To: CAHAN San Diego Participants
Date: February 14, 2019
From: Epidemiology Program, Public Health Services

**Kawasaki Disease Increased in San Diego**

This health advisory informs healthcare professionals about a recent increase in diagnosed cases of Kawasaki disease (KD) in the San Diego County region. It also contains recommendations and resources to help providers promptly diagnose and initiate hospital care for children with KD.

**Key Points:**

- Since January 1, 2019, 16 San Diego County residents have been diagnosed with KD at Rady Children's Hospital-San Diego (RCHSD), twice the expected number based on prior winters.
- KD is a seasonal disease that occurs in clusters, with March as the typical peak month for symptom onset in Southern California. A second, smaller peak occurs in mid-summer.
- KD should be considered in any pediatric patient presenting with sustained fever and any combination of rash, non-exudative conjunctival injection, red lips and pharynx, cervical adenitis, and extremity edema or erythema of the palms or soles.
- Although 85% of patients with KD are younger than 5 years, KD can present at older ages. Children of Asian/Pacific Island descent have the highest incidence.
- KD can initially be misdiagnosed as scarlet fever, measles, mumps, bacterial lymphadenitis, and adenovirus. Consider the possibility of measles especially if recent international travel or contact with an international traveler. Laboratory studies detailed in this advisory are helpful in confirming the KD diagnosis and excluding alternative diagnoses.
- Treatment of KD with high-dose IVIG and moderate dose aspirin should be initiated as soon as the clinical diagnosis can be confidently made. An echocardiogram by a pediatric sonographer should be performed within 24 hours of initiation of treatment.
- RCHSD has a dedicated KD specialist on call 24/7 to assist healthcare providers in diagnosing and managing KD (page via the RCHSD operator at 858-576-1700, ext. 0).

**Situation**

Since January 1, 2019, 16 San Diego County residents have been diagnosed with KD at RCHSD, at least twice the number that would be expected based on prior years. RCHSD cares for 80-100 new KD patients each year from San Diego and surrounding counties with a dedicated inpatient service and weekly clinic. A recent study published by the RCHSD team demonstrates that KD is a seasonal disease that occurs in clusters, with March the peak of the annual epidemic in Southern California. There is a

second, smaller peak in mid-summer. Sporadic cases occur all year long. The seasonality of KD is correlated with specific climatic conditions which are predicted to persist in San Diego County from mid-February into March. Clinicians should have a high index of suspicion for KD in any child presenting with fever and any combination of rash, bilateral conjunctival injection with sparing of the limbus and without exudate, red lips and pharynx, cervical adenitis, and extremity edema.

**Background**

KD is an acute vasculitis of childhood that can lead to coronary artery aneurysms in up to 25% of untreated cases. It is a self-limited febrile illness of unknown cause that predominantly affects children less than five years of age. KD is thought to result from genetic susceptibility and environmental trigger(s).

KD has not been a reportable disease in California, since June 2011, so the current incidence is unknown. Most local KD cases are cared for at RCHSD, so local epidemiology may be inferred from their cases. The RCHSD KD team recently published their experience with 788 KD patients from 2006 to 2015; over this period, the average incidence of KD in children less than five years old in San Diego County was 25 per 100,000 children, with the greatest incidence (50 per 100,000) for Asian/Pacific Islanders. Compared with other race/ethnicities, Asian/Pacific Islander patients with KD were younger, were diagnosed earlier in the course of their fever, had higher levels of inflammatory markers, and were more likely to develop aneurysms.

The American Heart Association (AHA) has established criteria for the diagnosis of complete and incomplete KD. The diagnosis of KD may be made in the presence of fever and four of the five classic criteria (exanthem, conjunctival injection, oropharyngeal changes, peripheral extremity changes, and cervical lymphadenopathy) or in the presence of fewer criteria with a coronary artery Z-score (internal diameter of the left anterior descending or right coronary arteries expressed as standard deviation units from the mean normalized for body surface area) greater than or equal to 2.5.

KD can mimic other rash/fever syndromes of children, and cases may be missed or misdiagnosed. Not all patients manifest the classic four of five criteria (aka “incomplete” KD), and clinical presentation may be more subtle in infants younger than 6 months of age. Fever is essentially invariant, and no one particular pattern is characteristic. The fever is often greater than >39° C (102.2° F) and accompanied by extreme irritability.

Consideration of each of the classic clinical signs follows.

> ***Exanthem:*** The exanthem of KD can take many different forms and is often polymorphous in the same patient. In its maculopapular presentation on the trunk and extremities, it can be easily confused with a drug reaction because many of these patients have been treated with antibiotics for erroneous diagnoses. Another common form of the rash is raised papules coalescing into plaques. This may be associated with target-like lesions with central clearing and can be confused with erythema multiforme. A pure erythroderma with no palpable component as in staphylococcal toxin–mediated disease is not associated with KD. Similarly, a confluent, fine maculopapular (“sandpaper”) rash extending onto the face as in scarlet fever is unlikely and should prompt consideration of scarlet fever. A fine micropustular eruption on the buttocks, thighs, and extensor surfaces can sometimes be seen and is perhaps pathognomonic of KD. Accentuation of the rash

with confluent erythema in the groin that peels during the acute, febrile phase is seen in up to 50% of patients.

***Conjunctival Injection:*** Prominent dilated vessels within the bulbar conjunctivae without edema or infiltration of inflammatory cells on conjunctival biopsy is the hallmark of KD. The lack of edema in the conjunctiva allows the limbus to be easily seen, giving the appearance of a white halo around the iris. The lack of edema and exudate are important features in distinguishing KD from other acute infections associated with fever and conjunctivitis, most notably adenovirus, enterovirus, and measles infection. Presence of exudative conjunctivitis should prompt search for a different diagnosis.

***Oropharyngeal Changes:*** Erythema of the lips with fissuring and erythema of the posterior pharynx are the most common mucocutaneous findings in acute KD. Sloughing of the filiform papillae of the tongue leaving a glossy red surface punctuated by the fungiform papillae creates the classic "strawberry tongue" appearance associated with both KD and streptococcal and staphylococcal toxin-mediated diseases. The presence of a true strawberry tongue essentially eliminates common viral infections from the differential diagnosis of a patient because these agents are not associated with this pattern of injury. The presence of exudative pharyngitis or discrete intraoral lesions should prompt search for an alternative diagnosis.

***Peripheral Extremity Changes:*** Edema of the dorsa of the hands and feet with or without erythema of the palms and soles often develops after several days of fever. The fusiform swelling of the digits accompanied by swelling and purple discoloration of the proximal interphalangeal joints is a classic finding. The painful arthritis may limit the child's use of their hands, and the swelling of the feet often discourages ambulation. The vasodilation of the palms and soles is distinct from the exanthem on the rest of body and is a diffuse, blanching erythema that may be fluctuating.

***Cervical Lymphadenopathy:*** This clinical sign is the least reliable feature and is seen in only 30% to 50% of patients. It is most commonly unilateral and inflammation in the sternocleidomastoid muscle often limits rotation of the head. The cervical mass should be at least 1.5 cm in diameter to qualify for this criterion. Studies have shown that correct diagnosis of KD is often delayed in patients who initially present with the cervical mass and fever (node-first presentation of KD) and are diagnosed with bacterial lymphadenitis. The appearance of the rash can further delay diagnosis when it is misinterpreted as a drug eruption, prompting a change in antibiotics. In distinguishing node-first KD from bacterial lymphadenitis, helpful features include a higher erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level, absolute band count, and imaging studies by ultrasound or computed tomography that demonstrate clusters of nodes (rather than one dominant node) and retropharyngeal edema.

There is no single laboratory test that confirms the diagnosis of KD. The laboratory evaluation of patients with suspected KD should include markers of inflammation and tests to exclude other competing diagnoses. The acute phase is associated with an elevated white blood cell count with neutrophil predominance and elevated acute-phase reactants including CRP and ESR. The platelet count usually rises during the second week after illness onset, whereas the acute-phase reactants normalize over two to four weeks after treatment.

**Recommendations for Providers**

- Consider KD in pediatric patients with sustained fever and any combination of rash, non-exudative conjunctival injection, red lips and pharynx, cervical adenitis, and extremity edema.
    - A flow diagram for the evaluation of incomplete KD is provided at the end of this advisory.

- Order appropriate laboratory studies in suspected cases or refer to RCHSD urgent care or emergency department for evaluation.
    - Studies should include: complete blood count (CBC) with manual differential, ESR, CRP, alanine aminotransferase (ALT), and gamma-glutamyl transferase (GGT).
    - Blood, throat, and urine cultures and viral polymerase chain reaction (PCR) panels should be ordered as appropriate to exclude other potential diagnoses. A positive PCR result for any virus does not rule out the diagnosis of KD as children may shed virus for weeks after an acute infection.
    - Typical findings are a neutrophil predominance with immature (band) forms, normocytic and normochromic anemia, normal to elevated platelet count, high ESR, and CRP.
    - ALT and GGT usually track together and can both be normal, or both elevated.
    - Urine may show an elevated white cell count with negative nitrites and leukocyte esterase consistent with sterile pyuria.

- Consider the possibility of measles, especially if recent international travel or contact with an international traveler. If measles or mumps is suspected in the differential diagnosis of a patient presenting with symptoms consistent with KD, contact the County Immunization Program **immediately,** during office hours by calling (866) 358-2966 (press 5 at the prompt) Monday-Friday 8AM-5PM and (858) 565-5255 after hours and on weekends. PCR testing for measles and mumps can be arranged in the San Diego Public Health Laboratory.

- Initiate treatment as soon as the clinical diagnosis of KD can be confidently made.
    - Patients must be hospitalized to receive high-dose IVIG and moderate dose aspirin.
    - An echocardiogram by a pediatric sonographer skilled in visualizing the coronary arteries should be performed within 24 hours of initiation of treatment.

- Consider consultation with the KD Team at RCHSD for diagnostic or management assistance or to discuss admission of a suspected case. The KD specialist is available 24/7 by paging the RCHSD operator at 858-576-1700, ext. 0.

**References**


- Centers for Disease Control and Prevention Kawasaki Disease website
- American Heart Association Clinical Statement and Guidelines: Diagnosis, Treatment, and Management of Kawasaki Disease
- RHCSD/UCSD Kawasaki Disease Research Center website
- Kawasaki Disease Foundation website

Thank you for your participation.

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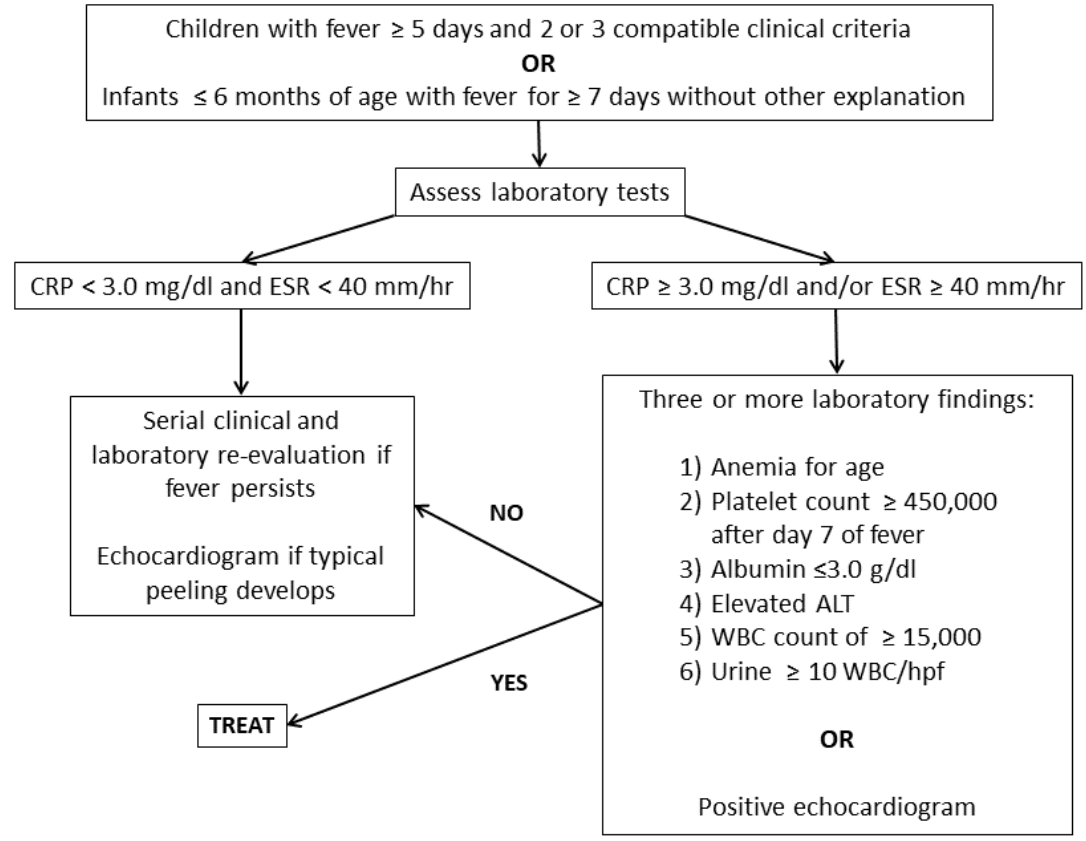
**Figure. Evaluation of Suspected Incomplete Kawasaki Disease.**




Adapted from McCrindle, et al 2017.

Notes: This algorithm represents the informed opinion of the expert AHA committee. Consultation with an expert should be sought any time assistance is needed. Clinical findings of Kawasaki disease are listed in the background section of this health advisory. Characteristics suggesting that another diagnosis should be considered include exudative conjunctivitis, exudative pharyngitis, ulcerative intraoral lesions, bullous or vesicular rash, generalized adenopathy, or splenomegaly. Infants ≤6 months of age are the most likely to develop prolonged fever without other clinical criteria for Kawasaki disease; these infants are at particularly high risk of developing coronary artery abnormalities. Echocardiography is considered positive for purposes of this algorithm if any of 3 conditions are met: *Z* score of left anterior descending coronary artery or right coronary artery ≥2.5; coronary artery aneurysm is observed; or ≥3 other suggestive features exist, including decreased left ventricular function, mitral regurgitation, pericardial effusion, or *Z* scores in left anterior descending coronary artery or right coronary artery of 2 to 2.5.