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Rapid Implementation of an Adult Coronavirus Disease 2019 Unit in a Children's Hospital

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Objective To describe the rapid implementation of an adult coronavirus disease 2019 (COVID-19) unit using pediatric physician and nurse providers in a children's hospital and to examine the characteristics and outcomes of the first 100 adult patients admitted.

Study design We describe our approach to surge-in-place at a children's hospital to meet the local demands of the COVID-19 pandemic. Instead of redeploying pediatric providers to work with internist-led teams throughout a medical center, pediatric physicians and nurses organized and staffed a 40-bed adult COVID-19 treatment unit within a children's hospital. We adapted internal medicine protocols, developed screening criteria to select appropriate patients for admission, and reorganized staffing and equipment to accommodate adult patients with COVID-19. We used patient counts and descriptive statistics to report sociodemographic, system, and clinical outcomes.

Results The median patient age was 46 years; 69% were male. On admission, 78 (78%) required oxygen supplementation. During hospitalization, 13 (13%) eventually were intubated. Of the first 100 patients, 14 are still admitted to a medical unit, 6 are in the intensive care unit, 74 have been discharged, 4 died after transfer to the intensive care unit, and 2 died on the unit. The median length of stay for discharged or deceased patients was 4 days (IQR 2, 7).

Conclusions Our pediatric team screened, admitted, and cared for hospitalized adults by leveraging the familiarity of our system, adaptability of our staff, and high-quality infrastructure. This experience may be informative for other healthcare systems that will be redeploying pediatric providers and nurses to address a regional COVID-19 surge elsewhere. (*J Pediatr* 2020;222:22-7).

The novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused a global pandemic.¹ By the end of February, due to the growing number of coronavirus disease 2019 (COVID-19) cases, the Centers for Disease Control and Prevention provided guidance on preserving the healthcare system functioning in anticipation of a public health crisis.² For inpatient facilities, this included a surge plan to care for high numbers of critically ill patients with COVID-19.²

"Surge capacity" is a health system's ability to meet increased demand for care by rapidly expanding beyond standard operating capacity.³ The Joint Commission defines "surge in place" as expanding the surge capacity of a functioning healthcare facility, as opposed to establishing temporary hospitals.⁴ To assemble personnel, hospital leaders can reallocate staff to areas most in need. As COVID-19 predominantly affects adult patients, the question of how to reallocate pediatric staff is challenging.

One approach is to redeploy individual pediatric providers and nurses to other parts of the hospital to work as part of integrated healthcare teams led by adult-medicine providers. This approach requires pediatricians and nurses to work in different team settings, as well as to learn new practice routines and culture of care. Alternatively, pediatric teams led by pediatricians can be maintained to care for adult patients. These teams can use adult-medicine providers as consultants. This latter approach maintains the team structure, practice routines, and culture of care in a familiar physical setting. Both approaches can expand the health system's surge capacity to care for patients with COVID-19.

COVID-19	Coronavirus disease 2019
ED	Emergency department
EHR	Electronic health record
ICU	Intensive care unit
NYC	New York City
PICU	Pediatric intensive care unit
PPE	Personal protective equipment
QI	Quality improvement
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2

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The first case of COVID-19 was reported in New York City (NYC) on March 1, 2020, and the number of cases rose exponentially to more than 40 000 by the end of the month.⁵ Up to 20% of cases required hospitalization.⁵ Similar to the overall NYC data, the average daily census of hospitalized patients with COVID-19 in the Montefiore Health System rose from 2 patients on March 11, 2020, to 675 patients on March 27, 2020. A further exponential increase in need for hospital beds in NYC was projected for the next 2 weeks.

To meet this extraordinary demand, our health system rapidly expanded the ability to care for adults with COVID-19 using all possible resources. For pediatrics, a plan to surge in place was developed, using a strategy of having pediatric teams led by pediatricians to care for adult patients with COVID-19. Pediatric physicians and nurses organized and staffed a 40-bed adult COVID-19 treatment unit within a children's hospital. In this report, we describe the rapid implementation of this unit, as well as the sociodemographic characteristics and outcomes of patients admitted. This experience may be informative for other healthcare systems that will be redeploying pediatric providers to address a regional COVID-19 surge elsewhere.

Methods

This is a descriptive report of the development of an adult COVID-19 unit and characteristics the outcomes of the first 100 adult inpatients with COVID-19 treated and managed by pediatric providers and nurses at the Children's Hospital of Montefiore during the period of March 30, 2020, to April 14, 2020. The study was approved by the institutional review board of the Albert Einstein College of Medicine (Bronx, New York).

Context

The Children's Hospital at Montefiore is 1 of 11 hospitals in the integrated, academic, Montefiore Health System. Located in the Bronx, New York, it is the centralized treatment center for children in the system and serves as the tertiary and quaternary referral center for children throughout the Bronx and the lower Hudson Valley. It shares a campus, electronic health record (EHR), laboratory, radiology, and pharmacy services with the system's largest adult hospital.

The inpatient units of the children's hospital are located in the same building and comprise 3 general medical units and 1 pediatric intensive care unit (PICU). Each unit holds 26-42 pediatric beds, is separated by floor, and contains pediatric hospital medicine and subspecialty care teams. Each of the units is staffed by inpatient teams, led by an attending physician who supervises care given by house staff (fellows and residents) and physician assistants. The care team includes pediatric nurses, respiratory therapists, pharmacists, medical students, social workers, and others. The hospital typically admits medical and surgical patients up to 21 years old.

Children's Hospital at Montefiore has a long-standing local quality improvement (QI) culture. Physician and

nursing leadership is present and visible. Unit-based and hospital-wide safety briefs occur daily. Leadership walking rounds occur monthly. Afternoon and evening safety huddles are common during times of high census. There is a dedicated QI group, multiple interprofessional QI committees, and a history of project collaboratives on all units.

Between March 27 and March 29, 2020, one medical floor in the children's hospital was transformed into an adult COVID-19 treatment unit. This 40-bed unit would treat patients aged 21 years and older with a primary diagnosis of COVID-19 and would be staffed by pediatric providers and nurses. Pediatric medical and subspecialty services were consolidated onto the remaining 2 medical units to remain separate from this unit.

An interprofessional, team-based approach to rapid implementation of an adult COVID-19 treatment unit staffed by pediatric providers and nurses is described.

System Logistics and Team Structure

The pediatric leadership team increased the frequency of routine quality procedures with daily calls, semiweekly division chief meetings, and frequent huddles with frontline staff. This included representatives from physician, nursing, and respiratory therapy leadership, attending physicians on service, and pediatric intensivists joining the daily unit-based safety briefs traditionally run by nurses and house staff.

The new adult COVID-19 unit was staffed by 3 care teams, 2 led by pediatric hospital medicine attending physicians and 1 by pediatric cardiology attending physicians. Each team admitted 12-14 patients. Attendings were present 24 hours per day. A dedicated adult hospital medicine consultant was available during the daytime. Pediatric subspecialty teams also were available for first-line consultative questions and coordinated care with adult subspecialist colleagues if necessary. All intubations and cardiac arrests were managed by the adult critical care rapid-response team in collaboration with the pediatric critical care team, as the pediatric team often responded more quickly due to their closer proximity. Once on mechanical ventilation, patients were transferred to either the adult intensive care unit (ICU) or PICU, depending on bed availability. Given their experience managing critically ill patients in the PICU, the cardiology team preferentially cared for those with more severe comorbidities or patients who were mechanically ventilated awaiting an ICU bed.

The pediatric nurses used their existing team-based model for care delivery. The charge nurse led unit nurses and nursing assistants in daily patient care. Nurse managers created models to maintain normal staffing ratios, accounting for a large percentage of nurses who were absent due to SARS-CoV-2 illness. Pediatric pharmacists, respiratory therapists, and social workers provided support in their areas of expertise.

The pediatric inpatient unit uses bedside and central monitors. These were checked for functionality and adjusted to an adult profile. The existing "code" carts already were equipped

for pediatric and adult patients. Carts to house equipment and supplies for emergent airway and central line placement were brought to the unit. The supply closet and medication-dispensing machine were modified to mirror an adult medical unit. When available, portable ventilators were stored on the unit to be used for emergent intubations.

Patients were admitted from any of 5 Montefiore Health System emergency departments (EDs). Patients either had a confirmed positive SARS-CoV-2 test or a pending test and symptoms consistent with a primary diagnosis of COVID-19. If testing was not confirmed before admission, the patient was admitted to a single room or one with another patient under investigation. In general, the unit charge nurse performed the initial screen for appropriateness of admission, which included adults up to 50 years of age and a limited number of comorbidities. If the patient did not meet these criteria, the attending physician did a further chart review to determine the appropriateness of admission to this unit. Because of the need for rapid transfer from the ED and the imperative to use all available beds to meet demand, the age and comorbidity restrictions for admissions were relaxed, particularly as the teams became more comfortable caring for adult patients. Patients were excluded from consideration for admission if the primary reason for admission was not management of COVID-19 or if they required ICU level care in the ED.

Clinical Care and Rapid Cycle Learning

In the weeks leading up to opening the unit to adults, pediatric providers and nurses had been constantly adapting to learn new COVID-19 policies for pediatric patients to minimize disease exposure and preserve personal protective equipment (PPE) when caring for pediatric patients. When the development of the new adult unit was announced, this rapid cycle learning expanded to include how to care for adults with COVID-19.

With adult-trained hospital medicine consultants, we identified the most efficient and effective ways to structure rounds, communicate with patients, and streamline care for patients with COVID-19. We reviewed and adapted institution-specific adult protocols for admission and treatment, respiratory management, laboratory follow-up, medication regimens, EHR note templates, and order sets. We compiled high-yield adult medicine clinical resources such as handbooks, video tutorials, and guidelines on a department-wide Web-based platform. We collaborated with our pediatric palliative care team to learn a streamlined approach to discuss advanced care directives and to use scripts to communicate about serious illness. An EHR-based note was created to ensure this information was documented effectively. Pediatric nurse educators regularly reviewed Advanced Cardiac Life Support protocols and reinforced proper PPE donning and doffing. All staff learned the essentials of the others' role, so that care could be clustered to limit exposure and preserve PPE. Everyone was empowered to obtain vital signs, give oral medications, or ask an important question.

An adult-trained hospitalist was present in a temporary consultative role. For the first 4 days, they were physically present during the day, and helped establish attending physician, house staff, and nursing approaches for caring for patients with COVID-19. They also reviewed management decisions related to common adult conditions, such as diabetes, hypertension, and opioid withdrawal. Similarly, a senior internal medicine resident check-in call was also scheduled each night for the overnight pediatric staff. By the end of the first week, the adult-trained hospitalist checked in with the pediatric care teams in-person 1-2 times a day and was otherwise available via telephone. Using a "train-the-trainer" model, providers who were on service first became the "experts" who trained the pediatric faculty and house staff who followed.

Statistical Analyses

We used patient counts and descriptive statistics to report sociodemographic, system, and clinical data available for the first 100 patients admitted to our unit from March 30, 2020, with data available to April 14, 2020.

Results

Our unit reached 100 admissions in less than 10 days. At that time, the total number of current inpatients with COVID-19 in the Montefiore Health System was 1832. The sociodemographic distribution of the first 100 patients admitted is presented in [Table I](#).⁶ The patients' median age was 46 years, and 69% were male. The high percentage of Hispanic (52%) and Non-Hispanic black (23%) patients, as well as the low socioeconomic status score, reflect the demographics of the Bronx community.

Clinical variables are shown in [Table II](#). The Charlson Comorbidity Index⁷ obtained through our EHR was 0 for 66% of patients. However, this score does not account for

Table I. Sociodemographic and system variables for patients admitted to an adult COVID-19 unit in a children's hospital, n = 100

Age, y	46.0 (38.0, 50.0)
Sex, male	69 (69)
Race and/or ethnicity	
Hispanic	52 (52)
Non-Hispanic black	23 (23)
Non-Hispanic other	17 (17)
Unavailable	8 (8)
Primary language spoken	
English	71 (71)
Spanish	28 (28)
Other	1 (1)
Socioeconomic status z score*	-2.4 (-5.7, -1.1)
Service team	
Pediatric cardiology	35 (35)
Pediatric hospital medicine	65 (65)

Values are median (IQR) or n (%).

*Socioeconomic status is reported as a z score calculated from small census tract data based on the patient's home address. It reports the deviation from the mean of the New York State population.⁶ Based on n = 79.

Table II. Clinical variables for adult patients with COVID-19, n = 100

Oxygen saturation on room air in ED	91% (88%, 94%)
Respiratory support on admission	
None required	18 (18)
Nasal cannula	56 (56)
Non-rebreather mask	22 (22)
Intubated immediately	4 (4)
Maximum respiratory support	
None required	12 (12)
Nasal cannula	46 (46)
Non-rebreather mask	26 (26)
High-flow nasal cannula	3 (3)
Mechanical ventilation	13 (13)
Age-adjusted Charlson comorbidity index*	
0	66 (66)
1	23 (23)
2	5 (5)
3	4 (4)
4	2 (2)
Number of comorbidities, including obesity, lung disease, cardiac disease, diabetes, or hypertension	
0	31 (31)
1	25 (25)
2	26 (26)
3	10 (10)
4	8 (8)
History of lung disease	19 (19)
History of cardiac disease	9 (9)
History of diabetes	26 (26)
History of obesity	48 (48)
History of hypertension	37 (37)
Maximum C-reactive protein, mg/dL	14.6 (8.5, 23.2)
Need for dialysis	5 (5)
Intubated on unit	13 (13)

Values are median (IQR) or n (%).

*Age-adjusted Charlson comorbidity index.⁷

obesity, which was present in 48% of our patients. Almost one-half of the patients had ≥ 2 comorbidities. The median oxygen saturation on presentation to the ED was 91% in room air, with 78% of patients requiring oxygen and 4% of patients requiring immediate intubation at admission. Ultimately, a total of 13 patients were intubated on our unit. Once on mechanical ventilation, they were transferred to either the PICU or the adult ICU, depending on bed availability.

From the time the unit opened to the submission of this manuscript, 74% of patients were successfully discharged and 20% are still admitted (Table III). One patient died during intubation and one died while receiving comfort care only on the unit. Four patients died after transfer to either the PICU or adult ICU.

Discussion

We report a rapidly implemented, children's hospital-based, surge-in-place adult COVID-19 unit using primarily pediatric physicians and nurses, after being trained by adult-trained medicine providers. In the current COVID-19 pandemic, hospitals may face an urgent need to increase their surge capacity. Our pediatric team screened, admitted, and cared for hospitalized adults by leveraging the familiarity of our system, adaptability of our staff, and high-quality infrastruc-

Table III. Current disposition for patients admitted to an adult COVID-19 unit in a children's hospital

Discharged (n = 74)	
To home	72 (97)
To long-term care facility	2 (3)
In-hospital mortality (n = 6)	
Died on the unit	2 (33)
Died after transfer to ICU	4 (67)
Length of stay, d	4 (2,7)
Currently admitted (n = 20)	
Inpatient unit (n = 14)	
RA	3 (15)
Nasal cannula	7 (35)
On non-rebreather	3 (15)
On noninvasive ventilation	1 (5)
ICU (n = 6)	
On mechanical ventilation	5 (25)
On noninvasive ventilation	1 (5)

Values are median (IQR) or n (%). RA, room air

ture, as well as long-standing, close collaborations with inter-nist teams.

The results of our first 100 patients highlight our specific intent to admit those patients who were relatively younger with fewer comorbidities to this unit in the children's hospital. The age and sex distributions align with those reported in China, and the majority of our patients had a low age-adjusted comorbidity score.^{7,8} Almost one-half of the patients had a history of obesity, a possible risk factor for mortality from COVID-19.⁹ The approach to minimize patients' chronic illness complexity allowed us to provide clinical care in alternative surge environments as independently as possible from adult-trained providers. Except to exclude patients who required ICU level care in the ED and limit the number of patient comorbidities, we did not limit admission of adult patients with COVID-19 based on disease severity. For example, 26% of patients required oxygen via non-rebreather mask, and an additional 13% required intubation and either died or required ICU level care. The mortality rate of 6% is similar to the rate reported in Wuhan, China, from a retrospective study by Zhou et al, who noted 54 deaths (6.6%) for a cohort of 813 adult patients hospitalized for COVID-19.¹⁰

A report from the Agency for Healthcare Research and Quality describes how pediatric hospitals should surge in response to emergencies that affect large numbers of children.³ There is limited literature discussing how a children's hospital should respond when the surge is needed for adults. In addition to developing a multi-stakeholder team, ensuring system readiness for escalating care, partnering with adult-trained staff, and consideration of scope of practice,¹¹ we learned several lessons from our approach to transform a children's hospital unit to manage adults with COVID-19.

As with all rapid changes, visible leadership, effective communication, and a foundation for QI allowed our system to address a specific healthcare crisis in a limited time period. During the transformation of our pediatric unit, we quickly identified and studied problems, implemented solutions, and observed outcomes. For example, the initial influx of

patients on the first few days was marked by limited ED communication and uneven flow to the unit. By the end of the week, we improved communications related to bed management and distribution of patient assignments to optimize patient management upon arrival to the unit.

Within a familiar and robust system, healthcare workers can adapt to care for new conditions or patient populations. Pediatric nurses adjusted their equipment, supplies, and medications to run a functional adult medical unit. Pediatric physicians learned to manage common adult conditions while gaining clinical expertise in COVID-19. Our cardiologists were trained to work in high-acuity settings. Our hospitalists were accustomed to coordinating care and planning discharges. We leveraged these skills with our team structure. All staff had a responsibility to ensure that the patient's physical and emotional needs were met while minimizing exposure and conserving PPE. For example, goals of care discussions were not left only to the palliative care team; all providers learned to lead conversations as patients' clinical status often changed relatively quickly.

Familiarity of our system and our team members outweighed the lack of familiarity with the treatment and management of common adult medical conditions. The advantage of using established teams and workflows, such as nursing structure, requesting consults, and escalating emergencies, allowed our efforts to focus on quickly adapting to care for adults, both logistically and clinically. Management of COVID-19 is new for all medical providers. As a result, learning about this disease in our own physical environment with the team we knew well counterbalanced the discomfort in providing such care. Nurses, hospitalists, cardiologists, and intensivists, who all had a history of previous collaboration, partnered to appropriately escalate care and manage patients who were awaiting transfer to the ICU after intubation on the floor. Our palliative care team supported us as we remained committed to providing family-centered care while adapting to adhere to COVID-19-specific visitor restrictions.

Support from our adult-trained colleagues was strategic. We modeled their rounding structure, followed their protocols, and used their order sets. This way, the adult-trained hospital medicine consultant present with us for the first few days could adapt quickly to our system and be maximally effective. To amplify the influence of the initial instruction and consultation from adult hospitalists, we developed a "train-the-trainer" model in which pediatric physicians who learned firsthand from this consultant became "experts" who trained future providers. We quickly were able to function independently and thus add value to the surge efforts of the entire hospital system.

There are several limitations of this study. Our results include a biased sample of patients with COVID-19, as patients were not admitted randomly to the pediatric unit. In general, our pediatric teams cared for patients who had fewer comorbidities, and therefore their risk for severe disease may have been lower. Regardless, this report offers a description of the types of patients who can be successfully managed by pediatricians in a Children's Hospital. In addition, we report on

a single children's hospital within a hospital in a large urban center. Adult-trained experts and an adult ICU were available in the same physical structure. Our results may not be generalizable to other children's hospitals. We extracted data from the EHR and chart review, and thus they are limited by the reliability and presence of documentation. Finally, we report a relatively small sample size compared with the overall burden of hospitalized patients with COVID-19.

When faced with a healthcare crisis of any kind, hospitals must be ready to treat patients beyond normal capacity. The COVID-19 pandemic presents an unprecedented need to surge. Leadership at children's hospitals may decide to redeploy pediatric attending physicians, house staff, and nurses to work as individual members of teams run by adult providers. Alternatively, we describe a strategy to maintain a pediatric team structure in a children's hospital environment to care for adults with COVID-19. Our system infrastructure and staff adaptability allowed us to implement this change rapidly. We believe these results and lessons learned may be helpful to providers in other pediatric communities faced with similar surge decisions in the near or distant future. ■

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References

- Centers for Disease Control and Prevention. Coronavirus Disease 2019, Cases in the U.S. [updated Apr 12, 2020; cited Apr 12, 2020]. <https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html>. Accessed April 12, 2020.
- Centers for Disease Control and Prevention. Interim Guidance for Healthcare Facilities: Preparing for Community Transmission of COVID-19 in the United States. [updated February 29, 2020; cited Apr 9, 2020]. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-hcf.html>. Accessed April 9, 2020.
- Boyer EW, Fitch J, Shannon M. Pediatric hospital surge capacity in public health emergencies (Prepared under Contract No. 290-00-0020.) AHRQ Publication No. 09-0014. Rockville (MD): Agency for Healthcare Research and Quality; 2009.
- Joint Commission on Accreditation of Healthcare Organizations. Surge Hospitals: providing safe care in emergencies; 2016. [cited April 9, 2020]. https://www.jointcommission.org/-/media/depended-unorganized/imported-assets/tjc/system-folders/topics-library/surge_hospital.pdf?db=web&hash=43EAC6444DE45A9528AEC0E346D32ACB. Accessed April 9, 2020.
- New York City Health Department. COVID-19 Data Archive [updated April 12, 2020; cited April 12, 2020]. <https://www1.nyc.gov/site/doh/covid/covid-19-data-archive.page>. Accessed April 12, 2020.
- Diez Roux AV, Merkin SS, Arnett D, Chambless L, Massing M, Nieto FJ, et al. Neighborhood of residence and incidence of coronary heart disease. *N Engl J Med* 2001;345:99-106.
- Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol* 1994;47:1245-51.

8. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020;382:1708-20.
9. Lighter J, Phillips M, Hochman S, Sterling S, Johnson D, Francois F, et al. Obesity in patients younger than 60 years is a risk factor for Covid-19 hospital admission. *Clin Infect Dis* 2020 Apr 9. <https://doi.org/10.1093/cid/ciaa415>.
10. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020;395:1054-62.
11. Jenkins A, Ratner L, Caldwell A, Sharma N, Uluer A, White C. Children's hospitals caring for adults during a pandemic: pragmatic considerations and approaches. *J Hosp Med* 2020;15(5):311-3.

50 Years Ago in *THE JOURNAL OF PEDIATRICS*

Spectrum of *GLI3* Mutations

Marshall RE, Smith DW. Frontodigital syndrome: a dominantly inherited disorder with normal intelligence. *J Pediatr* 1970; 77:129-33.

Marshall and Smith described a family in which affected members had craniofacial abnormalities, including a prominent forehead, hypertelorism, and polysyndactyly, with apparent autosomal-dominant inheritance. Affected individuals had normal intelligence. The clinical features of affected family members had overlapping features of Pfeiffer, Apert, Carpenter, Rubinstein Taybi, and Leri pleonosteosis syndromes, but lacked ocular, genital, growth, obesity, and cognitive deficits. Phenotypic features in this family were consistent with a syndrome characterized by polysyndactyly and craniofacial features originally described by Greig.¹ As more cases were reported cognitive deficits were subsequently added to the clinical spectrum of what is now known as Greig cephalopolysyndactyly syndrome (GCPS).

Mutations in a zinc finger transcription factor, *GLI3*, are associated with phenotypically overlapping but distinct conditions which include GCPS, Pallister-Hall syndrome (PHS, hypothalamic hamartomas, polysyndactyly, other malformations), and acrocallosal syndromes (partial or total absence of the corpus callosum, craniofacial features, and polydactyly) and nonsyndromic polydactyly. Some fairly robust genotype–phenotype correlations have been made for *GLI3* mutations.² Mutations in the middle third of *GLI3* that are truncating are null mutations, causing loss of the zinc finger binding domain resulting in PHS. As a result of these truncations, a constitutive *GLI3* repressor protein is formed, which affects sonic hedgehog signaling. GCPS is caused by large deletions/duplications, translocations, and a variety of point mutations encompassing nonsense, missense, in-frame deletions, splice and frameshift mutations, or truncating mutations in the amino or carboxy terminus of *GLI3*.

Because the phenotypic expression of *GLI3* mutations is broad, genetic testing for *GLI3* mutations should be considered in individuals with component clinical features of GCPS and PHS that may not meet criterion for clinical diagnosis.

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References

1. Greig DM. Oxycephaly. *Edinburgh Med J* 1928;33:189-218.
2. Johnston JJ, Sapp JC, Turner JT, Amor D, Aftimos S, Aleck KA, et al. Molecular analysis expands the spectrum of phenotypes associated with *GLI3* mutations. *Hum Mut* 2010;31:1142-54.