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.

efficacy against influenza B, especially in children, is therefore warranted.

Third, the optimal timing of immunisation during pregnancy remains unclear. Whether the gestational stage of pregnancy affects responses to vaccines has not yet been extensively studied and conflicting results on seroconversion after seasonal influenza immunisation exist. In this study, there was no difference in efficacy against PCR-confirmed influenza in infants when the mothers were vaccinated before or after 29 weeks of gestation. Concerning the mothers, there was no efficacy against PCR-confirmed influenza when they were vaccinated before 29 weeks gestational age (vaccine efficacy 30%, 95% CI −2 to 52). As explained by the authors, this absence of efficacy in mothers vaccinated before 29 weeks gestational age is probably due to statistical considerations (lack of power), rather than a real difference in efficacy, as this would be inconsistent with studies that have shown a waning serological response to influenza immunisation as pregnancy progresses.[9]

Fourth, these results confirm that seasonal influenza vaccination during pregnancy is safe. In addition to studies that did not show an increased incidence of adverse events in mothers,[3] safety in fetuses and newborns was also shown when considering low birthweight, stillbirth, preterm birth, and small for gestational age. However, contrary to what was suggested in the trials in Bangladesh[4] and Nepal,[7] the pooled data show no positive association between maternal immunisation and low birthweight. These findings would be a strong argument for recommending generalised maternal influenza immunisation in resource-limited countries and suggest that further research considering the heterogeneity of the findings across countries is needed.

In conclusion, these pooled data confirm that influenza immunisation during pregnancy is safe and effective for protecting both women and infants. Further research is warranted to consider more immunogenic vaccines to fill the protection gap in infants between 4 and 6 months of age and improve understanding of the association between maternal immunisation and child weight and length at birth at 6 months of age.

PL has received personal fees and non-financial support from Pfizer and Sanofi Pasteur. VT has received personal fees from Alexion and grants and personal fees from Roche Diagnostics and is a member of the scientific board of Obseva. OL has received personal fees from Sanofi Pasteur, grants, personal fees, and non-financial support from Pfizer, Janssen, and Sanofi Pasteur-Merck Sharp & Dohme, and grants, and non-financial support from GlaxoSmithKline.

*Paul Loubet, Vassilis Tsatsaris, *Odile Launay*
odile.launay@aphp.fr

VBMI, INSERM U1047, Université de Montpellier, Service des Maladies Infectieuses et Tropicales, CHU Nîmes, Nîmes, France (PL); Inserm, F-CRIN, Réseau Innovative Clinical Research in Vaccinology, Paris, France (PL, OL); Maternité Port-Royal (VT), FHU PREMA (VT, OL), and Inserm, CIC Cochin Pasteur (OL), Assistance Publique Hôpitaux de Paris, Hôpital Cochin, Paris 75014, France (OL); and Université de Paris, Paris, France (OL)

1 Neuzil KM, Reed GW, Mitchel EF, Simonsen L, Griffin MR. Impact of influenza on acute cardiopulmonary hospitalizations in pregnant women. *Am J Epidemiol* 1998; **148:** 1094–102.
2 Neuzil KM, Mellen BG, Wright PF, Mitchel EF, Griffin MR. The effect of influenza on hospitalizations, outpatient visits, and courses of antibiotics in children. *N Engl J Med* 2000; **342:** 225–31.
3 Loubet P, Kerneis S, Anselem O, Tsatsaris V, Goffinet F, Launay O. Should expectant mothers be vaccinated against flu? A safety review. *Expert Opin Drug Saf* 2014; **13:** 1709–20.
4 Zaman K, Roy E, Arifeen SE, et al. Effectiveness of maternal influenza immunization in mothers and infants. *N Engl J Med* 2008; **359:** 1555–64.
5 Madhi SA, Cutland CL, Kuwanda L, et al. influenza vaccination of pregnant women and protection of their infants. *N Engl J Med* 2014; **371:** 918–31.
6 Tapia MD, Sow SO, Tamboura B, et al. Maternal immunisation with trivalent inactivated influenza vaccine for prevention of influenza in infants in Mali: a prospective, active-controlled, observer-blind, randomised phase 4 trial. *Lancet Infect Dis* 2016; **16:** 1026–35.
7 Steinhoff MC, Katz J, Englund JA, et al. Year-round influenza immunisation during pregnancy in Nepal: a phase 4, randomised, placebo-controlled trial. *Lancet Infect Dis* 2017; **17:** 981–89.
8 Omer SB, Clark DR, Madhi SA, et al. Efficacy, duration of protection, birth outcomes, and infant growth associated with influenza vaccination in pregnancy: a pooled analysis of three randomised controlled trials. *Lancet Respir Med* 2020; **8:** 597–608.
9 Schlaudecker EP, Ambroggio L, McNeal MM, Finkelman FD, Way SS. Declining responsiveness to influenza vaccination with progression of human pregnancy. *Vaccine* 2018; **36:** 4734–41.

Challenges in the interpretation and application of typical imaging features of COVID-19

Published Online
May 18, 2020
https://doi.org/10.1016/
S2213-2600(20)30233-2

The detailed report by Timothy Harkin and colleagues[1] of an unusual case of respiratory illness eventually diagnosed as COVID-19 raises issues about the role of imaging in the management of the disease. The causative virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), can result in lethal pneumonia, so might chest imaging

have a central role in the detection or management of COVID-19? Is there a signature imaging appearance of the virus that could alert radiologists to its presence?

Early literature describes so-called typical imaging features of COVID-19 and reports high sensitivity for detection of COVID-19 by CT. This typical appearance of COVID-19 is peripheral or posterior ground glass and consolidative opacities with lower-lung predominance.[2] Notably, these features are similar to those described previously for SARS-CoV and Middle East respiratory syndrome-CoV.[3] However, the studies that reported high sensitivity of CT for detection of COVID-19 did not use these typical features to determine whether a CT scan is positive for disease, but rather used broad and non-specific findings of any airspace process.[4] This approach represents a deviation from standard clinical practice, with CT findings reported in a binary fashion as either positive or negative without clear delineation of criteria. Furthermore, the inclusion criteria for studies reporting high sensitivity were not well described and potentially reflect substantial selection bias of hospitalised patients with pneumonia in a region with a high prevalence of COVID-19. Early in the disease course or in asymptomatic patients, CT has been shown to be normal in around half of cases (in 20 [56%] of 36 cases reported by Bernheim and colleagues,[5] and 38 [46%] of 82 cases reported by Inui and colleagues[6]). Although some clinicians have advocated the use of CT as an adjunct to or in lieu of RT-PCR in settings where testing capacity is insufficient, this strategy would probably lead to false-negative results.

Where does this leave the radiologist or treating physician? Imaging can range from normal to typically abnormal for COVID-19. Furthermore, the so-called typical findings have substantial overlap with other infectious and non-infectious entities, including cryptogenic and drug-related organising pneumonias, pulmonary infarcts, and septic emboli. Although distinguishing these entities might be possible on the basis of clinical history, presentation clearly overlaps, and patients might have more than one infection simultaneously.

Two groups recently proposed standardised CT reporting guidelines: the Radiological Society of North America (RSNA)[7] and the Dutch Radiological Society.[8] The aims of these reporting guidelines are to familiarise all radiologists with the typical imaging findings of COVID-19, and to decrease inter-radiologist variation in the reporting of cases. Although these guidelines do represent important contributions, they should be applied with caution.

The first challenge for any reporting guideline system is defining the appropriate clinical context. The Dutch group calls its scheme the COVID-19 reporting and data system (CO-RADS), analogous to the established BI-RADS for breast cancer screening or Lung-RADS for lung cancer screening proposed by the American College of Radiology. When BI-RADS or Lung-RADS should be applied is clear: in patients who are being screened for breast or lung cancer, respectively. However, the specific scenarios in which the RSNA reporting guidelines or CO-RADS should apply are less clear. Do they apply to patients with known COVID-19, suspected COVID-19, no suspicion of COVID-19, negative COVID-19 testing, or another known diagnosis that might explain lung findings? Clearly, use in suspected cases is the intended application, although many specialty societies discourage CT use in this scenario.[9] In suspected cases, the authors of CO-RADS showed high diagnostic accuracy for the 105 cases on which the reporting system is based; notably, these were all symptomatic patients.[8] However, the applicability of the reporting categories in either the RSNA guidelines or CO-RADS is less clear in other clinical scenarios. For example, a patient with *Staphylococcus aureus* bacteraemia and peripheral opacities most probably has septic emboli; should that case also be reported as having typical features of COVID-19? Similar trouble arises when attempting to apply these categories to patients with known COVID-19, as with the case presented by Harkin and colleagues;[1] what should atypical manifestations mean in that setting? Finally, how should one interpret and apply so-called typical features in a patient with multiple negative COVID-19 tests?

The second challenge for a reporting system is its effects on patient management. This issue is arguably more important than the language radiologists use, yet it has unfortunately not been addressed by either set of guidelines. If we look to BI-RADS or Lung-RADS for comparison, both include solid recommendations for management of each assessment category (eg, BI-RADS 3 and Lung-RADS 3 necessitate 6-month follow-up imaging). Neither the RSNA guidelines nor CO-RADS recommend or even suggest subsequent patient management. This lack of guidance represents an acknowledgment that RT-PCR is the one and only


Colin Cuthbert/Science Photo Library

See **Case Report** page 644

approved method for diagnosis of COVID-19, as per WHO recommendations.[10] To re-emphasise, the management of any patient with suspected COVID-19 is one or both of RT-PCR testing and isolation, irrespective of RSNA or CO-RADS category. Typical does not mean specific for COVID-19.

CT remains a powerful diagnostic tool in the context of COVID-19 and should be used to trouble-shoot problematic cases like the one presented by Harkin and colleagues. Clinicians are still in the early stages of understanding COVD-19 and need to acknowledge the shortcomings of research to date. CT has been studied primarily in regions with a high prevalence of COVID-19, but its performance in lower-prevalence environments that we are likely to see in the coming months is not clear. A well designed, cross-sectional study is needed to define the sensitivity of typical CT findings and their specificity when multiple other disease processes are at play.

We declare no competing interests.

*Mark M Hammer, Constantine A Raptis, Travis S Henry, Amar Shah, Sanjeev Bhalla, *Michael D Hope*
michael.hope@ucsf.edu

Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA (MMH); Mallinckrodt Institute of Radiology, Washington University School of Medicine in Saint Louis, Saint Louis, MO, USA (CAR, SB); Department of Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, CA 94143, USA (TSH, MDH); Department of Radiology, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY, USA (AS); and Department of Radiology, San Francisco Veterans Affairs Medical Center, San Francisco, CA, USA (MDH)

1 Harkin TJ, Rurak KM, Martins J, Eber C, Szporn AH, Beasley MB. Delayed diagnosis of COVID-19 in a 34-year-old man with atypical presentation. *Lancet Respir Med* 2020; published online May 18. https://doi.org/10.1016/S2213-2600(20)30232-0.

2 Salehi S, Abedi A, Balakrishnan S, Gholamrezanezhad A. Coronavirus disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. *AJR Am J Roentgenol* 2020; published online March 14. DOI:10.2214/AJR.20.23034.

3 Das KM, Lee EY, Langer RD, Larsson SG. Middle East respiratory syndrome coronavirus: what does a radiologist need to know? *AJR Am J Roentgenol* 2016; **206:** 1193–201.

4 Ai T, Yang Z, Hou H, et al. Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. *Radiology* 2020; published online Feb 26. DOI:10.1148/radiol.2020200642.

5 Bernheim A, Mei X, Huang M, et al. Chest CT findings in coronavirus disease-19 (COVID-19): relationship to duration of infection. *Radiology* 2020; published online Feb 20. DOI:10.1148/radiol.2020200463.

6 Inui S, Fujikawa A, Jitsu M, et al. Chest CT findings in cases from the cruise ship "Diamond Princess" with coronavirus disease 2019 (COVID-19). *Radiol Cardiothorac Imaging* 2020; **2:** e200110.

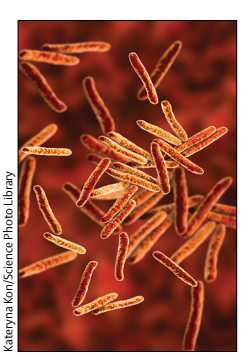
7 Simpson S, Kay FU, Abbara S, et al. Radiological Society of North America expert consensus statement on reporting chest CT findings related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA. *J Thorac Imaging* 2020; **2:** e200152.

8 Prokop M, van Everdingen W, van Rees Vellinga T, et al. CO-RADS – a categorical CT assessment scheme for patients with suspected COVID-19: definition and evaluation. *Radiology* 2020; published online April 27. DOI:10.1148/radiol.2020201473.

9 American College of Radiology. ACR recommendations for the use of chest radiography and computed tomography (CT) for suspected COVID-19 infection. March 22, 2020. https://www.acr.org/Advocacy-and-Economics/ACR-Position-Statements/Recommendations-for-Chest-Radiography-and-CT-for-Suspected-COVID19-Infection (accessed March 24, 2020).

10 WHO. Global surveillance for human infection with coronavirus disease (COVID-19). Feb 27, 2020. https://www.who.int/publications-detail/global-surveillance-for-human-infection-with-novel-coronavirus-(2019-ncov) (accessed April 27, 2020).

Tackling two pandemics: a plea on World Tuberculosis Day



Kateryna Kon/Science Photo Library

Published **Online** March 24, 2020 https://doi.org/10.1016/S2213-2600(20)30151-X

We are facing an unprecedented pandemic. A quarter of the world's population is infected and, between 2020 and 2021, it is predicted that 10 million people will have fallen ill, 3 million will not have been diagnosed or received care, and more than 1 million—mainly the most vulnerable—will have died.[1] This pandemic is not COVID-19 but tuberculosis. On World Tuberculosis Day, it is worth comparing the COVID-19 and tuberculosis pandemics to ensure that, while we focus on the former, we do not forget the latter.

A pandemic is defined as a disease that spreads across whole countries or the whole world. Tuberculosis and COVID-19 are both pandemics that show ongoing, sustained community transmission across continents. Indeed, no country is tuberculosis-free and this is likely to be the case soon for COVID-19.

There are striking similarities between the two pandemics. Both cause major infection-related morbidity and mortality around the world. Tuberculosis was the leading cause of mortality from an infectious disease worldwide in 2018, causing 1·2 million deaths.[1] COVID-19 has infected more than 300 000 people and caused over 13 000 deaths in the first quarter of 2020 alone.[2] Both COVID-19 and tuberculosis can present with respiratory symptoms, and diagnosis and treatment of people with tuberculosis, or tuberculosis and COVID-19 co-infection, are likely to be compromised during the COVID-19 pandemic. Older people and those with comorbidities are at increased risk of severe disease and adverse outcomes in both diseases.[3,4] And, as we are discovering for COVID-19, both diseases have considerable social impact—including stigma,