result on serum RT-qPCR assay for yellow fever. Liver-biopsy samples showed lobular necroinflammation, which included many foci of spotty necrosis, apoptosis, and hydropic hepatocyte degeneration in all lobular zones, without typical midzonal lesions associated with yellow fever, along with extensive hypercellularity and hypertrophy of Kupffer cells. Some of the patients had confluent necrosis. Among the patients who underwent liver biopsy, immunohistochemical analysis was positive for yellow fever antigen, which was found mainly in Kupffer-cell cytoplasm; such antigens are typically found in hepatocytes of the midzonal region in patients with acute yellow fever. All 26 patients recovered clinically with normal levels of liver enzymes.

In a 2019 report,[5] researchers described rebound hepatitis associated with yellow fever in two travelers who had returned to France from Brazil. Similar to these investigators, we hypothesized that such cases of late-onset liver inflammation result from an impaired immune transition from an antiinflammatory pattern to a proinflammatory pattern owing to the presence of the virus or its antigens after the acute phase. In our study, the administration of sofosbuvir did not appear to be associated with subsequent changes in levels of liver enzymes.

Thus, in this study, we characterized another possible clinical manifestation of yellow fever, a late-onset relapsing hepatitis occurring 1 to 4 months after the initial symptoms of severe acute yellow fever. Longer follow-up of the patients is needed to determine whether this condition will have serious health implications.

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Visualizing Speech-Generated Oral Fluid Droplets with Laser Light Scattering

TO THE EDITOR: Aerosols and droplets generated during speech have been implicated in the person-to-person transmission of viruses,[1,2] and there is current interest in understanding the mechanisms responsible for the spread of Covid-19 by these means. The act of speaking generates oral fluid droplets that vary widely in size,[1] and these droplets can harbor infectious virus particles. Whereas large droplets fall quickly to the ground, small droplets can dehydrate and linger as "droplet nuclei" in the air, where they behave like an aerosol and thereby expand the spatial extent of emitted infectious particles.[2] We report the results of a laser light-scattering experiment in which speech-generated droplets and their trajectories were visualized.

The output from a 532-nm green laser operating at 2.5-W optical power was transformed into a light sheet that was approximately 1 mm thick and 150 mm tall. We directed this light sheet through slits on the sides of a cardboard box measuring 53 × 46 × 62 cm. The interior of the box was painted black. The enclosure was positioned under a high-efficiency particulate air (HEPA) filter to eliminate dust.

When a person spoke through the open end of the box, droplets generated during speech traversed approximately 50 to 75 mm before they encountered the light sheet. An iPhone 11 Pro video camera aimed at the light sheet through a hole (7 cm in diameter) on the opposite side of the box recorded sound and video of the light-

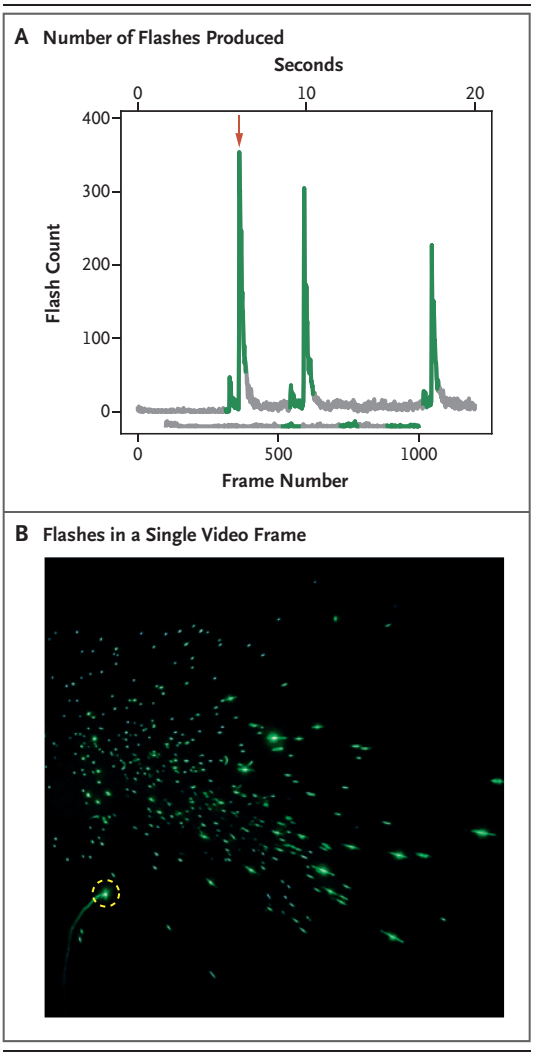

Figure 1. Emission of Droplets While a Person Said "Stay Healthy."

Droplets generated during speech produced flashes as they passed through the light sheet in this experiment. Panel A shows the flash count during each frame of a video produced at a rate of 60 frames per second, with and without a damp cloth covering the speaker's mouth. Green indicates spoken words. The number of flashes was highest (arrow) when the "th" sound in the word "healthy" was pronounced. The trace offset below the graph shows that when the speaker's mouth was covered with a damp cloth, there was no qualitative increase in the flash count during speech over the background level observed before the first trial of speech. The flash count during the silent periods between the spoken phrases remained above the background level, a finding that suggests that some of the speech droplets lingered inside the box for some seconds. Panel B shows frame 361 from the video, which corresponds to the red arrow in Panel A and to the highest number of speech droplets visualized in an individual frame of the video recording. The spots vary in brightness because of the differences in the size of the particles. Some of the spots are streaked, which suggests that the rate of 60 frames per second was insufficient to freeze the motion of the droplets. The feature highlighted by a dashed yellow circle corresponds to the tip of a very thin wire positioned just behind the light sheet; this wire provided a reference for setting the camera focus and gain before recording. (See the video, available at NEJM.org.)

scattering events at a rate of 60 frames per second. The size of the droplets was estimated from ultrahigh-resolution recordings. Video clips of the events while the person was speaking, with and without a face mask, are available with the full text of this letter at NEJM.org.

A video showing the experiment is available at NEJM.org

We found that when the person said "stay healthy," numerous droplets ranging from 20 to 500 μm were generated. These droplets produced flashes as they passed through the light sheet (Fig. 1). The brightness of the flashes reflected the size of the particles and the fraction of time they were present in a single 16.7-msec frame of the video. The number of flashes in a single frame of the video was highest when the "th" sound in the word "healthy" was pronounced (Fig. 1A). Repetition of the same phrase three times, with short pauses in between the phrases, produced a similar pattern of generated particles, with peak numbers of flashes as high as 347 with the loudest speech and as low as 227 when the loudness was slightly decreased over the three trials (see the top trace in Fig. 1A). When the same phrase was uttered three times through a slightly damp washcloth over the speaker's mouth, the flash count remained close to the background level (mean, 0.1 flashes); this showed a decrease in the number of forward-moving droplets (see the bottom trace in Fig. 1A).

We found that the number of flashes increased with the loudness of speech; this finding was consistent with previous observations by other investigators.[3] In one study, droplets emitted during speech were smaller than those emitted during coughing or sneezing. Some studies have shown that the number of droplets produced by speaking is similar to the number produced by coughing.[4]

We did not assess the relative roles of droplets generated during speech, droplet nuclei,[2] and aerosols in the transmission of viruses. Our aim was to provide visual evidence of speech-

generated droplets and to qualitatively describe the effect of a damp cloth cover over the mouth to curb the emission of droplets.

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Droplets and Aerosols in the Transmission of SARS-CoV-2

TO THE EDITOR: Anfinrud et al. now illustrate in the *Journal*[1] how liquid droplets exhaled during speech can linger in the air. The large particles to which they refer remain airborne only briefly before settling because of gravity; these particles may pose a threat of infection if they are inhaled by persons close by as well as a contact hazard if they are transferred to another person's nasal or oral passages. In this way, persons infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may contribute to the spread of the infection.

Breathing and talking also produce smaller and much more numerous particles, known as aerosol particles, than those visualized in the laser experiment of Anfinrud and colleagues.[2-4] Certain persons called "super spreaders" produce many more aerosol particles than other persons. The diameters of these particles are in the micron range. These particles are too small to settle because of gravity, but they are carried by air currents and dispersed by diffusion and air turbulence.

Inhaled droplets and aerosol particles have different sites of deposition in the recipient. Inhaled droplets are deposited in the upper regions of the respiratory tract, from which they may be removed in nasal secretions or carried upward by the mucociliary escalator, to be expelled or swallowed. In contrast, inhaled aerosolized particles can penetrate to the depths of the lungs, where they may be deposited in the alveoli.

A recent study, the results of which were also published in the *Journal*, showed that experimentally produced aerosols containing SARS-CoV-2 virions remained infectious in tissue-culture assays, with only a slight reduction in infectivity during a 3-hour period of observation.[5] Aerosols from infected persons may therefore pose an inhalation threat even at considerable distances and in enclosed spaces, particularly if there is poor ventilation. The possible contribution of infective aerosols to the current pandemic suggests the advisability of wearing a suitable mask whenever it is thought that infected persons may be nearby and of providing adequate ventilation of enclosed spaces where such persons are known to be or may recently have been.

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