current argument for mandatory testing in non-COVID patients, a proportion of patients may thus be missed despite testing.

As India transitions into a 'living with COVID' strategy, we will be encountering more of these patients in non-COVID settings. As patients and HCW are equally at risk of life-threatening complications of COVID infections, all efforts must still be made to protect all from getting infected. Also, HCW need to adapt themselves and work with each patient and attendant as if they are encountering a potential COVID carrier with universal precautions, appropriate PPE and standard steps for infection prevention. Another helpful strategy would be to develop teams of HCWs with 1-2 weeks of work followed by two weeks of quarantine, as is followed for COVID areas, even for non-COVID areas. In the event of an accidental exposure, this will prevent shutting down of services due to quarantining of staff.

Above all, a positive frame of mind is of utmost importance to tide over this difficult phase of for us and patients alike.

Published online: June 09, 2020; *PII*: S097475591600189

NITA RADHAKRISHNAN* AND SAVITRI SINGH
Department of Pediatric Hematology Oncology, Super Speciality Pediatric Hospital and PG Teaching Institute, Noida, Uttar Pradesh, India
**nitaradhakrishnan@yahoo.com*

REFERENCES

1. Ministry of health and Family Welfare, Government of India. Enabling Delivery of Essential Health Services during the COVID 19 Outbreak: Guidance note. *Available from: https://www.mohfw.gov.in/pdf/ Essential services during COVID19 updated 0411201.pdf.* Accessed May 14, 2020.
2. Terenziani M, Massimino M, Biassoni V, Casanova M, Chiaravalli S, Ferrari A, *et al*. SARS-CoV-2 disease and children under treatment for cancer. Pediatr Blood Cancer. 2020;e28346.
3. Seth R. *COVID -19* pandemic: The challenges for pediatric oncology. Indian Pediatr. 2020 May 4 [Early online]. Available from: *https://www.indianpediatrics.net/COVID 29.03.2020/CORR-00171.pdf.* Accessed June 7, 2020.
4. Ministry of health and Family Welfare, Government of India. Advisory on the use of hydroxyl chloroquine as prophylaxis for SARS-COV2 Infection. Available from: *https://www.mohfw.gov.in/pdf/Advisory on the use of Hydroxychloroquin asprophylaxis for SARS CoV2 infection.pdf.* Accessed May 14, 2020.
5. Director General Medical Education, Uttar Pradesh. Quarantine policy document for the health care workers (HCWS) working in COVID hospital/ward. Available from: *http://gsvmmedicalcollege.com/wp-content/uploads/2020/05/Quarantine-policy-DGME-4.4.2020.pdf.* Accessed May 14, 2020.
6. World Health Organization. Health workers exposure risk assessment and management in the context of COVID-19 virus: Interim guidance, 4 March, 2020. Available from: *https://apps.who.int/iris/ handle/10665/331340*. Accessed May 14, 2020.
7. Ministry of Health and Family Welfare, Government of India. Novel Coronavirus Disease 2019 (COVID-19): Guidelines on rational use of Personal Protective Equipment (setting approach for Health functionaries working in non-COVID areas). Available from: *https://www.mohfw.gov.in/pdf/GuidelinesonrationaluseofPersonalProtectiveEquipment.pdf*. Accessed May 14, 2020.
8. Ministry of Health and Family Welfare, Government of India. Novel Coronavirus Disease 2019 (COVID-19): Additional guidelines on rational use of Personal Protective Equipment (setting approach for Health functionaries working in non-COVID areas). Available from:*https://www.mohfw.gov.in/pdf/Additionalguidelinesonrational useofPersonalProtectiveEquipment settingapproachforHealth functionariesworkinginnon COVIDareas.pdf.* Accessed May 14, 2020.
9. ESMO guideline: Cancer patient management during the COVID-19 pandemic. Available from: *https://www.esmo.org/guidelines/cancer-patient-management-during-the-covid-19-pandemic.* Accessed May 14, 2020.
10. ICMR Strategy for COVID19 testing in India (Version 4, dated 09/04/2020) Available from: *https://main.icmr.nic. in/sites/default/ files/ upload_documents/ Strategey_for_ COVID19_Test_v4_09042020.pdf.* Accessed May 14, 2020.
11. Tahamtan A, Ardebili A. Real-time RT-PCR in COVID-19 detection: Issues affecting the results. Expert Rev Mol Diagn. 2020;20:453-4.

Seasonal Influenza Vaccination and the Heightened Risk of Coronavirus and Other Pandemic Virus Infections: Fact or Fiction?

During this ongoing severe acute respiratory illness coronavirus 2 (SARS-CoV-2) pandemic, few speculative reports on significant association of influenza vaccines with an increased risk of coronavirus infection appeared both in media and academic circles. The speculation of vaccines paradoxically increasing the risk of infections possibly originated first following 2009 influenza A (H1N1pdm09) pandemic when four Canadian studies suggested that receipt of seasonal influenza vaccine increased the risk of laboratory-confirmed 2009 pandemic influenza A (H1N1pdm09) virus infection [1]. This led to five additional studies, each of which substantiated these initial findings. One proposed mechanism behind this phenomenon is 'original antigenic sin' which was first used to describe how first exposure to influenza virus shapes the outcome of subsequent exposures to antigenically related strains. When an individual is

infected by an 'evolved' strain with a new dominant antigen, slightly different from the 'original' strain against which the person has been vaccinated, the immune system produces antibodies against the 'original' strain through preformed high-affinity memory B cells that inhibit activation of naïve B cells resulting in a weak immune response against the new 'dominant' strain. Hence, the risk of infection paradoxically increased in vaccinated individuals as compared to unvaccinated individuals [2].

Besides, viruses are known to interfere with the circulation of other viruses. For example, there is evidence that the circulation of rhinovirus in the community interferes and decreases the spread of seasonal and pandemic influenza viruses [3,4]. Viral interference is also well-known to interfere with "take" of oral polio vaccine. However, more recently a new phenomenon, 'vaccine-associated virus interference' has been suggested whereby a vaccine can paradoxically increase the circulation of other viruses. That is, vaccinated individuals may be at increased risk for other respiratory viruses because they do not receive the non-specific immunity associated with natural infection [5,6]. Rikin, *et al*. [5] found an increased incidence of acute respiratory infection in children by non-influenza respiratory viruses among 999 participants (out of which 68.8% were children) following influenza vaccination compared to unvaccinated children during the same period. In a study of 115 children [6], a significantly increased risk of virologically confirmed non-influenza respiratory virus infections was found to be associated with receipt of inactivated influenza vaccine. Coronavirus was one of the non-influenza respiratory viruses [6]. Wolff, *et al*. [7] recently performed a large study among defence personnel to investigate respiratory virus interference during the 2017-2018 influenza season by comparing respiratory virus status with their influenza vaccination status. They concluded that overall, receipt of influenza vaccination was not associated with virus interference among the study population. However, vaccine-derived virus interference by specific respiratory viruses was significantly associated with coronavirus and human metapneumovirus [7]. However, studies that have looked into the interference of influenza vaccine with specific non-influenza viral infections are scarce.

It is hypothesized that a respiratory virus infection confers immunity against the same and other respiratory viruses for a short time, perhaps a few weeks. This immune protection is associated with activation of the innate immune response to viral infection mediated by the release of type I interferons and other cytokines that have broad protective effects against a range of viruses [8]. This immunologic mechanism, known as heterosubtypic 'temporary non-specific immunity', has been proposed as the biological mechanism behind the paradoxical findings. Natural influenza infection that could have provided the host with some temporary immunity against other respiratory viruses is prevented by influenza vaccination. Hence, the risk of infection by non-influenza viruses (including the coronaviruses) is paradoxically increased [6].

The contentious issue of higher risk of non-influenza respiratory viruses to influenza vaccinated individuals has gained traction during the ongoing SARS-CoV-2 pandemic, which is also a coronavirus infection. Currently, we do not have sufficient data to establish or refute the association between influenza vaccination and higher susceptibility to coronavirus infection. We need to perform systematic studies urgently to find an answer to this question with regard to SARS-CoV-2. This is of vital importance since it is going to have far-reaching implications.

Published online: June 09, 2020; *PII*: S097475591600190

VIPIN M VASHISHTHA[1]* AND PUNEET KUMAR[2]
[1]Mangla Hospital and Research Center, Shakti Chowk, Bijnor, Uttar Pradesh; and [2]Kumar Child Clinic, KM Chowk, Dwarka, New Delhi; India.
**vipinipsita@gmail.com*

REFERENCES

1. Skowronski DM, De Serres G, Crowcroft NS, Janjua NZ, Boulianne N, Hottes TS, *et al*. Association between the 2008-09 seasonal influenza vaccine and pandemic H1N1 illness during spring–summer 2009: Four observational studies from Canada. PLoS Med 2010; 7: e1000258.
2. Zhang A, Stacey HD, Mullarkey CE, Miller MS. Original antigenic sin: How first exposure shapes lifelong anti-influenza virus immune responses. J Immunol. 2019; 202:335 340.
3. Linde A, Rotzén-Östlund M, Zweygberg-Wirgart B, Rubinova S, Brytting M. Does viral interference affect spread of influenza? Euro Surveill. 2009;14:19354.
4. Anestada G, Nordbo SA. Virus interference. Did rhinoviruses activity hamper the progress of the 2009 influenza A (H1N1) pandemic in Norway? Med Hypotheses. 2011;77:1132-4
5. Rikin S, Jia H, Vargas CY, Castellanos de Belliard Y, Reed C, LaRussa P, *et al*. Assessment of temporally-related acute respiratory illness following influenza vaccination. Vaccine. 2018;36:1958-64.
6. Cowling BJ, Fang VJ, Peiris JSM, Nishiura H, Chan KH, Ng S, *et al*. Increased risk of non-influenza respiratory virus infections associated with receipt of inactivated influenza vaccine. Clin Infect Dis. 2012;54:1778-83.
7. Wolff GG. Influenza vaccination and respiratory virus interference among Department of Defence personnel during the 2017-2018 influenza season. Vaccine. 2020;38:350-54.
8. Khaitov MR, Laza-Stanca V, Edwards MR, Walton RP, Gohde G, Contoli M, *et al*. Respiratory virus induction of alpha-, beta- and lambda-interferons in bronchial epithelial cells and peripheral blood mononuclear cells. Allergy. 2009;64:375-86.