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>> IBAD KHAN: Good afternoon, I'm Commander Ibad Khan, and I am representing the Clinician Outreach and Communication Activity (COCA) with the Emergency Risk Communication Branch at the Centers for Disease Control and Prevention. I'd like to welcome you to today's COCA Call: "Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with Coronavirus Disease 2019 (COVID-19)." Today's webinar will be closed captioned. The "CC" button in the Zoom webinar platform to enable closed captioning is located either on the top or bottom of your screen. All participants joining us today are in listen-only mode.

For participants using the Zoom platform to access today's webinar, if you are unable to gain or maintain access, or if you experience technical difficulty, please access the live stream of the webinar on COCA's Facebook page at www.Facebook.com/CDCD Clinician Outreach and Communication Activity. Again, that is www.Facebook.com/CDCD Clinician Outreach and Communication Activity. The video recording of this COCA Call will also be available immediately following the live call on COCA's Facebook page should you wish to view it at a later time. The video recording will also be posted on COCA's webpage and available to view on-demand, at Emergency.CDC.GOV/COCA a few hours after the call ends. Again, the web address is Emergency.CDC.GOV/COCA.

Continuing Education is not offered for this COCA Call.

After the presentations, there will be a Q&A session. You may submit questions at any time during the presentation through the Zoom webinar system by clicking the "Q&A" button at the bottom of your screen and then typing your question. If we are unable to ask the presenters your question, please visit CDC's COVID-19 website at www.cdc.gov/covid-19 for more information. You may also email your question to coca@cdc.gov. Facebook Live viewers, we will send your questions to the presenters after the webinar ends. If you are a patient, please refer your questions to your healthcare provider. For those who have media questions, please contact CDC media relations at (404) 639-3286 or send an email to media@cdc.gov.

For more clinical care information on COVID-19, you may contact CDC's COVID-19 Clinical Call Center at 770-488-7100. The center is available 24 hours a day. Again, that number is 770-488-7100.

We'd like to remind clinicians to please refer patients to state and local health departments for COVID-19 testing and test results. Clinicians should not refer patients to CDC to find out where or how to get tested for COVID-19 or to obtain test results.

Also, please continue to visit emergency.cdc.gov/coca over the next several days as we intend to host more COCA Calls to keep you informed of the latest guidance and updates on COVID-19. In addition to our webpage, COCA Call Announcements for upcoming COCA Calls will also be sent via email. Subscribe to receive these notifications by going to emergency.cdc.gov/coca/subscribe.asp. Again, that's emergency.cdc.gov/coca/subscribe.asp. Please share the call announcements with your clinical colleagues.

I would now like to introduce Dr. Sapna Bamrah Morris, the Clinical Team Lead for CDC's COVID-19 Response. Dr. Morris will kick us off with a brief introduction then she will turn it over to Dr. Ermias Belay, the Special Investigations Team Lead for CDC's COVID-19 response, to provide a short update. Following Dr. Belay will be today's first presenter-Dr. Michael Levin/Professor of Pediatrics & International Child Health at Imperial College in London, England; following Dr. Levin will be our second presenter, Dr. James Schneider/Chief of Pediatric Critical Care Medicine and Associate Professor of Pediatrics at Cohen Children's Medical Center; then today's third and final presenter will be Dr. Vincent Marconi who is a Professor of Medicine and Global Health at the Rollins School of Public Health at Emory University's School of Medicine.

Please note, Dr. Morris will not have presentation slides today nor will Dr. Belay. The slide presentation will resume when Dr. Levin begins his presentation.

I'll now turn it over to Dr. Morris. Dr. Morris, please go ahead.

>> DR. MORRIS: Thank you, Cmdr. I would like to start by thanking our speakers that are here today to share their experience and expertise. I would also like to acknowledge the intro task force workgroup that has been formed at CDC as well as our field team and partner more about this multisystem inflammatory syndrome in children. Or what we are calling MIS-C. We have been learning about how SARS-CoV-2 occurs with patience and how asymptomatic infections to severe COVID-19 with substantial morbidity and mortality. In adults is becoming clear. A second nonsevere symptomatic face and in some 1/3 severe respiratory phase leading to the need for critical care and mechanical ventilation. It is apparent in adults some of the most severe complications resulting in increased morbidity and mortality are linked to a cytokine release or storm. During and after the third phase.

While some mechanisms have been described we have a great deal more to learn about optimizing care and treatment. Dr. and Schneider will share their experiences related to infections with SARS-CoV-2. We invited Dr. Marconi on what he has learned about COVID-19 with adult and the treatments that are currently being studied. We hope this serves to describe aspects that may be similar but also to highlight the differences in the presentations in children and adults.

I would like to introduce two of my CDC colleagues. Will join us. Secondly, I would like to introduce

As doctor belay -- like him to give a brief summary of our activities.

>> DR. BELAY: Since MIS was first reported which children we are learning more about the condition. We formed a workgroup to better understand and learn about the disease. Created a work definition that is by no means perfect and will be revised as more data becomes available.

On May 14 there was a health advisory on the MIS with children and it was widely circulated in the public health community in the United States. The health advisory described what we knew about MIS at that time. It outlined they working case definition and requested clinicians to report suspected cases with a case definition to local and state health departments.

Working with the local and state health departments to establish national monitoring system to better understand the burden and assess any potential risk factors for MIS and its association with the COVID-19 pandemic.

We also try to better define the different clinical phenotypes of the illness. Redevelop the case to capture some critical data regarding the clinical and laboratory and epidemiology characteristics of the illness. As the COVID-19 pandemic continues and probably through the fall, we urge clinicians that contribute to this national monitoring system by reporting cases to local and state health departments.

At this point would like to introduce to tell us about his experiences with the group.

>> DR. LEVIN: Hello, and thank you very much for the invitation to share the experience we had in the United Kingdom with you. I would like to start by acknowledging that the data I will be presenting was developed by a wide group of pediatricians working at several London hospitals. I'm presenting on behalf of all of them.

I think perhaps the only good news there was on the COVID epidemic, seemed to be that children had mild disease. As the disease arrived in the UK I think that was the general patent. Most children seem to have very mild disease. Few needed or ended up critically ill.

There was a surprise amongst a number of us working in several London hospitals. Towards the end of March the pandemic had arrived in the UK in early January and cases were increasing during February.

It was towards the end of March that a number of pediatricians started noticing an unusual illness. We had children who were admitted to pediatric intensive care units, critically ill with a very unusual syndrome.

They had been unwell with variable symptoms including sore throat, headache, but particularly abdominal pain and

vomiting. Some had rash and conjunctivitis or conjunctivitis injection or similarity to Kawasaki disease and the syndrome progressed rapidly for shock and organ dysfunction.

The children had a remarkably similar laboratory appearance and that they had marked elevation of C-reactive protein, neutrophil, lymphocytes, and we noticed some had marked elevation of troponin and natural Reddick to pint -- peptides. The majority of children were negative for SARS-CoV-2 PCR. By the end of March and April we collected 37 cases from eight hospitals around London.

Because it seemed to be a syndrome distinct from other pediatric entities we thought it was necessary to review the cases an attempt to establish a case definition.

In order to develop a case definition all cases were systematically reviewed on the clinical and laboratory data placed on a database. The results were reviewed by a team that consisted of pediatric infectious diseases clinicians and intensive care clinicians. And in particular we focus on head, there be an exclusion of other causes of shock and multiorgan failure including bacterial sepsis, staphylococcal or streptococcal shock syndromes, infections associated with myocarditis such as antivirus and macrophage activation syndromes.

After this review we felt the disorder was sufficiently unusual and distinct from conditions that we knew about that we alerted the national health service in the UK on 24 April.

On 27 April the Royal College of pediatrics and Child health, which is the body connecting pediatricians in the United Kingdom issued guidance for a disorder that we termed pediatric multisystem inflammatory syndrome. Temporarily associated with COVID-19.

We use temporarily because at that stage of the Association wasn't clear and still remains unclear as to the exact mechanism by which the absurd and cases is related to the pandemic.

The case definition was child presenting with persistent fever, inflammation with neutrophil ES, elevated C-reactive protein and lymph anemia, evidence of single or multi organ dysfunction which shock, cardiac respiratory, renal, gastrointestinal or neurological disorders where possible. And with an additional set of features that waitlisted in appendix which I will come to.

In addition to meet the case definition needed to exclude other microbial causes include bacterial sepsis, staphylococcal or streptococcal shock syndromes, enter virus infection and autoimmune disease. And COVID incorporated to be positive or negative.

The cases identified in this short time. Came from areas with the red dots in London and South England.

The age range was one through 16 years with a median of 11 years. There was a male predominance with 62 percent being male.

Most of them were completely healthy children previously with only a small number of children having the common core morbidities. One child had epilepsy and one had asthma. But generally healthy children.

A striking feature in this first description was it seemed to be a predominance of children from black/African/Caribbean/British ethnicity. Who accounted for about 46 percent of the cases. Whereas in London, they account for 13 percent and an overall England and Wales about three percent. The proportion of white patients seemed lower than the proportion of white people in London or in the rest of England.

There was an increase proportion of South Asian, Indian Asian British with 11 percent in our series. London has a high incidence of the script, but higher than the rest of the UK.

The clinical presentation after the illness was the predominant presenting feature was shock and with evidence of myocardial failure. 75 percent of the patients had shock, 51 with clear features of myocardial impairment. Rash

occurred in half of the children, 13 percent had conjunct title injection and 20 percent had mucous membrane inflammation or red cracked lips.

A look proportion having features similar to Kawasaki disease.

A striking feature was abdominal symptoms are very prominent with a number of the children having abdominal pain, vomiting, diarrhea. And three children were severely worried enough that they ended up having a laparotomy to exclude appendicitis or interception with no obvious findings suggesting a surgical cause.

Renal injury was common with raised creatinine's but only one child required renal replacement therapy.

Unlike adults with COVID, only 1/3 had respiratory problems and generally the major management problems was a severe respiratory failure.

The laboratory features were quite striking. -- Laboratory features were striking. Anemia with a median of 84 and they all had neutrophil elevation and very marked depression of lymphocyte with a median of -- platelets tended to be low. There was elevation of D dimers suggesting coagulation activation. But despite -- levels were elevated and fibrinogen levels were markedly elevated.

I mentioned troponin levels were elevated and in the patients that it was measured it pro PMP was elevated. And C-reactive protein was markedly elevated.

Radiology findings on a chest x-ray, a range of findings. Some patients had normal findings, some bilateral pleural effusion's, others patchy consolidation, some had focal consolidation or eight selective systems.

Those patients that underwent a CT scan of the chest all had some areas of nodular round glass of pacification. Abdominal ultrasound or CT abdomen was undertaken in many of the patients with evidence of bowel inflammation, thickening of the bow and the particular intra-abdominal lymphadenopathy.

The cardiac findings were striking. A significant proportion of them, 8/19 who had echocardiograms initially had evidence of impaired ventricular function. Coronary artery aneurysms was present and a significant number of children. Five out of the first 19 had evidence of coronary artery and one child had a giant coronary artery aneurysm.

The management of the patients as they were all treated in high dependency or intensive care. The majority required fluid resuscitation and inotropes supports. And then a range of immunology treatments were given. Largely because of the extreme evidence of inflammation and laboratory findings and because some of the patients had features suggestive of Kawasaki disease. Intravenous evil globulin was the most common used with 62 percent of the patients receiving it.

And then some receiving it and steroids and a range of demodulator's and some were receiving erythromycin as part of COVID treatment.

The outcomes was the majority of patients responded quickly to treatment. Children required -- coronary artery dilation. In general the patients had a slower response than we see in many other infections. A number of them took an amount of time to come out of intensive care.

SARS-CoV-2 results, only one third were PCR positive for SARS-CoV-2 and often only after multiple testing from repeated respiratory samples, bronchial and stool samples.

In contrast a high proportion of the patients were positive for antibody. We first started sink the patient's antibody testing wasn't easily available. Subsequently, a high portion -- portion are anti- body positive against SARS-CoV-2.

The question in reviewing patients that we had, what was the illness? There was some features reminiscent of Kawasaki disease. Some were similar to the syndrome of Kawasaki disease shock syndrome. Symptoms of staphylococcal or streptococcal syndrome. Some features with macrophage activation syndromes and extreme inflammation. And there

was some similarity to a syndrome that we saw a lot during the 1980s, hemorrhagic shock and encephalopathy syndrome but it tended to affect younger children. And some evidence of overlap with the features of autoimmune conditions but we found no evidence of staphylococcal or streptococcal.

In order to compare these patients with Kawasaki disease and Kawasaki disease shock syndrome we were fortunate to have a long standing collaboration across the Atlantic with Jane Burns and her group at Children's Hospital in San Diego. There's a data collections of children with Kawasaki disease that includes over 1,000 children with Kawasaki disease.

It's remarkable tribute to the willingness of clinicians to share information and pull resources with COVID and new diseases so we telephone Jane Burns and asked if we could compare these new patients to her database. 24 hours later Jane and her team sent the complete database.

I'm showing you results that I collaboration between the UK and the San Diego group.

This slide summarizes the features comparing the new syndrome which we called and read pediatric inflammatory, multisystem syndrome. In blue is the Kawasaki disease patients, and in yellow, Kawasaki disease shock syndrome and the black is toxic shock syndrome caused by either Staphylococcus or strep -- we collected from an EU funded multicounty study.

The first box shows the children with the multisystem inflammatory system -- syndrome were older and ate significantly. The white cell count the next box were significantly higher than Kawasaki disease or Kawasaki shock syndrome. Overlapping that of -- the elevated relative to Kawasaki disease or Kawasaki shock. The lymphocyte counts were markedly depressed compared to Kawasaki or Kawasaki shock. Hemoglobin's were significantly lower. And all the other groups as in the middle pattern. The platelet counts were lower than Kawasaki or Kawasaki shock syndrome. C-reactive proteins were more elevated significantly than either Kawasaki or Kawasaki shock or toxic shock.

The -- levels were lower than those seen in Kawasaki or Kawasaki shock. The bottom panel the ferritin levels were significantly elevated compared to Kawasaki or Kawasaki shock as were troponin levels and D dimers.

I think the conclusion from our comparison of the laboratory features and some clinical features was the syndrome seem distinct from Kawasaki disease and from a new and unusual childhood illness which was emerging really a month behind the COVID curve in the UK. It had distinctive laboratory features which differ from other syndromes with marked troponin elevation, D dimers, high CRP and markers of cardiac injury.

This slide just shows the time course of the emergence of the syndrome in the UK with the red curve showing the cases of the pediatric inflammatory multisystem disorder and the blue cases showing the overall COVID in London. What we can see is the new syndrome has emerged a month after the curve of the COVID epidemic.

This is the distribution from the UK public health laboratory service data. With the aid distribution and also the severity of disease. What you can see is in children in the bottom part of the bars, virtually all the children were discharged. There were very few -- very few had ongoing care. A mild disease until the emergence of the syndrome.

What is the mechanism? I think we do not know but the timing after the COVID-19 curve, the majority of patients being negative for virus but positive for antibody would suggest the illness is mediated by the development of acquired immunity to COVID-19 rather than direct viral injury.

Since we establish the case definition for pediatric inflammatory multisystem disease in the UK, we have also become aware of a widening definition and widening number of cases.

First of all, the red at the tip of the pyramid is the pediatric inflammatory multisystem syndrome temporarily associated with SARS-CoV-2.

In addition throughout the UK and in many European countries there are now reports of typical Kawasaki disease

appearing in children with coronary artery disease, with all the usual features of Kawasaki disease but with a large upsurge in numbers.

And increasingly, we are seeing children with no features of Kawasaki disease, no multi-organ failure, but with persistent fever and with elevated inflammatory markers, Ray CRP, raised ferritin's, raised neutrophil and lymphopenia. It would seem this is a widening spectrum of disorder that has a common mechanism.

For the emergence of these disorders seem to have raised a number of urgent questions mostly don't know answers of yet, do patients progress for the less severe the febrile child with raised inflammatory markers to the more severe forms if we don't treat them?

What is the risk of coronary artery aneurysms in each group?

If there is a significant breach -- chance treatment for Kawasaki disease may be needed. What is the relationship of all three disorders to the pandemic?

Two anti-inflammatory drugs and immunomodulators such as immunoglobulins, steroids, anti-TNF, anti- IL-1, anti-IL-6? What are the mechanisms? And are there biomarkers that distinguish each group from COVID and from other conditions?

Those are the questions that we haven't grappling with in the UK and really need to be addressed at a multinational level in order to pool resources.

In the UK and Europe we have two studies which are attempting to address some of these questions. The first is diamonds, is an EU funded grant that was aborted, led from our group at Imperial College but includes 11 countries in Europe and it aims to understand the biology of the disease by undertaking RNA transcript told -- and genetic analysis not only of COVID but the emerging spectrum of disease but all infectious and inflammatory diseases.

We are attempting to recruit patients to the studies which are up and running in 11 EU countries in the UK. In the last study that I will mention which we think is perhaps a novel way of addressing some issues, a study that we termed the best available therapy study or bats, it is anonymized of the best treatments for pediatric multisystem inflammatory syndrome . The Kawasaki disease associated with SARS-CoV-2 and the principal of the study is we are inviting pediatricians all over the world to enroll patients.

Each clinician we know pediatricians generally give their best treatment for their patients.

At the moment because we don't know which treatment works and we don't know whether the treatments that usually work with Kawasaki disease will work.

We are comparing the rates of normalization of inflammatory markers in the rates of development of coronary artery aneurysms as well as time on ventilators and all patients are entered into the study.

While this isn't a randomized trial we would much prefer to be doing a randomized control trial, the cases have emerged to rapidly to be entered into the trial.

This site will let us propensity match with enrollment so we can actually get an idea of which treatments may work.

And if there is progression from the milder forms to the more severe forms.

We think it's possible to do because we have very good biomarkers of severity information in terms of the CRP, ferritin. And clear endpoints. We are hoping to be sending out invitations to research teams and clinicians in many countries towards the end of the week inviting people to participate and submit their patients.

It's an online database so we will be welcoming of patients.

I just want to say that we have had so much to learn in such a short time and I know that pediatricians across Europe and the United Kingdom have pulled patients and work together to try to understand the disease.

We've had wonderful collaboration with the teams in United States such as the San Diego team and are very keen to work on this in a collaborative way. The last slide is just to acknowledge that diamonds study is in the EU, Verizon setting with recruitment of patients. And acknowledging all my colleagues at the different hospitals. And NHS will lead the alert. Thank you very much.

>> IBAD KHAN: Thank you for sharing what I believe we have Dr. Schneider.

>> DR. SCHNEIDER: Thank you very much. I appreciate being able to share our experience in New York. If you go to the next slide.

First off a warm thank you to everyone for listening and participating. That was an outstanding description of what's been going on. You have led the charge in identifying this and helping us understand. It was the awareness that we shared from the UK in late April that led us in our institution on the side of the Atlantic to recognize there is this new syndrome that children are presenting with.

We've learned a lot from you and continue to learn together in the investigations you are undergoing I'm sure many of us would be willing to help as we learn together as a community.

What I will share some experience in our institution. For those not familiar with Cohens children. The one children hospital part of 23 hospital health system in New York. We capture a very broad net in our area and I am part of a 37 bed pediatric intensive care unit that offers all therapies known to critically ill children. And what I will share with you know is our experience. We have reported to the New York State DOH I believe in the mid-40s, 43 or 44 patients who have had the syndrome.

We were using a definition that was extrapolating from the original reports. They all fall under similar paradigm of children that had fever for at least days with any of the following clinical findings of gastrointestinal symptoms, rash, conjunctivitis or mucosal changes, respiratory symptoms of cough or neurologic symptoms.

Similar symptoms we see and Kawasaki disease. They had to have significant findings of inflammation, elevations and C-reactive protein, ferritin's, also cardiac involvement with troponin or Pro BNP. And lastly with the clinical features that fell under a different category of those that were classic Kawasaki type symptoms or those with incomplete Kawasaki symptoms as you see that are predefined characteristics from the American heart as well as kids that did not necessarily fall under those categories.

However, they were presenting with significant cardiogenic or distributive shock. We were now given this new case definition through the CDC which is helpful to at least standardize our approach so we can continue to learn more about this condition together.

Thankfully it seems, I will review the CDC definition per se, but I will say that our definition of the patients that we have included that I will report on all fit these definitions. At least we can move forward with that.

Overall we have -- like I mentioned we have had 43 kids as of yesterday I think it's 44 today who have met these criteria. I will report on 33 of them to limit to the timeframe when we have data to complete the definition. Mid-April through the past week.

Of the 33 children you will see a lot of similarities or hear a lot of similarities between what we've experienced here compared to what we just heard from the UK description that was eloquently described by Dr.

There was a male predominance, and racially we see about 1/4 were black and 10 percent were Asian or white and they may just reflect our particular demographic of where we are in New York.

However, as we collect more and share more data we will get a better sense of any racial disposition.

27 percent of the children were Hispanic.

I've also seen most of the children were previously normal healthy children with no underlying comorbidity sprayed only two children that had a comorbidity and that was not very significant.

Half of the children are normal weight and about 40 percent or so for obese and as we are familiar with the acute -- acute COVID infection obesity is a risk factor in the adult population that we haven't seen. About 15 percent of the children had underlying disease or asthma. This seems to be a condition that does not seem to be associated with any known predisposition.

What are these children presenting with in our experience here? The children had a median duration of fever for four days. Prior to arriving in a hospital. About two thirds had neurocognitive symptoms which were similar, headache, some lethargy, things of that nature. Almost all children presenting with gastrointestinal symptoms in abdominal pain, bottoming vomiting or diarrhea. Only a few had some type of radiograph, CAT scan of the abdomen. And of those that we do have results on they were nonspecific or normal. A few children had evidence of Italy -itis or bowel wall thickening. Nothing that was surgical or was the clear cause.

About half had respiratory symptoms and I will speak more coming up related to the respiratory support needs.

Interestingly I think we have all seen that these children, the respiratory systems are clear to be secondary to cardiovascular disease rather than primary lung infections. About two thirds of the children have presented with shock whether either required fluid resuscitation and the majority of whom required some type of -- care and the intensive care unit.

If we were to break down the presenting signs and symptoms and categorize the children in two meeting criteria for Kawasaki disease or not, two thirds met complete Kawasaki disease criteria and others patients three quarters had shock which is obviously as we are familiar very uncharacteristic of typical Kawasaki disease which is only five percent developed shock.

About 80 percent of our children have required ICU care and overall the length of stay for the children has been about four days.

The lab results are quite striking and illustrative of the inflammatory disease that we think is going on. Our children all had a fairly normal white count in general. Medians of 9.1.

With lymphopenia as we heard previously as well, 80 percent had. Mild anemia was fairly common with normal platelet count in general. The C-reactive protein levels were exceptionally elevated as you see the median is 206 which is quite high. The D dimers were quite elevated at 1700. Fibrinogen was elevated. We see higher than this you're just reporting the medians. Ferritin as well was elevated significantly as we are getting familiar, lactate D, mild elevation of INR. Pro BNP were remarkably elevated. Again, really putting emphasis on the incidence of cardiovascular system involvement right from the early presentation. And speaking to the amount of shock that we noticed and were treating saw significant increase. On our scale less than 14, so 31 being elevated. The procalcitonin is elevated knowing that the children did not have bacterial infections we will still learn for the relevance and the utility in managing the patients. There were significant incidents of hyponatremia. Mild levels of high in the children she see mild elevations of ALT and AST and as expected mild decreases. Lab results that reflect an active inflammatory system leading to other markers that we see in vascular buffets.

We look at the pages that are PCR positive or PCR negative for acute SARS-CoV-2 the mass majority were negative. No evidence at time of presentation of acute SARS-CoV-2. But the vast majority if not I believe all were positive for the IgG indicating the previous infection.

As we are describing this syndrome we are including clearly multiple organ involvement as part of the definition. Many of our children had various organ involvement. 21 percent had a degree of acute level -- liver injury. Three quarters had evidence of acute kidney injury rate I don't believe any required replacement therapy. But based on criteria they met significant portion met definition.

About half the children required some type of respiratory support either submental oxygen or ventilation but only a few I think six patients required incubation. What was striking is they were not primarily for lung disease that may indicate a direct injury to the lung from the virus rather they were -- the children were intubated. Those that remain such for three days.

A striking finding and what I put into my category of alarming with these group of children is half the children already had coronary artery abnormalities and you can see them described in front of you were looking at specifically with Z scores there were significant findings of coronary enlargement, aneurysms in which as we know is quite early if you compare to typical Kawasaki. And also significantly higher burden of coronary involvement compared to typical Kawasaki. Illustrating perhaps a different disease.

Many of the children already had myocardial dysfunction. Little more than half the children. Speaking to the need for critical care for the majority of the kids.

What have we been using for air therapies for the children? I've broken it down into a two-pronged approach. The first which is not up here, like to consider good old-fashioned critical care. The children need care for the shock they are in. The therapies including mechanical ventilation, that is one of the two areas that we are using to treat the children but specific to the inflammatory disease every one of the children received intravenous, thirds needed a second dose which is usually indicated for persistent fever for 24 hours duration of the first dose.

We also used a much more aggressive approach that intensified strategy for Kawasaki disease. We extrapolated from there. Most of the children received some quarter corticosteroid and aspirin. A few children earlier in the course or the timeframe that required other types of modulation which was generally indicated after persistence of ongoing inflammation by fever or blood test after the IV IG and steroids were being used.

Related to Oxley Perrin or blood thinning we are collaborating closely with our hematologist that to individualize the therapy based on some of the coagulation profiles and it is a very much area of interest in understanding how to best manage the children.

We know clearly from both the adult population and earlier pediatric experience with acute COVID there seems to be -- associated in some type of quagga -- anticoagulation.

Thankfully of our 33 reported and 43 that we've had or 44 now there have been no mortalities. Children are responding well to the therapies. 82 percent of the children in this cohort have been discharged alive and if you are hospitalized but seem to be responding. Interestingly there is still significant number of children leaving the hospital with some mild or depressed cardiac function or some cardiac involvement and on close follow-up with pediatric cardiologists -- [Inaudible].

Thank you very much for allowing me to share our data with you. As just one single center and I'm sure we will all continue to learn together in the collaboration associated with this has been fantastic. I think at this point I will pass the baton, if you will to Dr. Marconi.

>> DR. MARCONI: Wonderful talk. Thank you so much Dr. Schneider and thank you for who does to the CDC for being a part of this discussion. Perhaps a different take of COVID-19 I've been asked to talk about the adult perspective in terms of the inflammatory syndrome and what looks like for adults and some of the therapies that you heard discussed by Dr. Schneider and what's been talked about in trials.

Just to start off with a standard you've heard descriptions and children, but what is a usual presentation for an adult look like? This is for individuals that have gone on to have severe or critical COVID-19 disease.

This is a patient we saw early on around mid-March that presented to one of our hospitals in Atlanta. This individual was in their mid-50s and presentation and did have some underlying hypertension, was overweight but not obese and also underlying diabetes but no emphysema.

Usual state of health but presented initially with fever, cough, shortness of breath. Did not have earlier symptoms predating this but presented acutely shortness of breath in conjunction with the fever cough. And had significant diarrhea. The showing on the slides the colored bars running horizontally giving the time course of presentation.

Over time, the patient who had an oxygen requirement initially then progressed after a couple of days of being moved into the ICU and requiring intubation. As you can follow in the upper part of the figure, the temperature maximum red and minimum in blue. Remain febrile through the initial presentation and was intubated and brought into the ICU on hospital day 2 after being in the hospital for a couple of days required a significant amount of ventilation and oxygenation and requiring FAO to of 80 up to 100 percent.

Also the patient continued in this course for many days as you can see. It was intubated for the better part of more than 2 to 3 weeks. Through this time required they suppressors for shock because blood pressure dropped on day seven. Also predated by bacterial pneumonia as well as acute kidney injury.

While all this was happening, if you can view the top half of the figure you will see all the biomarkers that were described earlier were elevated for this individual.

CRP was very high, Sentry and D dimers 15,000 range. IL-6 well above the limits, upper limit of normal.

All of these inflammatory markers being elevated despite receiving some therapy the patient got -- working erythromycin remain febrile and intubated and experienced deep venous thrombosis on date 10 that did not progress into the lungs but in the lower extremities. And continued on for many days requires oxygen and slow to recover both from the inflammatory markers and oxygenation.

Fever did decrease by hospital day 11 and a few low-grade fevers after.

But was extubated on day 21 and moved out of the ICU. Very prolonged course.

As you can see requiring significant amount of hospital support at the time.

As was described earlier on by the others there are several phases to the disease we have seen in adults and perhaps what we are seeing and children some of the presentations are fitting part of the paradigm where others are not.

At the beginning there's a viral response phase characterized by constitutional symptoms, influenza like, dry cough, fever, headache and can have some diarrhea.

During this time there significant amounts of our replications occurring in the lungs as well as other parts of the body.

What can be seen traditionally is lymphopenia and sometimes profound and some of the elevations of the biomarkers as well. The vast majority of individuals will recover at this point and not progress on what was described as a pulmonary phase or what often in severity described as moderate presentation of COVID.

Now you are starting to see significant shortness of breath, hypoxia at this point and significant elevation of the same inflammatory biomarkers. Sometimes going in to several thousand, ferritin, LDH and the like.

It's at this point where patients will tend to progress very rapidly if they will go on to the hyper inflammatory phase of this stage III where biomarkers go extremely high and illness severity requiring intubation and ICU stay. Often seeing a shock syndrome and ARDS and micro thrombotic events we described.

What we have come to understand as the pathogenesis especially with this micro thrombotic phase is worth looking at to some extent and detail. The first aspect that is unique to this virus as opposed to other influenza or syndrome similar to these viral syndromes we are seeing is SARS-CoV-2 binds to the ace to receptor found in the lungs and also in the hyper pharynx, kidney, the gut, testes and brain and cardiac tissue. Once binding it becomes internalized into the cell and as a result much of the ace 2 receptor we have seen in the disease becomes down modulated or down expressed on the surface of the cells.

As a result there is a decrease in conversion of antigens and 2 and one - seven. Be -- due to this decrease and increase in 2 we see an increase in reactive oxygen species and a decrease in vasodilators. This is a perfect -- perfect set up for thrombosis -- and combining that with the inflammatory process and platelet activation that set off by the complement cascade, we have a terrible mix of thrombosis inflammation and this complement deposition that leads to the really terrible presentation of micro thrombosis throughout the body.

In understanding the therapies that may be useful here, it's worth looking at what happens immunologically to set all of this off. We believe initially in the viral replication face the innate has a host of antiviral campaign made up of type I interferons. These are alpha and beta interferons that are released to target cells that are infected eliminate the infection. And macrophage is also responding which trigger some involvement as the infection progresses unabated. Help the T cell involvements and adaptive immune system. And from this if the virus hasn't been contained and clear, results in a large elaboration of cytokines at this point including Iowa one and TH 17 cells as well as now this stage interferon gamma. Type II interferon release which is much more destructive especially in the lungs and causes much more of the information we are seeing.

Throughout this time there is a large depletion and killer cells that have a significant expansion and plasma cells at this point.

Whether or not this expanse of inflammatory syndrome is because of an ineffective neutralizing antibody and innate immunity remains unclear or if it can happen in that setting. But without effective clearance nonetheless there is this large expansion again of these inflammatory cytokines that seem responsible for a lot of the pathological consequences.

As you can see on the right half of the figure there are a number of areas and cytokines that have been targeted over many years for various different diseases which we will review that are being repurposed and leveraged for COVID-19 and maybe useful not only for adult therapy but as you heard today from our earlier seekers have been used in this Kawasaki presentation and MIS presentation and children.

To start off with probably the one that has been out earliest in studies and use is receptors. The once you have seen in the news and in literature including

They have been used across the spectrum in many different diseases including multi- century calcium disease cancers rheumatoid arthritis as well as systemic onset -- and even for the treatment of psychical release syndrome, vasculitis was somewhat similar somewhat overlapped with Kawasaki disease as well. Some of the downsides that you can see includes hypersensitivity reaction, hyperlipidemia described as well as respiratory tract infections some upper and lower resulting and black box warnings. Also with hypersensitivity rashes described in peripheral tenia. These are all given either IV or subcutaneously and can have liver effects.

This is just an initial look at some of the first three studies that were done. Two of them out of China and one from New York. These were small single arm studies have looked at patient populations in the hospital that were given various modalities.

Most of these were given methylprednisolone. Either considered critical or serious as you can see across the board. Majority were male. The US population was closer to being balance between the 2 and the low study on the bottom was out of patients that had been transplanted an average of six years prior.

Doses vary depending on the study although most receive 400 milligrams dose either a single time or repeated doses depending on initial response. And for the first China study, 67 percent showed a decrease in 20 percent died and 80

percent remained inpatient at time of publication in the second study from P NAS that shown on the bottom format figures describing decreases in CRP, temperature and SI 02 requirements with increases in PaO2. Had -- none of the patients died and 90 percent 20 chart -- discharged. The New York study showed about the same percentage died as the first Chinese study.

54 percent were discharged.

The study of the US population was amongst many of the drugs that were studied by just pulling out the 14 patients that received

The next target that was looked at and you heard Anna Kendra has uses in diseases including periodic fever syndrome and systemic onset juvenile and macrophages activating system that are described in some of the children as well.

KD blocks both Anakinra blocks Anakinra is being given and different studies depending on the study either in COVID or another study with an inferior blockade and Q ID or subcutaneously. Some of the side effects include headache, injection reaction similar lipids and infection risks as well as cited PDF.

Some question that potentially could be cancer risk although that has not been fully borne out.

One study with Anakinra showing cytokines reductions that we are seeing here. This is across the top C-reactive protein, ferritin and troponin elevations that was described in children seeing some declines as well as D dimer and oxygenation changes in clinical scores.

The next blockade is can block a lot of the downstream inflammatory biomarkers include sink -- including it's an attractive vital photo to be used and half a dozen that are in trials. A previous good track record in cytokine storm as well as rheumatoid arthritis, etc. Some of the adverse effects scenes with this blockade include hypertension, hypersensitivity and alveolar protein gnosis syndrome for some of these markers but not all as well as some shortness of breath. It's given IV and as you can see here in particular this is showing marked reduction in levels of -- and significant across the board inflammatory marker reduction. And consequent improvements in the xenograft that have been studied in vitro, waiting to see how this looks in human studies.

The other large number of trials that are looking at inhibitors around the world.

It's been looked across the board including rheumatoid arthritis, Myla fibrosis, etc. There are some adverse effects described in the previous studies including infections and primarily endemic fungi, tuberculosis and herpes virus diseases as well as a black box warning for thrombotic processes. There was an interesting finding this year showing that there submit that have antiviral where it appears that several entry points for the virus internalizing into the cell and being released are blocked in an independent process.

In fact one single arm study comparing to Kaletra standard of care and sequential historical comparison showed remarkable improvements in ICU.

Also showing in another study out of Italy patients not only the remarkable reductions in cytokines in blue and reductions in nasopharyngeal and oral parental swabs of the virus during treatment.

For those of you that are participating in the act 2 trial. If you are in act one, act 2 will be adjunctive therapy. 100 sites will be participating. We look forward, that started rolling about 10 days ago and we look forward to seeing the outcome of that study.

Finally to Moto process been described for the children like slept so mad a chart from the database that showed patients were on some of these therapies at the time of acquiring COVID-19. You can see 877 patients at the time of the publication. In receiving some agents. You can see those that have been giving without six and PA only one or two percent actually died and that compared to patients receiving parenteral steroids were 11 percent, is not a controlled study but observational data.

And also we know that the drugs have been used for treating Kawasaki disease and studies may bear be useful. So the adverse effects including side of pina, infection. Some ants if Alexis described in question about cancers arising as well.

In conclusion what's impressive is this is the first large-scale testing of anti-inflammatory for a deadly viral disease. A caution for off label use outside studies but recognize limitations of being able to participate in studies. They do appear to reduce the fever and cytokine store. At the time to recover and mortality date are lacking so looking for randomized controlled trials to look at this. And unclear impact of virus control also secondary infections, thrombosis and site of pina in the short term use compared to what we've seen more long-term use.

There are more classes that can fit in 15 minutes. Many more trials underway. We don't have time to discuss them.

I encourage you to look further into these.

Steroids have not been recommended by IDSA or by the NIH unless forced COVID-19. I recognize Kawasaki syndrome may have other recommendations but this is for adults.

An tremendous thanks to so many people who have been a part of the studies we participated in and helping putting together the slides and I will stop there.

>> IBAD KHAN: Thank you so much Dr. Marconi. I've been informed we have the honor of being joint by the Assistant Sec. for health of the US Department of Health and Human Services. Welcome, would you like to share some brief remarks at this time?

Trying again to see if he is able to unmute his phone. While we wait for him to join we will continue with our webinar. Presenters thank you for providing the audience with such a wealth of information on this evolving pandemic. We will go into our Q&A session. Please remember you may submit questions through the webinar by clicking the Q&A button at the bottom of your screen and typing in your question.

Our first question is can the presenters discuss similarities and differences in the epidemiology versus Kawasaki disease versus any adult -- [Inaudible].

>> DR. LEVIN: I think the Kawasaki disease that pediatricians have been familiar with for the last 30 or so years does have some distinct differences from the Kawasaki disease that appears to have had an upsurge in the numbers of cases associated with the COVID-19 pandemic. Perhaps the most striking feature is Kawasaki disease prior to COVID was a disease of young children. On the comparison that we have been comparing the patient's with post COVID Kawasaki disease as they tend to be older. I tried to show in my talk laboratory differences in which certainly for the shock patients there was a much higher level of many inflammatory markers particularly -- [Inaudible] Lower hemoglobin's and in particular higher proportion of patients with indicators of myocardial injuries.

I think while COVID and we are assuming the upsurge of Kawasaki cases that we are seeing is a response to COVID, COVID must be triggering an immunological response which has enough similarities to Kawasaki disease as we knew before COVID to results in the rash, conjunctival infection, medical changes in the pathophysiologic he tends to be different as indicated by the age of the children and the spectrum of laboratory results.

We have also had a striking understanding of the ethnic propensity to Kawasaki disease so patients from China and Japan and Asia generally have increased incidence of Kawasaki disease as we knew it before COVID.

Whereas COVID so far from the information we have had from Japan and my colleague Jane Burns have been in contact with Japanese colleagues doesn't appear to have been an upsurge of Kawasaki disease in Japan. It looks like COVID is triggering a response that has -- also important differences. I will stop there and see if Dr. Schneider has some comments on the same question.

>> DR. SCHNEIDER: There are a couple other general differences that this multisystem inflammatory system presents

with compared to Kawasaki. We generally think of Kawasaki disease and as a pediatric intensivist I think of it as a group of patients I don't get to see that frequently. Where we only think of about five percent of typical Kawasaki disease develop some type of shock syndrome with the end in our intensive care unit.

What we are seeing with this newer syndrome that seems related to COVID at least in our institution the majority of children are ending up requiring critical care where they present in shock, the fluid resuscitation, either tropes or laser pressers. To meet that is a clear characteristic difference. And shockingly where we think of the classic teachings about 23 to 25 percent of classic Kawasaki children untreated would lead to coronary anomalies and treated with the current regimen of immunoglobulins down 3 to 4 percent.

But in our current cohort of children we see close to half have had coronary abnormalities and at an early stage of the illness. That speaks to the inflamed state that they are in and the vascular apathy that is developing with the syndrome.

I think those are two really important characteristics. And in terms of how the children are presenting, the typical presentation we are noticing is the fever which clearly overrides and goes along with Kawasaki here but almost all of our children are presenting with abdominal symptoms. We know it can be part of the Kawasaki spectrum, however, it's almost universal in this group of patients we have seen. That would be some of the other characteristics I would like to highlight.

I would leave it to one of my other colleagues.

>> If I may add, clinically more patients with MIS -- as Dr. Schneider said there are G.I. symptoms specifically diarrhea and vomiting, particularly diarrhea which is uncommon in an addition to the other features.

One.
>> IBAD KHAN: Thank you everyone for your insight on the discussion. For we move on to our next question I want to try and see if the Adm. is on, the assistant secretary of health of the US Department of Health and Human Services. Are you able to unmute yourself?

We will try again in a few moments. Her next question is regarding testing. Can our presenters please discuss what kind of testing is recommended for a child or adult who presents with concerns for the syndrome?

>> DR. SCHNEIDER: I will take the first attempt. I think the key to this syndrome is a hyperactive inflammatory response. Getting evidence of inflammation is key to differentiating this from other syndromes.

When children show up with signs of fever and then some of the other clinical findings whether abdominal pain, vomiting or diarrhea or rash, oral or I changes those kids generally should be getting a full spectrum of complete blood count, complete metabolic panel, a CRP. We like to look at evidence of myocardial involvements, peptide levels and troponins it also other inflammatory markers as ferritin, D dimer, full coagulation panel, lactic hydraulic unit and evidence of current or previous SARS-CoV-2 so we get a PCR and now the capacity to do serology testing for antibodies which you should get right away.

The other important aspect is not to forget that children with bacterial sepsis or other forms of sepsis are out there and may be missed if we are not being vigilant.

Getting blood cultures and panels are important. A screening ECG is helpful and based on some results can determine the next phase of management. I will ask another colleague to see if they would like to add on.

>> That I think is a great summary and something many institutions are doing with some of the card manifestations you mentioned getting an echocardiogram and any kids they suspect the syndrome. If they see abnormalities on that they can follow that up during the hospitalization or beyond. Or at the very least it can serve as a baseline. For those with a normal echocardiogram from there many places are trending and getting follow-ups as indicated for clinical

deterioration or changes in the biomarkers.

>> DR. MARCONI: For adults, a slightly overlapping syndromes get in the same test in terms of progress Otori -- CRP source and what prompts us is cardiovascular instability or size of troponin elevation, EKG changes that prompt us for echocardiogram at that point.

>> IBAD KHAN: Thank you for that. Another question we have is
do children with underlying medical conditions have a high risk for the syndrome?

C5 based on what we have --
>> DR. SCHNEIDER: Based on what we have seen the cohort there do not seem to be any definitive underlying conditions that predispose children. I think as we collaborate and pull out data we may be able to find some other trends as we know in the adult acute COVID having obesity, hypertension, diabetes. These are things we know are classifying adults at higher risk. May be able to identify some other conditions that expose children.

>> IBAD KHAN: Thank you for that. Another question we had is for those that are PCR positive and IDD positive how do we distinguish between COVID-19 and MIS?

>> DR. BELAY: That is obviously very tricky. But one thing that could be helpful is among MIS patients there has been a delay of about 2 to 6 weeks between initial COVID-19 infection and the onset of MIS which is been reported in many patients. That could potentially help when there is very clear information. In patients with milder or asymptomatic antecedent COVID-19 infection distinguishing the acute infection for MIS it can be tricky.

Although, as discussed previously with the cytokine storm and the markers can be very suggestive of MIS and that could probably help favor the diagnosis of MIS as opposed to acute COVID-19 infection. Before I agree. It's been a difficult situation to distinguish.
>> DR. LEVIN: There is evidence of the virus certainly when we have patients that are both positive for virus on PCR and have the inflammatory syndrome it raises the concern about immunosuppression be harmful and maybe makes was a bit more cautious on thinking about using steroids. Obviously immunoglobulin we are comfortable with in using with a PCR positive patient.

I really don't know how to answer the question because the PCR positive patients are probably resembling closer to the adult patients who have COVID and develop an inflammatory syndrome and it would be interesting to hear from the physicians treating adults is the culmination of the virus and development of inflammatory features is what they are seeing in adults?

>> DR. MARCONI: The question is whether or not having a positive swab and the biomarkers being elevated at the same time is concurrent with the inflammatory syndrome?
>> DR. LEVIN: I think what I was raising is when we see children that are PCR positive for the virus and also have the inflammatory features, it seems more similar to what adults are seeing where patients evolve from being virally infected to developing an inflammatory problem with.

Whereas most of the children with the inflammatory syndrome don't have the acute viral type illness and come in with the inflammation being the only presenting feature.

>> DR. MARCONI: Exactly right. None of the patients we have seen and largely what's been described in the literature have had SARS-CoV-2 negative. Maybe a few exceptions. But severe disease if you see it in the bloodstream as well which is not commonly done in the clinical setting but in the research settings. If you are going to see SARS-CoV-2 presence, PCR positive in the blood usually with severe critical disease.

>> IBAD KHAN: Thank you for that. Before we move on let me do one more check and see if we have the Adm., assistant secretary for health on the line. You'll Adm., are you available for some brief remarks?

We will keep moving. Our next question is providers are seeing various presentations and younger kids more like

Kawasaki versus older kids like abdominal pain or headache or myocarditis. Can you comment about what kind of presentation you are seeing in young adults?

>> DR. SCHNEIDER: Just from our experience here, in general when we notice in the acute COVID infections, the presentation is varied. There is no obvious pattern. Related to MIS I think the pattern continues that it is slightly varied. What we have seen and some of the older kids I have 18 in the unit and it's more of a general fever, abdominal pain and chills and myalgias with the presentations.

I think we seen those in younger kids. It's in our experience it's not been an obvious pattern. Clearly as we gain more knowledge and experience and numbers we may be able to sort out the patterns. I don't know if Dr. Marconi has any other experience?

>> DR. MORRIS: Chemical to the next question? Dr. Marconi had to leave.
>> IBAD KHAN: Another question that came and is given the progression for shock and so many of the patients, went should a provider send a child to the ER? Similarly should children that are typically sent home from the ER with some be admitted and observed?

>> DR. SCHNEIDER: I will try to tackle this in a simplified fashion. In general we know that children who have classic Kawasaki disease need inpatient therapy and aspirin and we note this helps protect the coronaries. At the bare minimum. Depends on severity.

And we know that with this current syndrome there is a very high incidence of cardiovascular involvement early on in the course of the illness. I would think that any child who is at home who has a fever, abdominal pain or persistent fever, abdominal pain or abdominal symptoms as well as rash or injected by this should be seen by a pediatrician right away. I think as a pediatrician that evaluates a child if any signs or symptoms of Kawasaki disease the child should be referred for inpatient evaluation and the cardiologist Lisa see the child.

The child is looking unwell, any evidence of respiratory illness or stress or evidence of tachycardia in the office I think the child deserves further evaluation. We are seeing kids that do not fit classic Kawasaki criteria in terms of outward appearance related to the rash, the eyes and hands, etc.

I think we have to have a threshold for the evaluation because finding remarkable amount of kids with myocardial and coronary them are out -- abnormalities early on.

>> DR. LEVIN: I get maybe add to that from some of the experience in the UK. We had an impression with the earlier patients when we first recognized the syndrome that patients were arriving critically ill from the moment they arrived in hospital. What of the reasons for this may have been because of lockdown and fear of coming to hospitals. The public health message in the UK was that patients should try and stay at home and not attend hospital because the hospitals were under pressure.

Children were remaining at home with fevers for longer than they might have normally. And arriving in a very seriously ill state. Now that we become more familiar with the problem there's been a clear public health message that of children's have persistent fever they need to be evaluated in the -- laboratory tests, the white count will very quickly point to a group of patients that have elevated inflammatory markers and I think we would very much a great that if you have got inflammatory markers that are elevated even if there are no features of typical Kawasaki disease that warrants the child being investigated and bacterial infection excluded and watched very closely. Generally as an inpatient.

Certainly if there is any suggestion that the CRP is rising and there is lymphopenia the ferritin's are rising and certainly any markers suggestive of myocardial involvement with the troponins going up or PNP going up first patients deftly need inpatient assessment and careful evaluation.

>> I agree with everything that was said. Well said.
>> IBAD KHAN: Next question if a patient is admitted for the syndrome and is PCR negative do they need enhanced

precautions Mexican family members visit?

>> DR. BELAY: We do not know a lot about the dynamics. Even the PCR positive whether or not it is the shedding of the virus may not be told of the time. In the manifestations with PCR are negative I would think that maybe positive with some precautions but would like to know what others think from the panel.

>> DR. SCHNEIDER: We have noticed that during this era the PCR testing is not always 100 percent accurate. We have an important false negative rate.

All children with this syndrome we are testing at least twice 12 hours apart. We presume when the children are admitted to the hospital they are infectious I would treat them as AP UI until the second PCR becomes negative.

We have the luxury that every room is singular and every patient is treated the same grade we allow one family member to visit all patients in the intensive care unit but any patient that is PCR positive the family member is not allowed to leave the room other than using a specified restroom.

We do to tests it's hard to know if they are infectious even though we think noninfectious entity we are not quite sure yet.

>> IBAD KHAN: Thank you. Our next question is asking our hospitalizations a certainty in all cases?

>> DR. BELAY: We have heard a lot about the illness from the presentations and I think it's possible that there may be a spectrum and we are just catching the most severe cases that end up in the ICU. That has happened in Kawasaki disease. Severe forms of the disease and also a milder recitation of Kawasaki disease. It's possible that can also happen with a MIS.

To meet this is a reason we need to conduct more data to better understand the clinical phenotype of the illness. As it currently stands if not all of these cases are hospitalized and most of them end up in the ICU.

>> DR. LEVIN: I agree completely. We are certainly seeing children with mild illness, with just fever, no other features or organ failure or needing to go to intensive care but surprising elevation for C-reactive protein and other markers for which there is no other explanation.

While this patients don't look so ill when you see them, what we don't know is the direction of travel.

If we don't observe it or undertake echoes or follow them up as we would for a Kawasaki, will they progress to the more severe phenotype? Until we know more about it in the UK we are hospitalizing them, doing the complete investigations including echocardiography and ECG and only thinking of how management if we are sure that the CRP and the other inflammatory markers are progressively worsening on a daily basis.

>> IBAD KHAN: Thank you for that. Can we talk about the information or knowledge we have about the chances of death from the syndrome if the child receives appropriate care?

>> DR. BELAY: There have been deaths that have been reported among patients for MIS. Fortunately it appears to be rare and we are still understanding the disease. In one series I reviewed from over 80 suspected Casey's cases there have been deaths with MIS. As I say, fortunately, it is rare. But having said that the illness has most children ending up in the ICU. Anyone who would like to add to that?

>> DR. LEVIN: I think the experience from the UK is similar. So far we know of three deaths. One of them in a child with typical Kawasaki disease and thrombosis and aneurysm rupture. And others. But we have had very severe illness with patients needing -- oxygenation in a few cases. It can be very severe but the mortality rate seems similar to your experience in the states.

>> IBAD KHAN: Thank you so much for the information. We have time for one last question. The question states if

this syndrome can follow the mildest or asymptomatic of acute illness what are the implications of this syndrome for vaccine development testing?

>> DR. LEVIN: It is just speculation, but the timing of the illness does seem that it coincides with when acquired immunity would be developing. There is quite an extensive literature from go virus will are the same mechanism where antibodies enhance replication and is less likely for the syndrome we are seeing because PCR is negative. But in antibodies had macrophage activation and similar inflammatory process in primate and human tissue.

I think there's a concern we are seeing a dis-regulated immune response and for that reason I think understanding if this is a harmful immune response other than protective response we want from a vaccine I think it is an important area for research that we define exactly what is the antibody and T-cell recognition and is it different and what is underlying, genetically determined? And I think that information would be very important in ensuring safe introduction of vaccines. But.
>> DR. BELAY: I agree. The idea that we could understand the antiaging or the group of proteins that are triggering if we can identify them with a vaccine process that could help the problem.

In addition, and carefully monitoring and collection of data during the trials.

>> IBAD KHAN: Thank you very much. Before we conclude our call would Trinity Morris like to make any comments?

>> DR. MORRIS: Thank you, commanders. I would like to apologize. We were trying to get our assistant secretary of health on we are having difficulties with being able to add him on the speaker line. I apologize to him and his office for that. We were working behind the scenes and could not get it to work.

We wanted to thank all the speakers for their time today and just comment that CDC is working with other federal partners including NIH and the office of human health and collaboration describe the syndrome and to work towards understanding what care and treatment is most successful. The bar graph we hope to have future calls to share what we have learned and want to thank our speakers for spending all this time this afternoon with us.

>> IBAD KHAN: Thank you. A close caption video will be on COCA webpage at emergency be sure to visit the page for other calls and updates about COVID-19. In addition to our webpage COCA calls will be sent via email so remember to subscribe to receive the notifications by going to the stay connected to the latest news from COCA like and follow us on facebook@facebook.com/ CDC clinician outreach and community -- medication activity. Thanks for joining us on the call and have a great day.