with Gordon Holmes syndrome lead to synaptic and cognitive impairments via Arc misregulation. Aging Cell. 2017;16:281-92.
4. Shukla A, Das Bhowmik A, Hebbar M, Rajagopal KV, Girisha KM, Gupta N, *et al*. Homozygosity for a nonsense variant in AIMP2 is associated with a progressive neurodevelopmental disorder with microcephaly, seizures, and spastic quadriparesis. J Hum Genet. 2018;63:19-25.
5. Reijnders MRF, Ansor NM, Kousi M, Yue WW, Tan PL, Clarkson K, *et al*. RAC1 missense mutations in developmental disorders with diverse phenotypes. Am J Hum Genet. 2017;101:466-77.

Vinblastine-induced Acral Hyperpigmentation

A 5-year-old girl, diagnosed with multi-system langerhans cell histiocytosis (bone, liver, bone marrow and pituitary involvement), was started on induction chemotherapy (weekly cycles of vinblastine/ prednisolone for 12 weeks). Two months later, she developed progressive bluish-black discolouration over the nose and fingertips along with darkening of the nail beds without any itching, pain, redness, numbness, trauma or sun exposure.

Several differentials were considered, Chikungunya fever is well reported for causing an acute, brownish-black, centrofacial hyperpigmentation [1]. It can persist for three to six months after resolution of infection [1]. However, our child had no fever, arthralgia or cytopenias to suggest an infectious aetiology. Addisonian hyperpigmentation, which commonly involves mucous membranes, flexures, palmar and plantar creases, the areola, genitalia and pressure points (elbows and knees), was ruled out clinically, as well as by the absence of hyponatremia, hyperkalemia and acidosis [1]. Hyperpigmentation in thyroid disorders also has a similar distribution as in Addison disease [2]; however, the thyroid function test was normal. Exogenous ochronosis, secondary to topical hydroquinone use, responsible for bluish-black hyperpigmentation of the sun-exposed areas of the face, was also ruled out as there was no history of such application; neither was henna applied locally [1,2]. She had no preceding redness, scaling, pain, injury or cutaneous eruptions to suggest post-inflammatory hyperpigmentation [3]. Acanthosis nigricans, although classically noted over the nape of the neck, axilla and groin, can also develop over the face [4]. However, our child had neither hyperglycemia nor obesity and the lesion in question lacked the characteristic velvety thickening of acanthosis nigricans [3]. The involvement of distal phalanges, interphalangeal joints and oral mucosa, characteristic of Vitamin B_{12} deficiency, was absent in our child [2]. Moreover, her red blood cell indices were normocytic and normochromic, ruling out this possibility. Drug-induced acral hyperpigmentation was considered after ruling out other differentials and vinblastine was discontinued, following which the hyperpigmentation faded over a period of 3 weeks, but did not disappear completely.

Vinca alkaloids are notorious for causing extra-vasation injury [4]. Supravenous hyperpigmentation has been reported with the ABVD regimen which includes vinblastine (however, the causative drug was not implicated) [5]. Vinorelbine, a vinca alkaloid, in high doses is known to cause acral erythema [6]. Although drug-induced hyperpigmentation is responsible for 10-20% cases of acquired hyperpigmentation [2], it has not been reported with either vinblastine or prednisolone. Possible mechanisms of drug induced acral hyperpigmentation

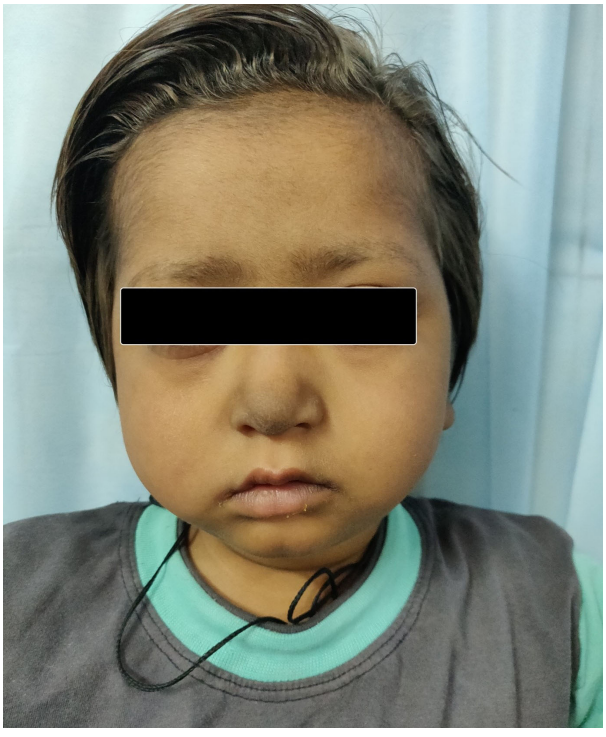

Fig.1

include increased melanin synthesis (secondary to cytotoxic effect on melanocytes), cutaneous drug accumulation or iron deposits following dermal vascular damage, and increased blood flow to acral areas causes drug deposition [4,5].

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REFERENCES

1. Khanna N, Rasool S. Facial melanoses: Indian perspective. Indian J Dermatol Venereol Leprol. 2011;77:552-64.
2. Bhalla M, Garg S. Acral melanosis. Pigment Int. 2018;5:14-27.
3. Vashi AN, Kundu RV. Facial hyperpigmentation: Causes and treatment. Br J Dermatol. 2013;169:41-56.
4. Payne AS, James WD, Weiss RB. Dermatologic toxicity of chemotherapeutic agents. Sem Oncol. 2006;33:86-97.
5. Pavey RA, Kambil SM, Bhat RM. Dermatological adverse reactions to cancer chemotherapy. Indian J Dermatol Venereol Leprol. 2015;81:434.
6. Heidary N, Naik H, Burgin S. Chemotherapeutic agents and the skin: An update. J Am Acad Dermatol. 2008;58:545-70.

Coronavirus Disease (COVID-19) With Relevance to Pediatrics

We read with interest the recent article on coronavirus disease (COVID-19) in children [1], which has, to some extent, as far as present knowledge is concerned, explained why children are less affected than the elderly. However, the possible reason why the illness is less, thus far, in our country needs to be highlighted.

We need to first understand the role of 'trained immunity'. Trained immunity represents an innate immune memory and it is formed by innate immunity cells that become memory cells after antigen exposure. The increased neutrophilic and low lymphocyte counts in COVID-19 patients during the cytokine storm, that occurs with severe deterioration of some patients, supports the hypothesis that innate immune response is both a protective and destructive phenomenon [2].

The WHO statement emphasizing that there is no evidence that BCG protects against SARS-CoV-2 virus infection was made primarily to prevent BCG being used as a prophylactic. The fact that the three studies referred to compared the incidence of COVID-19 cases in countries where the BCG vaccine is used with countries where it is not used and inferred that countries that routinely used the vaccine in neonates had less reported cases of COVID-19 to date [3] may suggest the protective effect of BCG at birth in countries where almost universal BCG vaccination is practiced.

It is known that seroconversion to oral polio vaccine (OPV) and rota virus vaccine has been poor in India compared to the developed world [4]. The frequent viral infections that probably prevent a new virus from getting a 'foothold', early immunizations like BCG, measles vaccine, 0-dose OPV, hepatitis B vaccine, maternal Tdap (or Tdvac) and influenza vaccine and exposure to atypical and typical bacterial and fungal infections expose our children to many antigens, which could contribute to effective defense against various infections – indicating the so-called trained immunity.

Telemedicine during the COVID-19 pandemic: The roles of teleconsultation, during a pandemic in outpatient and acute care settings, including virtual intensive care unit (ICU) are diverse [5] and need to be encouraged. Virtual care utilizing video and audio provider-initiated services is a well-established modality to provide direct care to patients. Hospitalized COVID positive cases could be managed by interviewing the parent and/or the adolescent and examining the child using video conferencing. It would be ideal, if possible, to provide high definition camera and digital peripherals, including stethoscopes, otoscopes, ophthalmoscopes, and dermatoscopes for this purpose. In-person visits should remain part of patients' care to ensure provider patient relationship [6]; however, telemedicine could still be deployed to provide direct care and monitoring of these patients. Nursing staff could use the facilities to conduct hourly rounds and limit unnecessary in-room visits. It definitely goes a long way in minimizing exposure of healthcare personnel and, in addition, helps conserve personal protection equipments (PPE). Triaging patients online or telephonically is useful in preventing high-risk patients from exposing others to infection. Prescription generation for in-patient and