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## Contents

### EDITORIAL

#### To help the Fight

*Daniel Kwok-keung Ng* ..... 1

### ORIGINAL ARTICLE

#### Peritoneal Drainage as a Safe Alternative to Laparotomy in Children with Abdominal Compartment Syndrome

*Beatrix Hyemin Choi, Rivfka Shenoy, Dina Levy-Lambert, Jason C. Fisher, Sandra S. Tomita* ..... 2

### INVITED COMMENTARYS

#### Complications of COVID-19 in Children and the Approach to the Affected Children in Pediatric Primary Care

*Petr Pohunek* ..... 6

#### After COVID - where now?

*Andrew Bush* ..... 11

## To help the Fight

The time now is December 2021 and this editorial is written with trepidation with the arrival of Omicron variant of the SARS-CoV-2. Measures are being tightened to contain the spread. Japan has closed its border to all outside traffic. This war on COVID now appears to be a drawn out one and resilience is essential in this fight.

For this journal, we are making good progress in catching up with the lost time.

The current issue sees the original report by Choi *et al.* about the emergency use of peritoneal drainage as a safe alternative to children with abdominal compartment syndrome. This is a handy bedside procedure for those sick children with potential of saving lives.

Professor Petr Pohunek reviewed the complications of COVID-19 in children even though SARS-CoV-2 has largely spared children. This might turn out to be timely as the Omicron variant might affect children more severely than the previous strains. COVID put a lot of pressure on the medical system and turn our routine practice, like clinic follow-up, very un-routine. It is not surprising that a lot of consultation is now done in a virtual manner. Professor Andrew Bush wrote an eloquent piece about how to go about setting up a virtual clinic to provide service without face-to-face contact.

I would like to end by wishing all the readers a very Merry Christmas and Happy 2022. By the way, 2022 does look like a lucky number to me. So, stay safe and stay well.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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# Peritoneal Drainage as a Safe Alternative to Laparotomy in Children with Abdominal Compartment Syndrome

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## Abstract

**Context:** Abdominal compartment syndrome in children carries a mortality of 40–60%. Although definitive treatment for this condition traditionally involves decompressive laparotomy, percutaneous catheter drainage of associated ascites is described as an alternative to laparotomy in adults. **Aims:** We explored the safety and efficacy of percutaneous catheter drainage of intraabdominal fluid for reversing abdominal compartment physiology in a critically-ill cohort of small children. **Materials and Methods:** We reviewed records of all children undergoing percutaneous catheter drainage for abdominal compartment syndrome from 2014 to 2018 in a single institution, excluding those who required drainage for other indications. Bedside sonogram-guided drainage using Seldinger technique or Penrose drain placement was performed by the pediatric surgical service, with drains removed on the resolution of compartment syndrome physiology and fluid output of <10 mL/day. Primary outcome measures were improvement in compartment physiology over 24 h. **Statistical Analysis:** Data were analyzed using descriptive statistics and paired Wilcoxon signed-rank tests. Statistical significance was assumed at  $P < 0.05$ . **Results:** Ten children ranging from 1.1 kg to 38 kg underwent 11 percutaneous catheter drainage procedures for abdominal compartment syndrome secondary to blood, serous fluid, air, or a combination. Significant physiologic improvement was seen across multiple variables including pulse rate, pH, and lactate. No patients later required decompressive laparotomy. Four patients died due to their primary disease. **Conclusion:** Percutaneous catheter drainage is safe and efficacious in reversing abdominal compartment physiology in children with intraabdominal fluid, and can be considered prior to surgical intervention when clinically appropriate.

**Keywords:** Abdominal compartment syndrome, abdominal decompression, ascites, intra-abdominal hypertension, paracentesis

## INTRODUCTION

Abdominal compartment syndrome is a life-threatening condition in which intraabdominal hypertension causes organ dysfunction.<sup>[1,2]</sup> This may develop after traumatic injuries that result in large intraabdominal bleeding or high-volume resuscitation related to abdominal surgery or sepsis.<sup>[1,3]</sup> The treatment of abdominal compartment syndrome traditionally involved early decompressive laparotomy.<sup>[4]</sup> Percutaneous catheter drainage has been used as an alternative in adults with massive ascites or hemoperitoneum as a presurgical intervention or a definitive treatment.<sup>[5–8]</sup> Although peritoneal drainage has long been used in the treatment of necrotizing enterocolitis in the neonate, its use in abdominal compartment syndrome in the pediatric population, specifically in infants and small children, has not been well described.<sup>[9]</sup> We hypothesized that percutaneous catheter drainage is a safe approach for abdominal compartment syndrome in a population of infants

and small children, and investigated its ability to reverse the physiology of abdominal compartment syndrome in small children with intraabdominal fluid.

## MATERIALS AND METHODS

We reviewed the records of all children 10 years of age or younger who underwent percutaneous catheter drainage for abdominal compartment syndrome physiology from January 1, 2014, to December 31, 2018, at Hassenfeld Children's

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Hospital at NYU Langone Health. Abdominal compartment syndrome was identified in the medical records as respiratory distress requiring increasing ventilatory support, tense abdomen on physical examination, decreased urine output, and a metabolic acidosis component indicated by decreased blood pH and elevated blood lactate. Both bedside and operating room-based interventions were included in this study. Children undergoing percutaneous catheter drainage for indications other than abdominal compartment syndrome were excluded from the analysis. Procedures were equally distributed across a single academic pediatric surgical division comprised the same four surgeons throughout the study period, all of whom utilized a standardized technical approach. Sonogram-guided percutaneous drainage was performed using a Seldinger technique with catheter diameters ranging in size from five Fr to 12 Fr or a direct placement of a Penrose drain. Catheters were removed when abdominal compartment physiology resolved and output was <10 mL/day. The study was approved by the institutional review board.

Clinical variables selected for univariate descriptive analysis included age, weight, indication for catheter placement, length of time of catheter placement, and amount of fluid collected in the first 24 h. The primary outcome measures consisted of changes to physiologic variables representative of abdominal compartment syndrome severity before and after drain placement, including heart rate, urine output, FiO<sub>2</sub>, SpO<sub>2</sub>, pH, pCO<sub>2</sub>, pO<sub>2</sub>, and blood urea nitrogen. Prior to comparative analyses, continuous variables were individually evaluated for distribution normality using a Shapiro–Wilk statistic and normality plots to guide nonparametric testing. Outcome variables were compared using paired Wilcoxon signed-rank tests. Results containing continuous variables are presented as median values with interquartile ranges unless otherwise noted. Statistical significance was accepted for  $P < 0.05$ . Data analyses were performed using the IBM Statistical Package for the Social Sciences (IBM SPSS 25.0, Armonk, New York, USA).

## RESULTS

We identified 46 children who underwent percutaneous peritoneal drainage over the 5-year study period and excluded 36 from the analysis because their drainage procedure was not related to abdominal compartment syndrome concerns. Most of these 36 excluded patients had drains placed for necrotizing enterocolitis. Of the remaining ten children who qualified for analysis, we identified 11 percutaneous catheter drainage interventions; one child underwent two discrete drainage interventions spaced 6 months apart for recurrent malignant ascites driving compartment physiology. Of note, over the study period, no children with abdominal compartment syndrome underwent decompressive laparotomy. Demographics and indications for percutaneous catheter drainage for the study sample are summarized in Table 1. The cohort was largely comprised infants and small children: ages ranged from 2 days to 7 years, including seven patients under 6 weeks of age. Drainage catheters remained in place

from 1 day to 35 days. The amount of fluid drained in the first 24 h following percutaneous catheter placement ranged from one to over 600 cc/kg.

Table 2 summarizes the physiologic response across the cohort following percutaneous catheter drainage, as measured by multiple objective parameters immediately before and 24 h after drainage. We observed improvement in all measured physiologic variables, with statistically significant improvements identified for pulse, SpO<sub>2</sub>, pH, pCO<sub>2</sub>, pO<sub>2</sub>, and lactate. No complications directly related to catheter occurred throughout the study period. While there were no procedure-related mortalities, four of the ten children in the study (30%) ultimately expired. Three of the deaths occurred within days after catheter placement in patients with congenital diaphragmatic hernia who succumbed to complications secondary to severe persistent pulmonary hypertension. One death occurred within 30 days of catheter placement in a patient with severe complications from acute megakaryocytic leukemia. Two children (Cases 6 and 7) had drainage consisting largely of air with trace intraabdominal fluid. While one (Case 6) experienced rapid improvement postpercutaneous catheter drainage of intraabdominal air, the other (Case 7) expired soon after the procedure secondary to the progression of his primary disease process.

## DISCUSSION

Abdominal compartment syndrome is an increasingly recognized morbidity affecting critically ill pediatric patients. Intraabdominal hypertension can lead to end-organ dysfunction in abdominal compartment syndrome through compression of the inferior vena cava and splanchnic vasculature. This subsequently impedes venous return to the heart, impairs cardiac output with disruption of systemic perfusion, and compromises renal function. The end result is progression to multisystem organ failure and death.<sup>[10]</sup> The traditional use of early decompressive laparotomy and supportive care to lower intraabdominal hypertension and maintain adequate abdominal perfusion pressure carries significant risk of complications including infection, hemorrhage, and abdominal wall hernias.<sup>[4]</sup> Furthermore, asystolic cardiac arrest has been noted in up to 25% of patients treated with decompressive laparotomy, believed to be induced by a reperfusion effect that triggers release of postischemic intracellular contents.<sup>[11–13]</sup>

Peritoneal catheter drainage can effectively lower intraabdominal pressure with less morbidity than laparotomy, and has been described in adults.<sup>[5,7,14,15]</sup> While no catheter-related complications occurred in this series, image-guided percutaneous drainage of intraabdominal fluid can be complicated by bleeding, bowel perforation, and bacterial peritonitis as noted by studies done in the radiology literature.<sup>[15,16]</sup> In a pilot study done on adult burn patients, percutaneous decompression was used in nine patients with abdominal compartment syndrome, relieving the intraabdominal hypertension in five successfully with

**Table 1: Clinical characteristics of patients undergoing peritoneal catheter drainage, original**

Procedure	Age	Weight of patient (kg)	Primary disease	Drain contents	Volume of liquid drainage over 24 h (cc/kg)	Drain duration (days)	Decompressive laparotomy required	30 days outcome
1	2 days	1.17	Fetal anemia requiring fetal intraperitoneal transfusion	Blood	60	3	No	Survived
2	7 years	38	Metastatic neuroblastoma status post-liver biopsy 1 week prior	Blood and serous fluid	136	8	No	Survived
3	3 days	1.6	Hydrops fetalis	Serous fluid	224	5	No	Survived
4	4 months	2.5	Congenital diaphragmatic hernia	Serous fluid	694	35	No	Died (due to primary disease)
5	4 days	2.9	Congenital diaphragmatic hernia requiring ECMO	Blood (over-anticoagulation)	114	10	No	Died (due to primary disease)
6	1 week	1.12	Spontaneous intestinal perforation	Air, trace serous fluid	<1	<1	No	Survived
7	2 days	2.86	Congenital diaphragmatic hernia	Air, trace blood (after vigorous/traumatic CPR)	<1	1	No	Died (due to primary disease)
8	14 months	12.7	Megakaryocytic leukemia	Serous (malignant ascites)	196	8	No	Survived
9	19 months	11	Megakaryocytic leukemia	Serous (malignant ascites)	130	6	No	Died (due to primary disease)
10	5 weeks	5	Septic shock	Serous	118	5	No	Survived
11	11 days	3.5	Hypoplastic right ventricle (cardiac failure)	Serous	74	11	No	Survived

ECMO=Extracorporeal membrane oxygenation, CPR=Cardiopulmonary resuscitation

**Table 2: Physiologic parameters before and after peritoneal catheter drainage, original**

	Prior to PCD	Post-PCD	P
UOP (mL/kg/h)	1.6 (1.0-2.3)	3.1 (2.0-3.6)	0.12
FiO <sub>2</sub> (%)	48 (25-64)	35 (21-40)	0.06
Pulse (bpm)	165 (150-183)	153 (112-159)	0.01
SpO <sub>2</sub> (%)	92 (85-96)	98 (96-99)	0.02
pH	7.17 (7.05-7.33)	7.32 (7.32-7.40)	0.02
pCO <sub>2</sub> (mmHg)	61 (42-66)	40 (39-40)	0.01
pO <sub>2</sub> (mmHg)	52 (33-61)	85 (60-95)	0.01
Lactate (mmol/L)	3.5 (2.2-6.1)	1.3 (0.66-2.7)	0.003
BUN (mg/dL)	26 (23-34)	26 (23-38)	0.87
Creatinine (mg/dL)	0.73 (0.58-1.1)	0.70 (0.67-1.0)	0.83

PCD=Peritoneal catheter drainage, UOP=Urine output, BUN=Blood urea nitrogen

four requiring laparotomy; no complications of percutaneous drainage were noted.<sup>[5]</sup>

While peritoneal drainage is accepted therapy for neonates with intestinal perforation such as in necrotizing enterocolitis,<sup>[17]</sup> its use in abdominal compartment syndrome in the pediatric population has not been as well described.

Isolated case reports have described the successful use of peritoneal drainage for emergent decompression of abdominal compartment syndrome in infants with septic shock and severe burns, and in older children after blunt trauma.<sup>[7,18-20]</sup> One retrospective series of percutaneous catheter drainage in 12 children with a median age of 3 years demonstrated reduction in intraabdominal hypertension and improvement in physiologic parameters.<sup>[9]</sup> Our study similarly showed a significant decrease in intraabdominal hypertension but in a much younger cohort. Like our study in which 30% of our patients died, this retrospective series had a similar mortality rate of 25%.<sup>[9]</sup> In our study, the deaths were not catheter related, but reflected the often severe underlying conditions that lead to abdominal compartment syndrome.

In this study, we analyzed the records of children undergoing peritoneal catheter drainage for abdominal compartment syndrome secondary to ascites, hemoperitoneum, and pneumoperitoneum with ascites. We found that peritoneal drainage in these children resulted in significant physiologic improvement with no catheter-related complications. We demonstrated the safety and effectiveness of this approach in our patient population, and suggest it continue to be studied



as a therapy for abdominal compartment syndrome in the pediatric population.

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### Conflicts of interest

There are no conflicts of interest.

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# Complications of COVID-19 in Children and the Approach to the Affected Children in Pediatric Primary Care

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## Abstract

Pandemics of the coronavirus SARS-CoV-2 has been circulating the world since the beginning of 2020 in several waves leaving behind many millions of affected individuals and very many fatalities. In children, the course of the disease has generally been milder than in adults; however, there was a wide range of possible serious complications observed including the pediatric fatalities. In this article, we review possible complications of COVID-19 in children and also focus on the role of pediatric primary care practitioners in the diagnosis and management of this serious disease.

**Keywords:** Children; complications; COVID-19; epidemiology; MIS-C; novel coronavirus; PIMS-TS; primary care; SARS-CoV-2

## INTRODUCTION

Since the first reports of novel coronavirus virus infection (SARS-CoV-2) causing pneumonia in adults came from China in the end of 2019,<sup>[1]</sup> very soon also the pediatricians became highly alerted. Along with the reports of growing number of cases of the new COVID-19 disease in adults, first reports also came about children affected by the same disease.<sup>[2]</sup> The first papers about the symptoms and severity suggested that children did suffer from similar symptoms as adults; however, from the very beginning, the reported experience was that the course of the disease in children was milder than that in adults and also the ICU admissions and fatalities were much less frequent than in the adults.<sup>[3]</sup> Nevertheless, first Chinese epidemiological analyses suggested that individuals of all ages were susceptible to COVID-19 with no significant sex difference. Especially young children, particularly infants, were vulnerable to this infection. Most infections in children came from the family clustering, and children were specific victims of the human-to-human transmission with the close family contacts representing the highest risk.<sup>[4]</sup> The first reported hospitalized infants from China due to the COVID-19 infection had at least one family member infected, with the infant's infection occurring only after the family members' infection. Fortunately, none of these children required intensive care or had any severe complications.<sup>[5]</sup>

With the ongoing pandemics and growing numbers of cases worldwide, the experience and knowledge about the disease have substantially expanded.

As of April 5, 2021 there have been 131,020,967 confirmed cases of COVID-19 globally, including 2,850,521 deaths, reported to WHO. This makes the current overall mortality rate 2.18%. Interestingly, in some initial reports, the overall published mortality was higher. By April 16, 2020, 1,991,562 confirmed cases were reported with 130,885 deaths and thus the mortality rate was 6.57%. This change apparently reflects changing of the approach to the disease and the increased testing of asymptomatic individuals, mainly because of increased detection of contacts and higher rate of regional testing in some areas of the world. Also, there has been a substantial progress in the treatment as several treatment modalities have been introduced during the last year that may have improved prognosis in severe cases. However, the reporting of severity of the COVID-19 may still be biased

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by many factors and may be largely dependent on the local systems of detections and organization of epidemiological surveillance and health care. Initially, the reported overall mortality rate in the highly affected areas was rather variable but currently has stabilized around 2% of all cases (1.8% in the USA, 2.5% in Brazil, 1.3% in India, 2.2% in Russia, 3% in Italy, and 2.9% in the UK).<sup>[6]</sup>

The epidemiological data in children may be even less reliable than in adults as many cases may escape detection. In the initial reports, children represented about 2% of all reported cases in China and approximately 1.5% in Europe and in the USA. Children are certainly much less tested, and many of those tested come from testing of the family contacts. This may increase the probability of positive result even in an asymptomatic child. There were no systematic studies testing large population-based cohorts of children that could provide more accurate data about the true incidence of SARS-CoV-2 positivity of children in various age groups and in different regions of the world. Logically, the initial reports about the symptoms, severity, and course of the disease in children came from the most affected areas of the world such as China and Italy. Some studies indicated that symptomatic children often presented with mild symptoms, mostly presenting as mild febrile upper respiratory tract disease. However, even these data were somewhat inconsistent as the frequency of such symptoms was reported in a rather wide range, between 10% and 60% of all diagnosed children. This again may be related to imprecise denominators as the studied populations were definitely somewhat preselected, based on the presentation and reason for testing. The course of the disease in diagnosed children tended to be shorter than that in adults. Besides mild respiratory symptoms, also gastrointestinal symptoms were reported, such as abdominal pain, nausea, vomiting, and diarrhea. Nevertheless, children with severe disease were also reported from the very beginning of the data gathering. Again, the initial data came from the first areas of the disease outbreak. Chinese studies of various powers and various numbers of evaluated subjects indicated that between 2.5% and 5% of all pediatric cases had some form of severe disease.<sup>[4,7]</sup> One systematic review from China reported moderate course of the disease, mostly clinically presenting as mild pneumonia, in 39–82% of the patients. However, in a German study among children admitted to the hospital, up to 8% of the children presented with severe or very severe disease, including deaths.<sup>[8]</sup>

Interestingly, while in adults the most vulnerable age group includes seniors, in children the age comes apparently as an inversely related risk factor for a severe course of the disease. The early CDC reports from the United States found rather a wide range of hospitalized children (5.7–20%), most of these being infants.<sup>[9]</sup> Similarly, reports from Italy mapping the situation in 11 pediatric hospitals and 51 pediatric units found that admissions were

more needed in the younger age groups.<sup>[10]</sup> Fortunately, compared with adults and seniors, the overall mortality in children remains very low. The current US CDC analysis (as of April 5, 2021) shows the children in the age from 0 to 17 years to comprise 11.8% of all US COVID-19 cases with the mortality  $\leq 0.1\%$ .<sup>[11]</sup>

## COMPLICATIONS OF COVID-19

Although most symptomatic patients with COVID-19 manifest with fever and respiratory symptoms of various severity, SARS-CoV-2 infection may also affect other organs and present with more or less expressed extra-respiratory symptoms. Loss of smell and diminished taste have been described as rather typical early symptoms in about 10% of adults with possible persistence for some time after resolution of the respiratory manifestation. These symptoms were, however, much less prevalent in younger children.<sup>[12]</sup> In a growing number, some adult case reports and small series reported extra-pulmonary manifestations, including gastrointestinal, cardiac, hepatic, renal, neurological, ocular, or hematological symptoms. Occasionally, these extra-respiratory symptoms were the initial manifestation of SARS-CoV-2 infection, prior to development of fever or respiratory manifestations. Initially, complications were mainly reported from seniors and patients with pre-existing chronic conditions such as obesity, cardiac disease, hypertension, or diabetes. It has not yet been fully elucidated to what extent complications are caused by the deterioration of a pre-existing condition in a general cytokine-driven inflammation during the infection and how much these complications may be caused by a direct effect of the virus attacking the target tissue. More and more reports pointed to the vascular involvement, including endothelial injury, microangiopathy, and thromboembolic complications. Comparison of the autopsy findings in the lungs of patients who died from COVID-19 and those who died from influenza-related ARDS showed a marked difference in the vascular involvement, with severe endothelial injury associated with the intracellular detection of the virus, thrombosis with microangiopathy, and marked angiogenesis characteristic for the COVID-19-related deaths.<sup>[13]</sup> A vascular damage has also been documented in skin as vasculitic rash or chilblains; a concurrent occurrence of chilblains and retinal vasculitis has also been described.<sup>[14,15]</sup>

Fortunately, such thrombotic episodes were much less reported in children than in adults. Generally, it seems that the vessels of children do not respond to the virus-induced cytokine-driven endothelial injury as much as in adults.<sup>[16]</sup>

Nevertheless, the most severe complications in children have been reported from various SARS-CoV-2-affected areas as series of Kawasaki-like disease. While the

presentation and clinical course shared most features with the classical Kawasaki disease, reported cases were not limited to the young children but also occurred in older children and adolescents. In a French report of 21 cases [median age 7.9 (range 3.7–16.6) years] with Kawasaki-like multisystem inflammatory syndrome, 12 (57%) presented with Kawasaki disease shock syndrome and 16 (76%) with myocarditis. Most patients (17–81%) required intensive care support. All of these 21 patients had marked gastrointestinal symptoms and high inflammatory activity. All patients received intravenous immunoglobulin (IVIG) and 48% also received corticosteroids. The outcome was good in all patients with moderate coronary artery dilations found only in 24%.<sup>[17]</sup>

In another report, a 30 times increased incidence of Kawasaki-like disease after the outbreak of COVID-19 has been reported from the highly affected Bergamo area in Italy.<sup>[18]</sup> Affected children presented with intense inflammatory response resembling macrophage activation syndrome and with frequent cardiac disease. In a series of 35 children admitted in 14 centers in France and Switzerland over a 2-month period with cardiac injury and cardiogenic shock associated with SARS-CoV-2 infection, 28% required ECMO support. They responded favorably to IVIGs with one-third requiring additional systemic corticosteroids (CS).<sup>[19]</sup>

This clinical presentation has been later defined as a separate disease labeled as PIMS-TS (pediatric inflammatory multisystem syndrome temporarily associated with SARS-CoV-2) or MIS-C (multisystem inflammatory syndrome in children). In a recently published meta-analysis analyzing 953 reported patients from 68 carefully selected studies, the median age of affected children was 8.4 years which was significantly different from the non-COVID children with Kawasaki disease (median age 2.0–2.7 years). Fever was a leading symptom in almost all patients (99.4%), in 27% lasting more than 5 days. Gastrointestinal symptoms, such as abdominal pain, diarrhea, and vomiting, were present in 85.6% of cases. Cardiovascular manifestations were frequent (79.3%): mainly tachycardia, hypotension or cardiogenic shock, myocarditis, and decreased left ventricular ejection fraction. Coronary dilatation or development of aneurysms of coronary arteries was found only in 11.6% and 10.3%, respectively. About half of the patients had respiratory symptoms, mainly multiple pulmonary infiltrates, dyspnea, or upper airway symptoms. Polymorphous exanthema (54.9%) and non-purulent conjunctivitis (49.8%) were frequent. Among biological markers, C-reactive protein, ferritin, and interleukin-6 were typically markedly elevated. Interestingly, the inflammatory activity was substantially higher when compared with historical Kawasaki disease cohorts.<sup>[20]</sup> Treatment of this condition has been originally derived from the recommendations in the Kawasaki disease, mainly using IVIG and CS. Gradually, with

growing experience, some management recommendations and guidelines were published that address the complexity of treatment. Besides the well-established IVIG and CS, great attention is given to management of the coagulation system using the anti-coagulation and anti-aggregation treatments.<sup>[21,22]</sup> From the available data, it can be concluded that if this condition is recognized early and treatment started immediately, the prognosis is very good and long-term sequelae are rare.

Neurological complications have also been described mainly in adults but some reports about pediatric cases also appeared. These may be part of the multiorgan systemic inflammatory syndrome or as an isolated complication.<sup>[23]</sup> Isolated cases of COVID-19 disease-associated Guillain-Barré syndrome have been described.<sup>[24]</sup>

Attention has been paid also to the children who may be at risk of severe course of the disease because of pre-existing conditions and comorbidities. Interestingly, preliminary data about children on immunosuppressive treatment because of underlying autoimmune diseases did not reveal higher susceptibility to the SARS-CoV-2 infection or more severe course of the disease.<sup>[25]</sup> Patients with a congenital heart disease are also considered at potential high risk of complications. Interestingly, in an Italian study in 4 children and 72 adults with congenital heart disease, no severe symptoms or complications were registered.<sup>[26]</sup> Still, as there is a well-documented risk of myocardial affection by the virus, these patients should be closely followed. Traditionally, patients with chronic respiratory diseases are mentioned as carrying higher risk of infection and possibly also a more severe course of the disease. However, it seems from the available evidence that patients with cystic fibrosis are not affected with any marked difference to the general population. This may, of course, be result of generally much higher compliance of these patients and their families with all the suggested protective measures.<sup>[27]</sup> There are no consistent data on pediatric patients with other chronic respiratory conditions, such as primary ciliary dyskinesia or bronchiolitis obliterans. Patients with asthma have also been traditionally considered at higher risk; however, there is no real evidence that children with well-controlled asthma do carry any higher risk of infection or severe disease. Patients with asthma should mainly properly follow their treatment plans and use their prescribed preventative medication with the exception of nebulizers because of the possibility of aerosolizing the infection in their environment.<sup>[28]</sup> More studies are definitely needed, and long-term follow-up of children and adults with asthma may show long-term prognosis of SARS-CoV-2-infected patients in the future.<sup>[29]</sup>

## APPROACH TO THE CHILDREN WITH COVID-19 IN THE PEDIATRIC PRIMARY CARE

The COVID-19 pandemic represents a new challenge to the pediatric primary care. So far, there has been no similar



situation with a wide-spread highly transmissible infection and so many asymptomatic potentially infective carriers. Asymptomatic children may act as a reservoir of the infection and may disseminate the infection, especially if in close contact with their peers in schools. Symptomatic children mostly do present with mild respiratory complaints that are hardly distinguishable from any other viral infections. This will be even more difficult during the autumn and winter with emergence of other usual viruses and especially during the usual influenza outbreaks. Pediatric primary care physicians need therefore to modify their practice, introducing more preventative measures and precautions into their routines. They should be aware of the epidemiological situation in their areas and follow closely the development of COVID-19 incidence. Children with respiratory symptoms (cough, sore throat, and fever) should generally be considered positive and isolated primarily within the family. Children with positive family contacts should be tested depending on the availability or at least followed up as there is a high risk of asymptomatic or oligosymptomatic infection. The arrangement of primary care practice should be re-arranged to reduce any contacts between patients. For children with mild symptoms, the visits should be reduced and distant follow-up arranged (phone consultations or video conferencing if possible). Parents should be properly instructed about the symptoms and made aware of signs of respiratory compromise (more frequent dry coughing, tachypnea, retractions, dyspnea). In case of any signs of more severe course, the patient should be seen with all the precaution measures and oxygen saturation checked. Patients with any hypoxemia need to be referred to the hospital for oxygen supplementation and further care. Always, the cardiac status should be properly checked. Inappropriate tachycardia, arrhythmia, chest pain, and fatigue may signal the development of myocarditis that also needs referral to the hospital for further diagnosis and treatment. This may go isolated or appear as part of the PIMS-TS. All patients should be always thoroughly evaluated for other possible complications such as gastrointestinal disease, neurological complications, etc. In young patients with more pronounced gastrointestinal symptoms, proper hydration should be maintained. The younger the child, the lower the threshold for referring for admission and inpatient treatment.

Of course, any patients with some underlying condition that might increase the risk of severe course of the disease should be referred rather early. These are mainly patients with severe immunocompromised conditions (current or recent chemotherapy, any post-transplant patients, primary immunodeficiency, HIV infection, severe heart disease, severe persistent asthma or other chronic lung diseases, chronic lung disease of immaturity, neuromuscular disease, severe poorly controlled diabetes, chronic kidney failure). In children with prolonged fever, the PIMS-TS should be considered irrespective of the history regarding possible COVID-19. As PIMS-TS can develop even in children with very mild disease or even

asymptomatic SARS-CoV-2 positivity, the symptoms and signs of this condition should be searched for actively.

Primary care physician is also responsible for evaluation of any possible collateral social issues. There have been reports of increased occurrence of home violence on children during the coronavirus lockdown, including sexual abuse. Other mental issues that must be detected early and referred timely to the psychologist or psychiatrist may be related to the isolation and lack of contact with other children or an overload with tasks during the remote education.<sup>[30,31]</sup>

## CONCLUSION

The new global pandemic of SARS-CoV-2 comes as a new experience and brings new challenges to the healthcare professionals on all levels of care. So far, in pediatric patients, the disease presents as milder than in adults but the risk of severe course or severe complications is not negligible. Primary care physicians must be aware of the epidemiology of the disease, modify their practice, and increase their alertness. Any possible complications, especially signs of respiratory failure, should be detected early, and the patient must be referred for specialized inpatient care. The threshold for referral must be rather low in patients with any significant underlying condition that might be associated with increased risk of severe disease or impaired prognosis.

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## Conflicts of interest

There are no conflicts of interest.

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# After COVID - where now?

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CoVID-19 has shattered our complacent assumptions about the best ways to practice medicine, and it is clear that there is no going back to 2019, whether or not there is another surge of CoVID or a new viral pandemic.<sup>[1]</sup> Here we look back to the way we were and consider the changes mandated by CoVID. Finally, we propose a road map for the future, critically considering which of the rapid, non-evidence-based changes worked, and what needs to be refined for the future. Illustrations are taken from respiratory medicine, but the principles are likely applicable to many other specialities.

**2019: *The way we were.*** Outpatient practice had not changed in living memory. A child and carer would make sometimes a very long journey; join an unruly scrum in the clinic waiting areas; be summoned to a (usually brief) consultation with an often quite junior doctor, who may never have seen the child before and may never see them again, before departing on the long return journey; the whole sterile process being repeated a few weeks or months later. A new referral would be seen at the hospital, but often investigations would have to be scheduled for a second visit. An emergency admission was usually prefaced by a prolonged wait in a crowded emergency department.

**2020: *In the throes of CoVID.*** The imperatives were to reduce travel to the minimum, and reduce face-to-face contacts, to minimize the risk of infection. The default was that the child should stay at home unless it was absolutely essential. The hospitals were flooded with severely ill adults, and children's services severely cut back. Children frequently presented late with serious illnesses, partly through bad advice and partly through parental reluctance to go to hospitals which were perceived as hotbeds of infection.<sup>[2,3]</sup> Outpatient clinics were initially mainly conducted over the telephone and then by video link. Equipment such as spirometry was increasingly provided at home.

**2021: *Going forward.*** We are going to continue with the default that the child only comes to hospital if it is absolutely necessary, for example, for a sophisticated test requiring expensive equipment. Much can be done in the local primary care center if we can connect up care for children. The obvious example is measurement of height and weight, which should be plotted on an electronic growth chart with access by the family and all carers.

The first area to consider is referral for a specialist opinion. Hitherto, a referral from primary to secondary care in many cases leads to all responsibilities being devolved away from the community, but this should change. Logically, the first specialist consultation should be by video link, and part of the process would be to plan the next steps. If, as is often the case, sophisticated investigation is determined to be needed, then a hospital visit is required during which a physical examination is performed and all necessary tests are carried out, because they have been pre-planned and booked, preferably as a day case. Also during this visit, the child should be provided with any necessary monitoring equipment and its use demonstrated. In the case of a child with asthma, this could include an APP allowing the mobile phone to be used as an electronic stethoscope; a portable spirometer; and an exhaled nitric oxide meter. A cheaper alternative might be to install these in primary care unless infection control is a major issue, as for example, in cystic fibrosis. Electronic monitoring devices (e.g. SmartInhaler™) would be attached to the relevant inhalers to monitor adherence<sup>[4]</sup>; hopefully, future devices would monitor

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inhalation as well as activation.<sup>[5]</sup> Directly observed therapy by mobile phone video link is well established in a research context,<sup>[6]</sup> but there is no reason why it should not also be utilized in clinical settings. All data would be stored on the carer's mobile phone and be accessible remotely in primary and secondary care.

Follow-up will also be transformed. Remote video supervision of treatment such as airway clearance and monitoring techniques such as spirometry are readily feasible. Intermittent video consultations are also eminently feasible. The advantages to the family of these approaches are obvious: minimal time off work and school, travel costs minimized, and far greater objective monitoring than previously. Pre-CoVID there was increasing emphasis on home visits by specialist hospital teams, but travel time was a problem; much can be done remotely.

Acute care provides different challenges. Video triaging in a virtual emergency room is one obvious way to improve on telephone consultations. There is potential to arrange direct admission from the home, bypassing the emergency department. Parental education in the recognition of a sick child is also essential, to avoid the twin pitfalls of missing serious problems and over-reacting to trivialities.

*2021: Unresolved problems.* The first prerequisite is a step change in technology, allowing storage and remote exchange of data in a manner compatible with data protection and personal security. The NHS has a poor record for Information Technology commissioning, and these difficulties cannot be understated. Also a concern is those for whom the modern world of electronic communications is a closed book, in particular the elderly. For these groups, safety nets must be in place, and remote monitoring will be much less feasible. Another vulnerable group is children for whom there are child abuse and safeguarding concerns; remote access may equate to no access for such children, leaving them trapped in an abusive home. This is no trivial issue; in severe asthma at least, safeguarding concerns are common.<sup>[7]</sup>

There may also be as an as-yet unresolved legal issue; could failure to see a child face to face be seen as negligent? As far as we are aware, this has not been tested in the Courts, so it is only possible to speculate about a ruling. Perhaps, an important principle is that if the family wants a face-to-face consultation, then that should be provided if at all possible. Secondly, if at the end of the remote consultation, the pediatrician is in any doubt of the clinical circumstances, at the very least a follow-up should be organized within a short time. Indeed, families may find a video or even a telephone call to check out progress to be reassuring. As with all consultations, critical is to ensure that the family feels that their concerns have been heard and they are happy with the proposed plan. The Courts

should certainly take into account that, compared with a year ago, remote consultations have become a mainstream part of medicine.

There is also a societal challenge. At least in some hospitals, attendance for asthma attacks<sup>[8,9]</sup> and other emergencies<sup>[10]</sup> has dropped dramatically, and this must be driven by behavioral changes which we should support continuing. The exact reasons are unclear, but are likely multifactorial. Lockdown and isolation have probably greatly reduced the transmission of non-CoVID respiratory viruses, a major trigger of asthma attacks. Environmental pollution has dropped dramatically.<sup>[11,12]</sup> Perhaps lockdown has reduced exposure to aeroallergens such as pollens, albeit at the price of increasing indoor exposures if parents smoke or vape. Hypothetically, parents may have had more time to supervise their children's medications and adherence has improved.<sup>[13]</sup>

Another key societal challenge is obesity, which has been a worse pandemic than CoVID-19 for far longer. Whereas the threats of cardiovascular disease and cancer in obesity have been largely ignored, the realization that obesity is associated with worse CoVID infection outcomes<sup>[14,15]</sup> has stung regulators into action. Weight loss is now on the public health agenda, and it needs to stay there.

Funding is another pertinent challenge. In care systems in which reimbursement is on the basis of face-to-face consultations, devolving these to remote care may cause consternation. The cost of the equipment may well be offset by savings in travel costs and loss of income, but these come from different pots of money!

Finally, as with all sweeping changes, there needs to be in place robust means of assessment, including safety and cost-effectiveness. In the rush of the onset of the pandemic, there was little or no time to do this, and we all learned how to cope as we went along. We now can and should go to more measured appraisals, ensuring we preserve the best of what we learned during CoVID and refining and reworking that which worked less well.

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## Conflicts of interest

There are no conflicts of interest.

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# 鼻敏感噴 鼻眼適

## 舒緩症狀話咁易<sup>1</sup>

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\*2歲或以上適用<sup>1</sup>

有效舒緩鼻敏感症狀，包括鼻塞、打噴嚏、流鼻水、鼻痕、眼痕、眼紅及流眼水<sup>1</sup>

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- ✓ 藥霧可直達鼻腔，針對敏感根源部位<sup>3</sup>
- ✓ 每日一次，藥效持續24小時<sup>1</sup>
- ✓ 舒適易用<sup>3</sup>，獨特設計榮獲醫學金獎<sup>2</sup>



**Safety information:** AVAMYS is contraindicated in patients with hypersensitivity to any of the ingredients. Adverse reactions: Epistaxis (the incidence of epistaxis was higher in longer-term use [more than 6 weeks] than in short-term use [up to 6 weeks] in adults and adolescents; in paediatric clinical studies of up to 12 weeks duration the incidence of epistaxis was similar between fluticasone furoate and placebo), nasal ulceration and headache. A reduction in growth velocity has been observed in children treated with fluticasone furoate 110 µg daily for 1 year. Therefore, children should be monitored on the lowest dose that delivers adequate symptom control.

**AVAMYS NASAL SPRAY abbreviated prescribing information: QUALITATIVE AND QUANTITATIVE COMPOSITION** Fluticasone Furoate 27.5 mcg/spray. **INDICATIONS** AVAMYS is indicated for the treatment of the symptoms of seasonal and perennial allergic rhinitis in patients 2 years of age and older. **DOSAGE AND ADMINISTRATION** Administer AVAMYS 27.5 mcg/spray by the intranasal route only. Adults & adolescents 12 years and older: The recommended starting dosage is 110 mcg (2 sprays in each nostril) once daily. When the symptoms have been controlled, reducing the dosage to 55 mcg (1 spray in each nostril) once daily may be effective for maintenance. Children 2-11 years: The recommended starting dosage in children is 55 mcg (1 spray in each nostril) once daily. Children not adequately responding to 55 mcg may use 110 mcg (2 sprays in each nostril) once daily. Once symptoms have been controlled, the dosage may be decreased to 55 mcg once daily. **CONTRAINDICATIONS** Hypersensitivity to any of the ingredients. **WARNINGS AND PRECAUTIONS** Based on data with another glucocorticosteroid metabolized by CYP3A4, co-administration with ritonavir is not recommended because of the potential risk of increased systemic exposure to fluticasone furoate (see Interactions). Systemic effects with nasal corticosteroids have been reported, particularly at high doses prescribed for prolonged periods. These effects are much less likely to occur than with oral corticosteroids and may vary in individual patients and between different corticosteroid preparations. A reduction in growth velocity has been observed in children treated with fluticasone furoate 110 mcg/spray daily for one year. Therefore, children should be monitored on the lowest dose which delivers adequate symptom control (see Dosage and Administration). As with other intranasal corticosteroids, physicians should be alert to potential systemic steroid effects including ocular changes. **INTERACTIONS** In a drug interaction study of AVAMYS with the potent CYP3A4 inhibitor ketoconazole there were more subjects with measurable AVAMYS plasma concentrations in the fluticasone group compared to placebo. The enzyme induction and inhibition data suggest that there are no clinically significant pharmacokinetic interactions between AVAMYS and the cyclosporine P450-mediated metabolism of other compounds at clinically relevant doses. Therefore, no clinical studies have been conducted to investigate interactions of AVAMYS with other drugs. **PREGNANCY AND LACTATION** Adequate data are not available regarding the use of AVAMYS during pregnancy and lactation in humans. AVAMYS should be used in pregnancy only if the benefits to the mother outweigh the potential risks to the foetus. Following intranasal administration of AVAMYS at the maximum recommended human dose (110 mcg/day), plasma AVAMYS concentrations were typically non-quantifiable and therefore potential for reproductive toxicity is expected to be very low. **ADVERSE REACTIONS** Epistaxis, nasal ulceration, growth retardation in children, hypersensitivity reactions including angioedema, rash, and urticaria. Headache, rhinorrhoea, nasal discomfort (including nasal burning, nasal irritation and nasal soreness), nasal dryness, nasal septum perforation. **OVERDOSE** Acute overdose is unlikely to require any therapy other than observation. Abbreviated Prescribing Information based on PI version GDS101P09.

Please read the full prescribing information prior to administration, available from GlaxoSmithKline Limited. Full Prescribing Information is available upon request. For adverse event reporting, please call GlaxoSmithKline Limited at (852) 3188 8888 (Hong Kong), or send an email to us at HKAdverse@glaxo.com.

**References:** 1. Avamys Hong Kong Full Prescribing Information (Version GDS101P09) 11/09. 2. Medical Design Excellence Awards 2004 available at: <http://www.designex.com/awards/winners/index.php?cat=11-year+2004&view=win>. Accessed 26 November 2000. 3. Berger BE, Gidycz AE, Siller AL. Expert Opin. Drug Deliv. 2007; 4(8): 689-701. 4. CYP3A4 Sales Data (GP Channel) in class R01A1 (NASAL CORTICOID AND ANALOGS), 2010-2020. 5. HPA Sales Data (Private) in class R01A1 (Nasal Preparation), 2000-2014.

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# Nasal tissue.

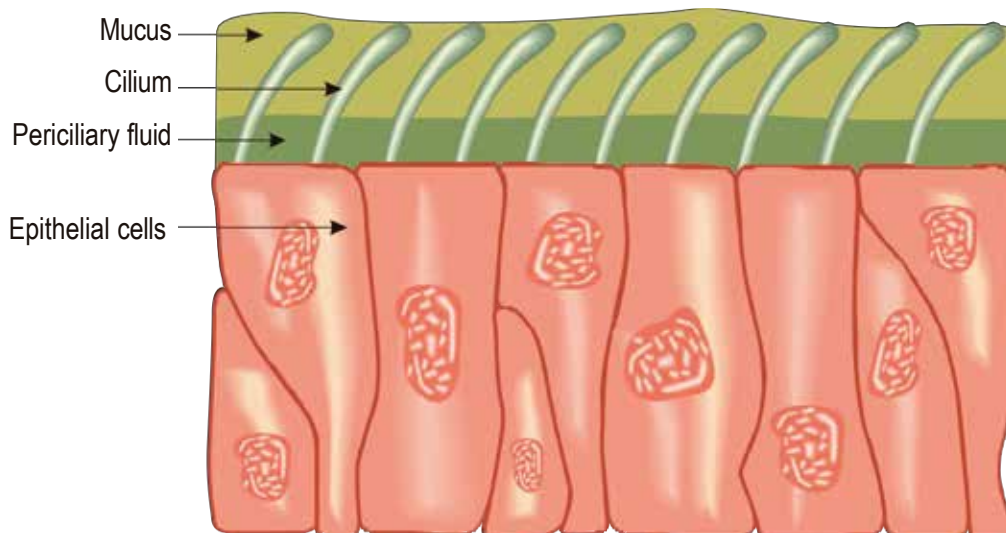
## What it is all about

Nasal tissue comprises a complex of integrated systems involving the following structures and functions.

### Structures and functions at the epithelial/mucus junction

- Epithelial cell
- Mucus producing cells (goblet cells)
- Mucus
- Cilia
- Periciliary fluid
- Cellular Repair
- Cellular inflammation

*Every component has a complex interaction with others and each process has complex biochemical chemistry*



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#### Reference:

1. Ringer-Lactate solution versus isotonic saline solution on mucociliary function after nasal septal surgery. Unal M et al The Journal of Laryngology and Otology Oct 2001 Vol 115 pp 796-797

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## 專家訪談

母乳餵哺 從營養著手

### 趙振瑞教授

臺北醫學大學營養學院院長

美國俄亥俄州立大學人體營養與食品管理博士



**"為了預防寶寶日後出現食物過敏的情況，授乳媽媽必須遵循各種飲食上的限制?"**

**趙教授：**

如媽媽本身有食物過敏，當然需要作出膳食調整。但如媽媽和寶寶都沒有確診過敏的情況，為此戒口對防敏沒有特別幫助，國際權威包括歐洲過敏及臨床免疫學會 (European Academy of Allergy and Clinical Immunology, EAACI) 亦不建議因此刻意避免任何膳食致敏原<sup>1-3</sup>。母乳當中的乙型轉化生長因子 (transforming growth factor- $\beta$ , TGF- $\beta$ ) 有助寶寶免疫系統完善發展，促進免疫球蛋白A (immunoglobulin A, IgA) 的製造，並降低誘發早期過敏病徵的機率<sup>4</sup>。

**"有推薦給授乳媽媽的簡單食譜嗎?"**

**豬腳燉花生<sup>5</sup>**

材料: 豬腳、花生 (亦可加入海帶)、適量鹽

做法: 洗淨材料，豬腳汆水，加入清水、花生 (及海帶)，燉熟即可。

營養價值: 豬腳含豐富膠原蛋白; 花生含豐富葉酸; 海帶含豐富碘質。

注意: 海帶含碘量非常高，建議每次吃一點點即可。

**More recipes and Q&As in the full interview >>>**

<https://hongkong.wyethnutritionsc.org/maternal-health-nutrition/interview-dr-jane-c-j-chao>



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**UP TO 72% REDUCTION**

**SIGNIFICANT EXACERBATION REDUCTION**  
in annualized severe exacerbations at Week 24 with  
DUPIXENT 200 mg Q2W + SOC vs placebo + SOC (P=0.0003)<sup>1</sup>

**200 mL IMPROVEMENT**

**RAPID AND SUSTAINED IMPROVEMENT  
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**86% OF PATIENTS**

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by Week 24 with DUPIXENT 300 mg Q2W + SOC vs 68% with  
placebo + SOC (P<0.001)<sup>1</sup>

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**HIGH RESPONDER RATE**

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limitations, and breathing<sup>1</sup>



**SELF-INJECTABLE**

Convenient subcutaneous  
injection<sup>1</sup>

**LIBERTY ASTHMA VENTURE Study Design:** 1,902 patients who were 12 years of age or older with uncontrolled asthma were randomly assigned in a 2:2:1:1 ratio to receive add-on subcutaneous DUPIXENT at a dose of 200 or 300 mg every 2 weeks or matched-volume placebo for 52 weeks. The primary end points were the annualized rate of severe asthma exacerbations and the absolute change from baseline to week 52 in the forced expiratory volume in 1 second (FEV<sub>1</sub>) before bronchodilator use in the overall trial population. Secondary end points included the exacerbation rate and FEV<sub>1</sub> in patients with a blood eosinophil count of 300 or more per cubic millimeter. Asthma control and DUPIXENT safety were also assessed.

**LIBERTY ASTHMA QUEST Study Design:** 1,902 patients who were 12 years of age or older with uncontrolled asthma were randomly assigned in a 2:2:1:1 ratio to receive add-on subcutaneous DUPIXENT at a dose of 200 or 300 mg every 2 weeks or matched-volume placebo for 52 weeks. The primary end points were the annualized rate of severe asthma exacerbations and the absolute change from baseline to week 52 in the forced expiratory volume in 1 second (FEV<sub>1</sub>) before bronchodilator use in the overall trial population. Secondary end points included the exacerbation rate and FEV<sub>1</sub> in patients with a blood eosinophil count of 300 or more per cubic millimeter. Asthma control and DUPIXENT safety were also assessed.

EOS, eosinophils; FEV<sub>1</sub>, fractional expired volume; SOC, oral corticosteroid; Q2W, once every 2 weeks; SOC, standard of care.

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**Indications:** Dupilumab solution for injection is a pre-filled syringe with needle shield. **Indications:** Acute Dermatitis (AD). Moderate-to-severe AD in adults and adolescents 12 years and older who are candidates for systemic therapy. Asthma. In adults and adolescents 12 years and older with severe asthma with type 2 inflammation characterized by elevated blood eosinophils and/or raised FeNO, who are inadequately controlled with high-dose ICS plus another inhalational product for maintenance treatment. **Dosage & Administration:** Subcutaneous injection. AD adults initial dose of 600 mg (two 300 mg injections), followed by 300 mg every other week. AD adolescents initial dose of 400 mg (two 200 mg injections), followed by 200 mg every other week. Body weight 400 kg. Same dosage as adults. Dupilumab can be used with or without topical corticosteroids. Topical calcineurin inhibitors may be used, but should be reserved for problem areas only, e.g. face, neck, intertriginous and genital areas. Consider discontinuing treatment in patients who have shown no response after 16 weeks. Asthma: Initial dose of 400 mg followed by 200 mg every other week. For patients with severe asthma and/or oral corticosteroids or with severe asthma and/or oral corticosteroids to severe AD: Initial dose of 600 mg, followed by 300 mg every other week. Patients receiving concomitant oral corticosteroids may reduce steroid dose gradually once clinical improvement with dupilumab has occurred. The need for continued dupilumab therapy should be considered at least annually as determined by a physician. If a dose is missed, administer it as soon as possible and resume dosing at the regular scheduled time. **Contraindications:** Hypersensitivity to dupilumab or any of the excipients. **Precautions:** Safety and efficacy in children <12 years not been established. Not to be used to treat acute asthma symptoms, acute exacerbations, acute bronchospasm or status asthmaticus. Do not discontinue corticosteroids abruptly upon start of dupilumab. Reduction should be gradual and performed under supervision of a physician. It may be associated with systemic, arthralgic symptoms and/or urinary conditions previously suppressed by systemic corticosteroid therapy. Disorders of type 2 inflammation may be suppressed by systemic corticosteroid use. If systemic hypersensitivity reaction occurs, discontinue dupilumab and initiate appropriate therapy. Be alert to vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in patients with eosinophilia. Treat pre-existing helminth infections before initiating dupilumab. If patients become infected while receiving dupilumab and do not respond to anti-helminth treatment, discontinue dupilumab until infection resolves. Patients who develop conjunctivitis that does not resolve following standard treatment should undergo ophthalmological examination. AD patients with uncontrolled asthma should not adjust or stop asthma treatments without consultation with physicians. Carefully monitor patients after discontinuation of dupilumab. Do not give live and live attenuated vaccines concurrently with dupilumab. Patients should be brought up to date with immunizations before starting dupilumab. **Drug Interactions:** Immune response to Tdap vaccine and meningococcal polysaccharide vaccine were assessed. Patients receiving dupilumab may receive concurrent inactivated or non-live vaccinations. **Pregnancy and lactation:** Should be used during pregnancy only if potential benefit justifies potential risk to fetus. Unknown whether dupilumab is excreted in human milk or absorbed systemically after ingestion. Decision must be made whether to discontinue breast-feeding or dupilumab taking into account benefit of breast-feeding for the child and benefit of therapy for the woman. **Undesirable effects:** AD: Most common adverse reactions reported: injection site reactions, conjunctivitis, dry mouth and oral herpes. Safety profile observed in adolescents consistent with that seen in adults. Asthma: Most common adverse reaction reported: injection site reactions. For other undesirable effects, please refer to the full prescribing information. **Preparation:** 2 x 300mg/2mL in pre-filled syringe with needle shield, 2 x 200mg/2.5mL in pre-filled syringe with needle shield. **Legal Classification:** Part L, Part 3 Third Schedule (Prescription Only). **Full prescribing information is available upon request.** AD: H-046-20-03

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