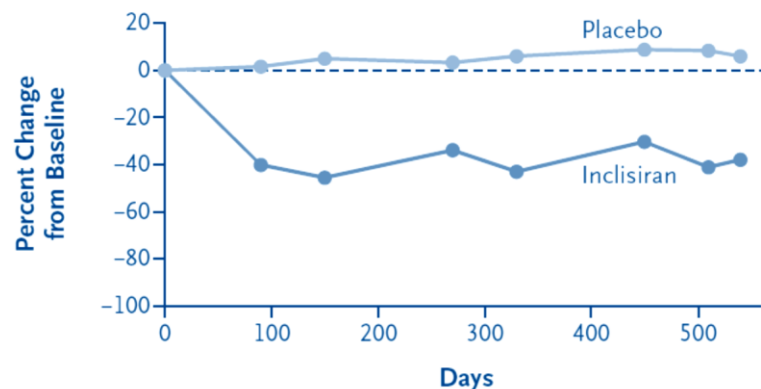
Familial hypercholesterolemia is characterized by an elevated level of low-density lipoprotein (LDL) cholesterol and an increased risk of premature atherosclerotic cardiovascular disease. Monoclonal antibodies directed against proprotein convertase subtilisin-kexin type 9 (PCSK9) have been shown to reduce LDL cholesterol levels by more than 50% but require administration every 2 to 4 weeks. In a phase 2 trial, a twice-yearly injection of inclisiran, a small interfering RNA, was shown to inhibit hepatic synthesis of PCSK9 in adults with heterozygous familial hypercholesterolemia.

In this phase 3, double-blind trial, we randomly assigned, in a 1:1 ratio, 482 adults who had heterozygous familial hypercholesterolemia to receive subcutaneous injections of inclisiran sodium (at a dose of 300 mg) or matching placebo on days 1, 90, 270, and 450. The two primary end points were the percent change from baseline in the LDL cholesterol level on day 510 and the time-adjusted percent change from baseline in the LDL cholesterol level between day 90 and day 540.

Inclisiran significantly lowers levels of LDL cholesterol

The median age of the patients was 56 years, and 47% were men; the mean baseline level of LDL cholesterol was 153 mg per deciliter. At day 510, the percent change in the LDL cholesterol level was a reduction of 39.7% (95% confidence interval [CI], -43.7 to -35.7) in the inclisiran group and an increase of 8.2% (95% CI, 4.3 to 12.2) in the placebo group, for a between-group difference of -47.9 percentage points (95% CI, -53.5 to -42.3; $P < 0.001$). The time-averaged percent change in the LDL cholesterol level between day 90 and day 540 was a reduction of 38.1% (95% CI, -41.1 to -35.1) in the inclisiran group and an increase of 6.2% (95% CI, 3.3 to 9.2) in the placebo group, for a between-group difference of -44.3 percentage points (95% CI, -48.5 to -40.1; $P < 0.001$). There were robust reductions in LDL cholesterol levels in all genotypes of familial hypercholesterolemia. Adverse events and serious adverse events were similar in the two groups.

A Change in LDL Cholesterol Level



No. of Patients

Placebo	240	237	238	235	233	233	229	232
Inclisiran	242	240	239	240	237	237	231	232

Among adults with heterozygous familial hypercholesterolemia, those who received inclisiran had significantly lower levels of LDL cholesterol than those who received placebo, with an infrequent dosing regimen and an acceptable safety profile.

Source: Frederick J et al. Inclisiran for the Treatment of Heterozygous Familial hypercholesterolemia. ACC 2020.



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