

This Month In **The JOURNAL** of **PEDIATRICS**

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A picture of severe COVID-19 in US children and youth emerges

— Sarah S. Long, MD

The reports of Chao et al and DeBiasi et al from the Children's Hospital at Montefiore in New York City (NYC) and Children's National Hospital in Washington, DC (DC) provide their SARS-CoV-2 experience over 4- and 6-week periods, respectively, beginning on March 15, 2020. Although SARS-CoV-2 generally has been said to be a mild infection in the pediatric age group, a picture of severe COVID-19 in US children and youth emerges through these reports. Together, 91 hospitalized patients with 22 critically ill are reported, with demographic and other patient characteristics compared between groups. Hospitalized patients were representative of the Bronx, NYC, and DC communities served, with high proportion of Hispanic/Latinos in NYC and Hispanic/Latinos and African Americans in DC. Obesity (BMI >30kg/m²) was present in 26% of Bronx patients and 2% of DC patients. Although underlying medical conditions were common in hospitalized patients, 37% of hospitalized and 22% of critically ill patients in DC had no underlying condition. Of the combined studies' 22 critically ill patients, 63% were male and 82% were >10 years of age. PICU admission predominantly was due to respiratory compromise and was associated with briskly elevated inflammatory markers, lung opacities on chest radiograph, and systemic inflammatory response syndrome (SIRS). Both reports show that approximately 20% of COVID-19 hospitalizations were comprised of patients with asthma, but neither shows an excess of asthmatics among the critically ill. Because substantial SAR-CoV-2 testing of symptomatic outpatients was occurring in DC (1804 tests over 6 weeks), we also know that 21% of infected outpatients had asthma. Taken together,

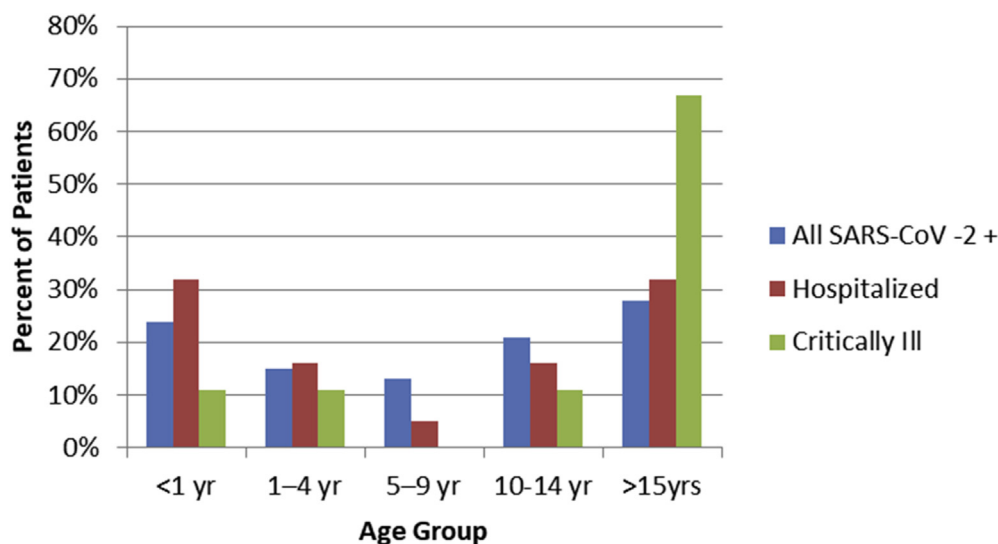


Figure. Age Distribution of SARS-CoV-2- Infected, Hospitalized, and Critically Ill Cases.

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there likely is a signal that SARS-CoV-2 may exacerbate asthma but itself is not a major risk factor for the severe COVID-19 pulmonary syndrome. Additionally, from the DC study, we see that although children <1 year and >15 years of age were over-represented among hospitalized patients with COVID-19, only those >15 years were overrepresented among the critically ill (Figure).

These 2 reports have limitations of small numbers. Characteristics of COVID-19 in these dense urban populations of special racial/ethnic groups where there is known high transmission of SARS-CoV-2 may not be generalizable to all pediatric and US populations. They provide, however, a sobering reality check that is vital to our current and upcoming considerations of social distancing. Children and youth are susceptible to life-threatening COVID-19.

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Thanking families for research participation

— Raye-Ann deRegnier, MD

For many years, neonatologists and endocrinologists have debated the question: “What is a normal blood glucose level in the first days after birth?” In this volume of *The Journal of Pediatrics*, Harris et al publish results of the GLOW study that was carefully designed to provide high quality answers to this question. The authors found that glucose levels stabilized at adult levels by 4 days of age, but before then, glucose levels <47 mg/dl were a common occurrence. De Leon and Stanley explain the importance of these findings in an accompanying editorial.

To obtain these data, healthy newborn infants underwent interstitial glucose monitoring for 5 days after birth as well as twice daily capillary blood sampling. This was a big contribution for families during those first special days after birth and we would be remiss not to recognize their vital role in this landmark study. Surely without their participation we may never have this important information.

This is true for all children and their families who participate in research. They pave the way for a better understanding of health and disease and improve our care for children in the future. The publication of this study provides a good opportunity for us to extend our thanks and appreciation to not only these infants and their families, but to all children and families who participate in clinical research.

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General anesthesia adds to the cognitive sequelae of childhood cancer

— Paul G. Fisher, MD

The impact of the total number of administrations and the cumulative dosage of anesthetics and sedatives on the developing brain is not a new topic for readers of *The Journal* (*J Pediatr* 2019;204:285–90). In this volume, Jacola et al report the effects of anesthesia exposure in 111 children with medulloblastoma from a retrospective, secondary analysis of patients at St. Jude Children’s Research Hospital enrolled on a multisite clinical trial (<https://clinicaltrials.gov/ct2/show/NCT00085202>). The children were all treated with surgical resection of tumor, followed by radiotherapy and chemotherapy. This patient population is already well known to be vulnerable to adverse long-term neurocognitive outcomes resulting from these therapies as well as underlying young age and a developing brain. Over 12 months these children were exposed to general anesthesia an average of 19 times for an average cumulative 21 hours. At 3 years after diagnosis, anesthesia exposure significantly and negatively affected intelligence, attention, working memory, processing speed, and reading, independent of other aforementioned risk factors.

The negative effect of general anesthesia on intellectual dysfunction has previously been given little consideration in these children. Yet, anesthesia is deployed over and over again for myriad procedures, such as lumbar puncture, bone marrow sampling, and placement of central venous catheter; administration of daily radiotherapy in younger children; and years of surveillance imaging with MRI or CT. These experiences are not unique to children with medulloblastoma and brain tumors, but rather routine to other children with cancer and even

some with other complex or chronic diseases. Although this study was retrospective and limited to only those anesthesia exposures in the first 12 months following medulloblastoma diagnosis, the results should be concerning to all children with complex disease, their families, and their providers. Have we gone too far in the omnipresence of anesthesia to streamline or even escalate the care of children with complex disease, or to spare them any physical pain or psychological trauma? Prospective collection of anesthesia exposure in childhood illnesses is certainly warranted, as the authors suggest, but such an effort will take many years. Perhaps here and now we should reconsider how many procedures are truly required and management-altering in pediatric patients, minimize those procedures, and ask when is anesthesia truly a must.

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Paradoxical hypertension

— Thomas R. Welch, MD

A host of physiologic factors contribute to the maintenance of blood pressure. Of these, intravascular volume is perhaps the most important. Thus, when confronted with low or elevated blood pressure, clinicians rightly consider reduced or elevated intravascular volume, respectively. Volume expansion is usually a correct response to hypotension; similarly, volume expansion in the context of hypertension is counter intuitive.

As with any clinical heuristic, however, there are exceptions to this association. Scattered reports of paradoxical hypertension in patients with hypovolemia have appeared over the years. Although the physiology underpinning these cases is not clear, central or hormonal mechanisms have been suggested. Although this scenario is obviously rare, it is important to recognize. Despite their apparent hypertension, such patients actually require volume expansion, and pharmacologic lowering of blood pressure could be hazardous.

In the current volume of *The Journal*, DePiero et al report a large series of children with severe diabetic ketoacidosis (DKA), who at some point during their therapy exhibited significant hypertension. Although the mechanism is also not certain, there is good evidence that central factors play a role in these children; specifically, the children had more severe acidosis and evidence of CNS involvement.

The management of severe DKA is a clinical challenge, in which a dizzying array of interconnected physiologic perturbations can be present. Before intervening to address hypertension in a child with DKA, it is incumbent on clinicians to be aware of this phenomenon and not worsen the situation with an ill-advised therapy.

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Skin to skin care: More than meets the eye

— Robin H. Steinhorn, MD

Skin-to-skin care, often referred to as kangaroo care, was developed decades ago in South America as a supplement to the care of the preterm infant—primarily to provide warmth and facilitate earlier release from the hospital. Since then, skin-to-skin care has been associated with improved breastfeeding, reduced maternal stress, and improved maternal attachment and post-discharge confidence in the care of her preterm infant. In a previous volume of *The Journal*, Sehgal et al provide additional rationale indicating that skin-to-skin care directly improves physiologic stability of the preterm infant. Sehgal studied 40 spontaneously breathing, preterm infants (mean gestational age of 30.5 weeks and birth weight of 1378 ± 133 grams) at a median age of 12 days by echocardiography before and one hour after skin-to-skin care. Skin-to-skin care reduced pulmonary vascular resistance, improved contractility of the right ventricle, increased stroke volume, and increased superior vena cava and cerebral blood flow. It will be important to determine whether these powerful physiologic benefits are due to reduced stress/cortisol levels, reduced sympathetic tone, or

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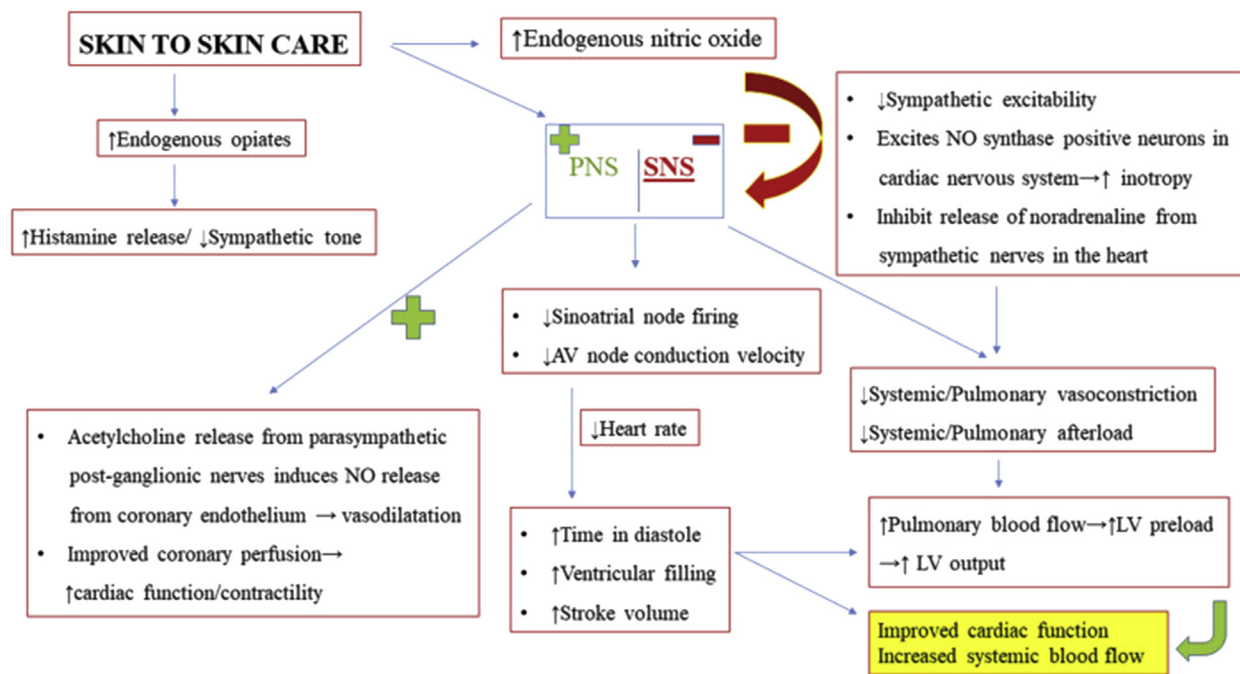


Figure. Putative mediators of the effect of skin-to-skin contact on cardiovascular system. AV, atrioventricular; LV, left ventricular; PNS, peripheral nervous system; SNS, sympathetic nervous system.

other physiologic adaptations (Figure), and whether these findings might apply to smaller and sicker infants requiring mechanical ventilation support.

See article in *J Pediatr* 2020;222:91-7.e2 ►

Subtle forms of vaccine hesitancy affecting children and adolescents are unreasonable and risky

— Sarah S. Long, MD

Vaccine refusal and hesitancy have clear adverse effects on the nonvaccinated individual as well as on the community. Related research has been performed largely in the general pediatric population. Two studies have focused their lenses on subtle forms of vaccine hesitancy, in special groups—children with Down syndrome and the general adolescent population. In this volume of *The Journal* Langkamp et al administered the Parental Attitudes about Childhood Vaccines Survey (PACV) (a validated tool for the general pediatric population) to 55 parents of children ≤8 years of age attending the Down Syndrome Clinic at Akron Children’s Hospital and matched results with their child’s immunization record to assess association with up-to-date status for standard vaccines at 19 months of age. In all, 7% of parents refused all vaccines, and 18% considered themselves as vaccine hesitant, but almost one-half reported that they were concerned that their child would have a serious side effect, thought it better to have fewer vaccines at the same time, and had decided not to have their child receive an injection for reasons other than illness or allergy. Not surprisingly at 19 months, only 58% of children with Down syndrome were up to date for all 8 vaccines and only 31% also had had no delays. The percentage of children up to date declined with higher PACV scores. Both percentages of delayed and non-completion are substantially higher than in the general population and in some children studied with other chronic conditions, and are especially disconcerting in Down syndrome patients who have undo susceptibility to severe vaccine-preventable disease.

The study by Robison et al in *The Journal of Pediatrics: X* used Oregon’s electronic immunization registry ALERT IIS to assess the prevalence in >240 000 adolescents

receiving only a single vaccine injection per visit at ≥ 9 years of age and its relationship with initiating and completing a valid human papillomavirus (HPV) vaccination series. The study also probed the relationship of earlier injection limitation at ≥ 4 years of age with later injection-limiting behavior and HPV vaccination. In accordance with school requirement of Tdap receipt for 7th grade entry, 93% of all adolescents had received Tdap, but only 79% had received MenACWY and 70% had initiated the HPV series. For adolescents who received multiple injections on at least one visit at ≥ 9 years of age, 61% completed the HPV series compared with only 8% of injection-limiting adolescents. Data further showed that injection limitation at an earlier age (likely parent choice) was associated with similar behavior at ≥ 9 years of age (likely patient choice or parent choice/acquiescence). When a second visit occurred for an injection-limiting teen, MenACWY rather than HPV was chosen as the next single injection, reducing further the likelihood that the 2 required additional visits to complete HPV series would occur.

There is no lack of safety or excess rate/severity of side effects in children with Down syndrome. There is no superior immunologic or safety basis, or evidence of psychological benefit, for separation of vaccines or injections. There is evidence from these 2 studies that such practices are associated with excess risk of achieving vaccine protection. Considering that for adolescents multiple highly beneficial vaccines now are standard recommendations, and that there is falloff of healthcare visits through teen years, the unreasonable practice of limiting injections per visit especially jeopardizes the age-sensitive, cancer-prevention opportunity of HPV vaccination. These studies expand and reinforce what should be every provider's strong recommendation to immunize *all* children and adolescents, *on time*, at *all eligible encounters*, and *without limiting vaccines or number of injections* per visit.

[Article pages 64 and at J Pediatr: X 2020;3:100024](#) ►