Smoking and COVID-19

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1.　Smoking and the aggravation of COVID-19 symptoms

 (1) Direct evidence

　About 7 days after the onset of initial COVID-19 symptoms, COVID-19 related pneumonia often becomes more severe.　According to novel coronavirus infection (COVID-19) medical treatment guide, version 4.1, of the Ministry of Health, Labor and Welfare; aggravating factors include smoking, being elderly (aged 65 and over), or having malignant tumors, chronic obstructive pulmonary disease (COPD), chronic kidney disease, Type 2 diabetes, hypertension or dyslipidemia (high cholesterol). Most of these diseases are also known to be directly caused by smoking[1].　For example, chronic obstructive pulmonary disease (COPD) is present in 95% of patients who are or were smokers. The relative risk of contracting end-stage kidney disease from chronic kidney disease is 1.44 for past smokers and 1.91 for current smokers. The relative risk of type 2 diabetes is 1.44 for current smokers, and smoking is also known to be significantly correlated with dyslipidemia and obesity.　Smoking also raises the risk of developing cancer in about 20 organs, mainly in the respiratory system, and it has been reported that active smoking is associated with 90% of lung cancer patients. In sum, smoking is correlated with most kinds of serious diseases.

　Therefore, it therefore seems reasonable that past and present smoking are also associated with more severe COVID-19 symptoms.

(2) Epidemiology

　Hitherto, several reports have included meta-analysis, but some of these studies are suspected to have received funding from the tobacco industry.　So when searching the literature on tobacco, one should reject articles whose authors have conflicts of interest, articles that have not been peer-reviewed, and articles with studies that violate their inclusion criteria of test subjects. In these senses, the articles from Miyara et al. and the article from Simon D et al. should be considered suspect.

　In addition, there are five other meta-analysis articles that deserve scrutiny.

Author	Journal	Significance of aggravated symptoms or death for smokers	
Patanavanich[2]	Nicotine Tob Res	1.9	aggravation
Salah[3]	Cureus	2.07	death
Rahman[4]	Int J Clin Pract	1.71	aggravation

| Dai[5] | China. Front Physiol. | 1.825 | death |
| Kunchok[6] | Plos One | 1.3 | death |

Thus, significant values (t-statistics) were found on both sides of two-tailed tests, and it has already been shown that smoking is significantly correlated with the aggravation of COVID-19 symptoms and mortality.

2. Ease of infection
 (1) Direct evidence

A paper by Tung et al.[7] reported that particulate matter ($PM_{2.5}$ and other diameters) increases novel coronavirus infections. The paper confirmed in animal experiments and in experiments with human alveolar cells that the ACE2 receptor acts as an entry point for the novel coronavirus and that exposure to particulate matter such as $PM_{2.5}$ increases respiratory ACE2 receptor expression. It was epidemiologically confirmed that $PM_{2.5}$ exposure increased the mortality rate of the novel coronavirus.

Wu et al.[8] examined the relationship between $PM_{2.5}$ exposure (2000-2016 average level) and the mortality rate from the novel coronavirus in 3000 counties in the United States, and the mortality rate was shown to increase 8% for every 1 $\mu g/m^3$ increase in $PM_{2.5}$ exposure (95% confidence interval 2%-15%) after controlling for 20 variables including population, age distribution, population density, number of days since an outbreak, number of days since an announcement of a stay at home order, number of hospital beds, number of PCR tests, weather, obesity rate and the tobacco smoking rate.
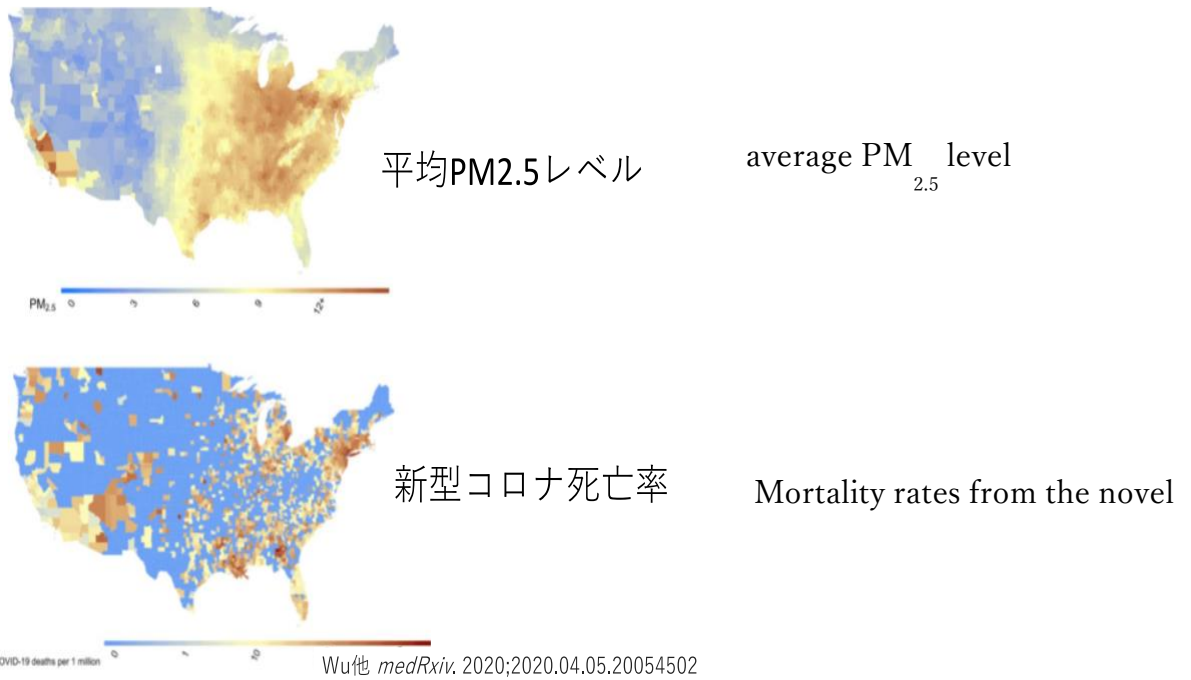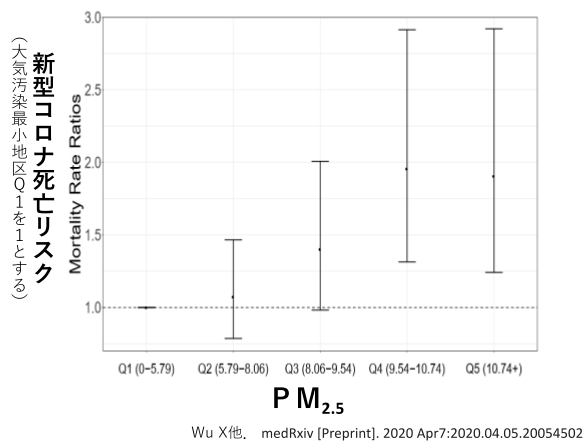
平均PM2.5レベル　　average PM$_{2.5}$ level

新型コロナ死亡率　　Mortality rates from the novel

Wu他 *medRxiv*. 2020;2020.04.05.20054502

図 1

Figure 1

新型コロナ死亡リスク（大気汚染最小地区Q1を1とする）

Mortality Rate Ratios

Q1 (0-5.79)　Q2 (5.79-8.06)　Q3 (8.06-9.54)　Q4 (9.54-10.74)　Q5 (10.74+)

P M$_{2.5}$

Wu X他． medRxiv [Preprint]. 2020 Apr7:2020.04.05.20054502

図 2）

Figure 2

　　In addition, Wu et al. show that PM$_{2.5}$ exposure increases by about 10 μg/m^3 to 100 μg/m^3 from indoor passive smoking (so that a 10 μg/m^3 increase in exposure increases mortality rate by 80%).　It is therefore imperative to quit smoking and to eliminate exposure passive smoking indoors protect against infection from the novel coronavirus.

　　Environmental Research has recently reported animal experiments from Japan, which show how PM$_{2.5}$ affects the lungs and makes them more susceptible to COVID-19 infection. According to the report, the amount of protein that the virus sticks to and the amount of

enzymes that the virus uses to enter the cells on the surface of the lungs are dozens of times higher when exposed to $PM_{2.5}$.　In brief, the virus can more easily invade lung cells when they are exposed to $PM_{2.5}$.

In conclusion, smoking significantly increases $PM_{2.5}$, and inhaled smoke contains 20,000 $\mu g/m^3$ of $PM_{2.5}$.　As exposure to $PM_{2.5}$ increases, it increases ACE2 receptor expression. An increase of $PM_{2.5}$ exposure by 1 $\mu g/m^3$ will increase the mortality rate of the novel coronavirus by 8%. The same relationship applies to passive smoking, and indoor passive smoking creates $PM_{2.5}$ exposure of about 10 $\mu g/m^3$ to 100 $\mu g/m^3$.

(2) Epidemiology

A survey of approximately 50,000 representatives of the general population in the United Kingdom found that smokers are at a 79% higher risk of novel coronavirus infection than never smokers[9]. Furthermore, according to Gaiha et al.[10], young people who use cigarettes and e-cigarettes are more susceptible to the novel coronavirus. According to the report, the number of people diagnosed with the new coronavirus infection was 5 times higher (95% confidence interval: 1.82–13.96) for e-cigarette only users (current and past), and 7 times higher for both tobacco cigarette and e-cigarette users (current and past) (95% confidence interval: 1.98–24.55) and 6.8 times higher (95% confidence interval: 5.43–15.47) for users of both in the past 30 days.

According to England's Smoking Toolkit Study[11], a monthly survey of England's population, smokers are now 1.34 times more likely to be infected than never smokers (1.04-1.73).

But the evidence of smoking and infection risk is not robust because even though all patients are tested for PCR, the tests do not use a random sample from the population, likely causing a sampling bias.

About 40% of new coronavirus cases are asymptomatic after infection is detected, and about 2/3 of recent antibody tests in Tokyo show similar results.　Thus, it is necessary to perform antibody tests on an appropriate sample to determine the population of infected persons, instead of relying only on results from PCR.

In any case, the incidence of infection remain high, and the effects of $PM_{2.5}$ data remain without doubt.

3. In conclusion

I think that it is important that WHO, CDC, and the Ministry of Health, Labor and Welfare explain the danger of smoking during the contagion of the novel coronavirus.

The WHO[12] suggests that smoking is associated with increased disease severity and mortality in inpatients infected with COVID-19. Given the established hazards associated with tobacco use and exposure to passive smoking, WHO recommends that tobacco users discontinue use.

CDC[13]: Current smokers or past smokers are more likely to become seriously ill with COVID-19.

Ministry of Health, Labor and Welfare[14]: Risk factors for aggravation: elderly (age 65 and over), malignant tumors, HIV infection (especially CD4 $<200/\mu$L)12), chronic obstructive pulmonary disease (COPD), pregnancy, chronic kidney disease, Type 2 diabetes, hypertension, dyslipidemia, obesity (BMI 30 and above), smoking, immunodeficiency after solid organ transplantation.

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