Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Kits [Epitope Diagnostics, San Diego, CA, USA]; and IgA and IgG with Euroimmune ELISAs [Euroimmun, Lübeck, Germany]).

25 (63%) patients were asymptomatic on physical examination, and the remaining patients had only mild symptoms compatible with COVID-19. 24 (60%) patients reported contact with a person suspected of having COVID-19. However, no patient was PCR positive at the time of consultation, a finding that is inconsistent with the PCR positivity of all three cases reported by Guarneri and colleagues.[1] Our results are not surprising considering no patient reported having fever or signs of upper or lower respiratory tract infection in the past 3 days. However, COVID-19 serology was positive in 12 (30%) patients: seven had only IgA antibodies, three had only IgG antibodies, one had IgM and IgG antibodies, and one had IgA and IgG antibodies. This proportion is substantially higher than expected for our area (estimated at 3·4%[6]). Although these results require further investigation, they suggest that in young patients SARS-CoV-2 is completely suppressed before a humoral immune response is induced.

Taken together, our results suggest that chilblain-like lesions are associated with mild or asymptomatic SARS-CoV-2 infection, and in this respect our findings are in accordance with the cases reported by Guarneri and colleagues.[1] However, physicians should be aware that most patients presenting with chilblain-like lesions will probably have negative PCR results at the time of presentation.

We declare no competing interests.

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Biostatistics to better detect fishy findings

We commend Srinivas Mantha[1] for the much needed clarification of the differences between risks, ratios, and rates, and of the latter's underlying notion of time. There is, however, an additional and important difference.

The main scientific basis for epidemiology is biostatistics,[2] which applies rigorous mathematical laws of probability and statistics to the fascinating but unpredictable diversity of living organisms. This is done by accepting some measure of uncertainty. If the sample in which we document data is large enough and representative of the population from which the sample is selected, then we can be confident—at a usually chosen 5% risk of being wrong—that the measure in the population is close to that found in the sample and situated within a range of values called the confidence interval (CI). The CI is a fundamental statistical tool for estimating values and comparing them between groups. Upper and lower bounds of the CI of a risk or ratio computed using a normal or a binomial distribution are equally distant from the estimated value.

Unlike risks and ratios, however, rates are usually very small numbers: their numerator can vary but their denominator is usually much larger, especially when composed of a number of people exposed multiplied by a number of days, weeks, or months of exposure.[3] CIs for rates, especially for rates of repeatable events, are computed using a Poisson distribution and can be substantially skewed towards the upper bound. This skew has important consequences: when calculating incidence rates of COVID-19 endpoints to compare them between different populations or groups (especially repeatable events such as hospital admissions or repeat clusters over a time period), computing their CIs using a normal instead of a Poisson distribution would wrongly cut them short on the right. This might result in a statistically significant difference between groups' incidence rates when there would not be any under a Poisson distribution. This also has consequences when estimating the sample size needed to achieve desired power before comparing incidence rates between samples.[4]

The emergence and rapid global expansion of COVID-19 within weeks and implementation of lockdowns worldwide have made epidemiology a household word.[5] We enthusiastically welcome increased awareness among clinicians, researchers, and indeed the general public of the importance of epidemiology and biostatistics. As we progress from computing percentages in observational studies to comparing rates and CIs within or among groups, clinicians and researchers must be aware that—unlike risks or ratios—incidence rates follow a Poisson distribution.

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Surfing the COVID-19 scientific wave

Since the beginning of the COVID-19 pandemic, the number of articles published in scientific journals has skyrocketed; unfortunately, the quality of many of these articles leaves much to be desired.[1,2] We read with interest two publications from the same group[3,4] whose objectives were to demonstrate that normal speech generates droplets that can be suppressed by covering the mouth of a speaker and aerosols that persist for several minutes. Briefly, the authors used fluorescent green light to illuminate particles emitted by a person's mouth when speaking normally in a confined black box and filmed the interior of the black box. The words spoken by the participant were "stay healthy", chosen by the authors as the "th" sound is known to emit droplets. Unsurprisingly, the authors found that the speaker emitted droplets of various sizes that were suppressed by covering the mouth.[3] On the basis of a set of assumptions, the group produced a model suggesting that aerosols smaller than 5 μm were generated. The group concluded that normal speaking is associated with airborne transmission.[4]

We have issues with several assumptions made by the authors.[4] First, the main assumption in the model is that dehydration is key to reducing the diameter of the expelled droplets, allowing droplets to become aerosols. The experiment was done in an environment with a relative humidity of 27%, which is below the minimum recommended indoor relative humidity of 40%.[5] Second, the authors assumed an average viral load in saliva of 7×10^6 copies per mL on the basis of a prospective study[6] wherein viral load was measured in sputum. Thus, they assume that viral load in sputum is the same as in saliva. The group also assume that every RNA copy detected is a potentially infectious virion, without acknowledging that in the cited study samples containing fewer than 10^6 copies per mL never resulted in a viable virus being isolated. An additional required proof would be to show that the viable virus is infectious and that the load is higher than the infectious dose.[7]

The studies[3,4] have methodological flaws that limit their generalisability. We were surprised that experiments in one person were published in leading scientific journals. No report of the loudness, measured in decibels, was found in either manuscript, although in the videos it seems that in some cases the study participant was shouting, so the claim of normal speech is dubious.[3,4] The air in the black box might have been filtered by a high-efficiency particulate air filter, but in the 2·33 min preceding the beginning of the speech, we counted at least 12 instances where flying particles were observed.[4] Also, the size of the box was small; the authors did not show that these particles could be found more than 60 cm away from the speaker (the maximum length of the black box). The duration of recorded speech was 25 s, but the results were artificially extrapolated to 1 min.[4] Also, the presence of a fan at the bottom of the black box during the speech and for 10 s after the end of speech does not represent real-life conditions; a control condition with no fan would have been expected. Neither aspect is discussed.

In the abstract of one of the articles,[4] it is stated that asymptomatic transmission is plausible, but its role has not been clearly elucidated and indeed is highly disputed.[8] The authors were mistaken when stating that high viral loads were found in asymptomatic patients while referring to the study by Wölfel and colleagues.[6] Only one patient reported being asymptomatic in the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak in Bavaria, Germany,[9] and that patient was not included in Wölfel and colleagues' study,[6] which included only hospitalised patients.

The title of one of the articles[4] mentions SARS-CoV-2 transmission, yet the experiment had more to do with sialoquence than with SARS-CoV-2. Although the objectives of these studies are worthy, their findings have no immediate implications.

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