BETTER MANAGE

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Bronchiolitis/Kawasaki/clinical scenarios

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BRONCHIOLITIS- AAP 2014 GUIDELINES

- **Clinicians should not administer albuterol (or salbutamol)** to infants and children with a diagnosis of bronchiolitis (Evidence Quality: B; Recommendation Strength: Strong Recommendation).

- **Clinicians should not administer epinephrine to infants and children** with a diagnosis of bronchiolitis (Evidence Quality: B; Recommendation Strength: Strong Recommendation).

- Nebulized hypertonic saline should not be administered to infants with a diagnosis of bronchiolitis in the emergency department (Evidence Quality: B; Recommendation Strength: Moderate Recommendation).
- **Clinicians may administer nebulized hypertonic saline to infants and children hospitalized for bronchiolitis** (Evidence Quality: B; Recommendation Strength: Weak Recommendation [based on randomized controlled trials with inconsistent findings]).

- Clinicians should not administer systemic corticosteroids to infants with a diagnosis of bronchiolitis in any setting (Evidence Quality: A; Recommendation Strength: Strong Recommendation).

- **Clinicians may choose not to administer supplemental oxygen if the oxyhemoglobin saturation exceeds 90% in infants** and children with a diagnosis of bronchiolitis (Evidence Quality: D; Recommendation Strength: Weak Recommendation [based on low level evidence and reasoning from first principles]).

- Clinicians may choose not to use continuous pulse oximetry for infants and children with a diagnosis of bronchiolitis (Evidence Quality: D; Recommendation Strength: Weak Recommendation [based on lowlevel evidence and reasoning from first principles]).

- **Clinicians should not use chest physiotherapy for infants** and children with a diagnosis of bronchiolitis (Evidence Quality: B; Recommendation Strength: Moderate Recommendation).

- **Clinicians should not administer antibacterial medications to infants** and children with a diagnosis of bronchiolitis unless there is a concomitant bacterial infection,or a strong suspicion of one (Evidence Quality: B; Recommendation Strength: Strong Recommendation).

- **Clinicians should administer nasogastric or intravenous fluids** for infants with a diagnosis of bronchiolitis who cannot maintain hydration orally (Evidence Quality: X; Recommendation Strength: Strong Recommendation).

PREVENTION

- **Clinicians should not administer palivizumab to otherwise healthy infants** with a gestational age of 29 weeks, 0 days or greater (Evidence Quality: B; Recommendation Strength: Strong Recommendation).

- **Clinicians should administer palivizumab during the first year of life to infants with hemodynamically significant heart disease or chronic lung disease** of prematurity defined as preterm infants <32 weeks 0 days' gestation who require >21% oxygen for at least the first 28 days of life (Evidence Quality: B; Recommendation Strength: Moderate Recommendation).

- Clinicians should administer a maximum 5 monthly doses (15 mg/kg/dose) of palivizumab during the respiratory syncytial virus season to infants who qualify for palivizumab in the first year of life (Evidence Quality:B; Recommendation Strength: Moderate Recommendation).

- **All people should disinfect hands before and after direct contact with patients**, after contact with inanimate objects in the direct vicinity of the patient, and after removing gloves (Evidence Quality: B; Recommendation Strength: Strong Recommendation).

- **All people should use alcohol based rubs for hand decontamination** when caring for children with bronchiolitis. When alcohol based rubs are not available, individuals should wash their hands with soap and water (Evidence Quality: B; Recommendation Strength: Strong Recommendation).

- **Clinicians should inquire about the exposure of the infant or child to tobacco smoke** when assessing infants and children for bronchiolitis (Evidence Quality: C; Recommendation Strength: Moderate Recommendation).
- Clinicians should counsel caregivers about exposing the infant or child to environmental tobacco smoke and smoking cessation when assessing a child for bronchiolitis (Evidence Quality: B; Recommendation Strength: Strong)..
- **Clinicians should encourage exclusive breastfeeding for at least 6 months to decrease the morbidity of respiratory infections**. (Evidence Quality: B; Recommendation Strength: Moderate Recommendation).

- Clinicians and nurses should educate personnel and family members on evidence-based diagnosis, treatment, and prevention in bronchiolitis. (Evidence Quality: C; observationalstudies; Recommendation Strength: Moderate Recommendation

REFERENCE: www.pediatrics.org/cgi/doi/10.1542/peds.2014-2742 doi:10.1542/peds.2014-2742

KAWASAKI'S DISEASE

Guidelines for medical treatment of acute Kawasaki disease: Report of the Research Committee of the Japanese Society of Pediatric Cardiology and Cardiac Surgery (2012 revised version)

Treatment of acute KD

- The principal objective in treating acute KD is minimizing the risk of developing CAL(coronary artery lesion). In practice, this means quickly suppressing the acute-phase inflammatory reaction caused by KD. **Except in cases of very mild KD, IVIG should be started before illness day 7.** Histological studies have shown that arteritis typically develops by 8 or 9 days after KD onset. Therefore, treatment should begin before this point, to suppress arteritis and hasten resolution of fever and normalization of inflammation markers.

- In patients with incomplete KD, IVIG should also be begun as soon as possible after a diagnosis of KD, especially if fever is present. In approximately 80% of cases, fever should be lowered to ≤37.5°C within 48 h of starting IVIG. In 40% of IVIG resistant patients, fever can be reduced to ≤37.5°C with additional IVIG of 1 g/kg**. Persistent fever after 48 h of starting IVIG should be regarded as evidence of IVIG-resistant KD.** Prevention of CAA in such patients may largely depend on the selection of subsequent treatment.

- In addition to CAL, other cardiovascular complications may develop in patients with acute KD, including myocarditis, pericardial effusion, valvular regurgitation, and, rarely, arrhythmia. Specific treatment may be required for these sequelae, as well as for cardiac dysfunction or heart failure.

- Furthermore, other symptom-specific treatment may be required for systemic complications such as edema, hypoalbuminemia, electrolyte imbalances (i.e. hyponatremia), paralytic ileus, hepatic dysfunction, cholecystitis, impaired consciousness, convulsions, anemia, diarrhea, vomiting, and dehydration. Particularly during highdose IVIG infusion, care must be taken to prevent volume overload so as to protect the patient from complications such as heart failure.

- There is currently no universally accepted classification system to evaluate KD severity and need for IVIG use, although many such scoring systems have been proposed. Initial attempts were made by Asai and Kusakawa,5 which were followed by the Iwasa score6 and Harada score.7

- **More recently, predictive models designed to evaluate the possibility of IVIG resistance were proposed, including the Kobayashi score,8 Egami score,9 and Sano score**.10 In general, such predictive models consider factors such as age, gender, days of illness, white blood cell count, %neutrophils, hematocrit, platelet count, C-reactive protein (CRP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, sodium, and albumin.
- **Recently, a randomized controlled trial found that IVIG plus steroid as initial therapy for patients predicted to be at high risk for IVIG resistance improved clinical and coronary arterial outcomes.**11–13 The effectiveness of such predictive models, however, has not been confirmed in large-scale prospective cohort studies or meta-analyses, and controversy remains as to whether initial therapy with IVIG plus steroids is the optimal treatment.

Choice of treatment for IVIG-resistant patients

- Several second-line treatment options are available if fever persists or has reappeared at 24 h after first-line treatment. The efficacy of these second-line treatments for resistance to first-line treatment is currently being investigated by researchers in manycountries, but evidence remains limited due to the lack of randomized controlled trials.

- **Options for second-line treatment include additional IVIG, i.v. methylprednisolone pulse (IVMP), prednisolone (PSL), IFX, ulinastatin (UTI), CsA, MTX, and plasma exchange (PE)**. The decision to use any of these treatments requires careful consideration of patient characteristics.

- At present, the most commonly used second-line treatment is additional IVIG,1 which is sometimes given in combination with other medications. As for steroids, a retrospective study noted a high incidence of giant aneurysms.14 That small uncontrolled case study reported that several patients had received steroids before rupture of coronary arteries, which suggests that physicians should carefully consider the decision to use steroids for patients with KD if CAA are already present.
- When steroids, biologics, or immunosuppressants are given to infants, there is also a risk of long-term sideeffects, and questions remain regarding the general safety of such medications. Thus, a careful risk/benefit evaluation should be done to consider the likelihood of such adverse effects versus the possibility of CAA formation.

Algorithm for selecting optimal treatment

- **To decrease the risks of first-line IVIG resistance and CAA, it seems reasonable to consider risk stratification using predictive models and to select more-aggressive initial treatment for patients at high risk of IVIG resistance. Such patients should be treated with 2 g/kg of IVIG in combination with either 2 mg/kg per day PSL or 30 mg/kg per day IVMP**.

- If the patients fail to respond to these treatments, a third-line treatment will be upgraded to a second-line treatment. Because few studies have assessed the efficacy of medications other than IVIG retreatment, it is impossible at this time to assign an objective order of

these treatment options. The present guidelines, however, offer evidence levels and grades to assist physicians in selecting appropriate alternatives.

- In recent years, various scoring systems have been developed to evaluate the likelihood of IVIG resistance at the time of diagnosis. Representative scoring systems are listed in Table 3.8–10 If such scores suggest that patients are at high risk of IVIG resistance,more aggressive primary therapy in combination with the usual first-line treatment of 2 g/kg IVIG plus aspirin can be considered. In the RAISE study, Kobayashi *et al*. found that IVIG plus PSL, started at 2 mg/kg per day and halved every 5 days, was effective in preventing CAL formation and initial treatment failure.8,13 In addition, Egami *et al*. and Ogata *et al*. as well as Sano *et al*. and Okada *et al*. reported the effectiveness of methylprednisolone (MP; 1–3 doses of 30 mg/kg of IVMP) in combination with IVIG.9–12 As compared with patients receiving only IVIG plus aspirin, defervescence was significantly more likely, and the incidence of CAL was significantly lower, among patients receiving IVIG plus steroids

Representative scoring systems for evaluating potential IVIG resistance

	Cut-off point	Points
Kobayashi score[8] (≥5 points; 76% sensitivity, 80% specificity)		
Sodium	≤133 mmol/L	2
Day of illness at initial IVIG (= KD diagnosed)	Day 4 or earlier	2
AST	≥100 IU/L	2
Neutrophil ratio	≥80%	2
CRP	≥10 mg/dL	1
Platelet counts	$\leq 30.0 \times 10^4/mm^3$	1
Age	≤12 months	1
Egami score[9] (≥3 points; 78% sensitivity, 76% specificity)		
ALT	≥80 IU/L	2
Day of illness at initial IVIG (= KD diagnosed)	Day 4 or earlier	1
CRP	≥8 mg/dL	1
Platelet counts	$\leq 30.0 \times 10^4/mm^3$	1
Age	≤6 months	1
Sano score[10] (≥2 points; 77% sensitivity, 86% specificity)		
AST	≥200 IU/L	1
Total bilirubin	≥0.9 mg/dL	1
CRP	≥7 mg/dL	1

AST, aspartate aminotransferase; CRP, C-reactive protein; IVIG, i.v. immunoglobulin; KD, Kawasaki disease.

Treatments other than IVIG for acute KD

General name	Mode of action	Treatment route, dose, and methods	Principal side-effects	Important notices
Methylprednisolone	Suppresses transcription of inflammatory proteins arising from glucocorticoid receptors Suppresses immune cells and inflammatory cytokines arising due to non-genomic activity, such as functional changes in cell membranes etc.	When used in combination with first-line IVIG: 1 dose of 30 mg/kg methylprednisolone. When used to treat IVIG-resistant patients: 30 mg/kg methylprednisolone once a day, for 1–3 days. Some reports suggest additional prednisolone (started at 1–2 mg/kg/day and gradually tapered over a period of 1–3 weeks) after methylprednisolone.	Sinus bradycardia (6–82%), hypertension (10–91%), hyperglycemia (6–55%), hypothermia (6–9%) etc. In rare cases, patients may develop infections, gastrointestinal ulcers, mental disorders, femur head necrosis, and suppressed adrenal function.	Vital signs – including electrocardiogram, body temperature, and blood pressure – should be continuously monitored
Prednisolone	Inhibits gene transcription of inflammatory proteins and promotes gene transcription of anti-inflammatory proteins	During fever: 2 mg/kg/day of prednisolone, i.v. in 3 divided doses After defervescence: Once patient is no longer febrile and general status has improved, prednisolone is given orally. When CRP normalizes, the dose of prednisolone is tapered over 15 days, in 5 day steps, from 2 mg/kg/day in 3 divided doses to 1 mg/kg/day in 2 divided doses to 0.5 mg/kg/day in a single dose.	Some viral infections (a few percent), moon facies (most who receive this treatment), hypothermia immediately after defervescence (a few percent), occult blood positivity (approx. 1%), hyperlipidemia (a large proportion), neutrophil-predominant leukocytosis (in almost all cases) etc. General side-effects of steroid treatment: infections, gastrointestinal ulcers, mental disorders, femur head necrosis, suppressed adrenal function etc.	
Infliximab	Neutralizes biological activity of soluble TNF-α Damages membrane-bound TNF-α-expressing cells, with complement- and antibody-dependent cell damage Dissociates TNF-α bound to TNF-α receptors	i.v. drip infusion of 5 mg/kg (may only be given once)	Of 708 adult cases in Japan, nasopharyngitis (19.6%), fever, (11%), exanthema (8.9%), headache (5.8%), cough (5.1%), elevated ALT (12.6%), elevated AST (9.9%), elevated LDH (9.3%) etc.	
Ulinastatin	Inhibits elastase release from neutrophils and platelets, and rendering it inactive after release	i.v. drip of 5000 units/kg, 3–6 times a day, for 3–4 days No treatment may exceed 50 000 units.	Anaphylaxis, hepatic dysfunction (0.5%), leukopenia (0.2%), allergic symptoms such as exanthema and pruritus (0.1%), diarrhea, angiodynia (0.1%), elevated AST, elevated ALT, eosinophilia, vascular pain at injection site etc.	Avoid mixing with IVIG in treatment route
Cyclosporine A	Suppresses cytokine production such as IL-2 by inhibiting nuclear factor of activated T cells	Start on 2 divided oral doses (1 each before meal) of 4–5 mg/kg/day Target trough level: 60–200 ng/mL	Subclinical hyperkalemia (with lower values in plasma than in serum; no reports of adverse events such as arrhythmia etc.) General adverse reactions include increased blood pressure, nausea and vomiting, shivering, hyperglycemia, hyperuricemia, hyperlipidemia (1–5%) etc.	
Methotrexate	Suppresses proliferation of several immunomodulatory cells by inhibiting synthesis of DNA as a folic acid antagonist	One oral dose of 10 mg/body surface area per week	Side-effects appearing at standard doses (gastrointestinal injury, hair loss, myelosuppression etc.) are not reported at lower doses	
Plasma exchange	Mechanical removal of inflammatory cytokines	Displacing solution set at 5% albumin; 1–1.5x the patient's circulating plasma volume is exchanged Usually given for 3 continuous days (upper limit: 6 days)	Hypotension, hypovolemia, shock, anaphylactoid reactions, hypocalcemia, fever/coldness/shivering, nausea/vomiting, coagulopathies, pneumothorax at time of catheter insertion	
Aspirin	Blocks synthesis of PGE2 from arachidonic acid during PG synthesis	Febrile period: Oral dose of 30–50 mg/kg/day, in 3 divided doses After defervescence: Single oral doses of 3–5 mg/kg/day	Bleeding, hepatic dysfunction, gastrointestinal ulcer, hematemesis, induction of asthmatic attacks, urticaria, exanthema (incidence unknown), loss of appetite (0.1 to < 5%), nephropathy (<0.1%) etc.	Special care should be taken when patient has chickenpox or influenza, as aspirin might induce Reye syndrome

Antiplatelet, anticoagulant, and thrombolytic drugs

Name of medication (trade name)	Mechanism of action	Dose and method of treatment	Side-effects (%)	Important considerations
Flurbiprofen	Anti-inflammatory effect by inhibiting cyclooxygenase	3–5 mg/kg, in 3 divided doses	Gastric discomfort (1.56%), loss of appetite (1.03%), rash (0.24%), rare cases of thrombopenia etc.	
Dipyridamole	Inhibits phosphodiesterase	2–5 mg/kg, in 3 divided doses	Headache (0.91–4.37%), palpitations (0.43–0.56%); severe side-effects: worsening of angina symptoms (<0.1%), tendency to bleed (incidence unknown) etc.	
Ticlopidine	Suppresses antiplatelet coagulation; reinforces activity of platelet adenylate cyclase	2–5 mg/kg, in 3 divided doses	TTP, agranulocytosis, severe liver damage (incidence unknown) etc.	Indications for treatment should be carefully examined. Blood tests required every 2 weeks during initial treatment.
Unfractionated heparin	Displays anticoagulant activity by binding AT-III, a factor in physiological inhibition of coagulation factors II, VII, IX, X, XI, XII	Start patient on slow i.v. 50 units/kg (duration of treatment: ≥ 10 min), then continuous i.v. infusion with 20–25 units/kg /h	Hemorrhage is the principal side-effect (incidence unknown) HIT (incidence unknown), impaired hepatic function (0.1 to <5%), rash (incidence unknown), hair loss/vitiligo (incidence unknown) etc.	APTT should be controlled within 60–85 s (1.5–2.5× that of controls)
LMWH	Displays anticoagulant effect through AT-III indirectly	Infants <12 months Treatment: 300 units/kg/day in 2 divided doses (every 12 h) Prevention: 150 units/kg/day in 2 divided doses (every 12 h) Children/adolescents Treatment: 200 units/kg/day in 2 divided doses (every 12 h) Prevention: 100 units/kg/day in 2 divided doses (every 12 h) Subcutaneous injection	Lower incidence of hemorrhage than unfractionated heparin Subcutaneous bleeding (3.8%), HIT (0.4%), headache/vertigo (1 to <10%), constipation/diarrhea (1 to <10%), abnormal hepatic functioning (1 to <10%) etc.	APTT should be controlled within 60–85 s (1.5–2.5× that of controls)
Warfarin	Achieves anticoagulant effect by inhibiting biosynthesis of vitamin K-dependent coagulation factors II, VII, IX, and X	0.05-0.12 mg/kg, in a single dose Orally	Hemorrhage (incidence unknown), allergic reactions (incidence unknown), impaired hepatic function/jaundice (incidence unknown) etc.	PT-INR should be adjusted to 1.6–2.5 and thrombotest to 10–25% Because warfarin is passed through the placenta, it is contraindicated for pregnant women in their first trimester
Urokinase	Degrades fibrin and encourages activation of plasmin	Systemic treatment 10 000–16 000 units kg (maximum 960 000 units), given in an i.v. drip over 30–60 min Intracoronary thrombolysis 4000 units/kg over 10 min, maximum 4 times	Hemorrhagic cerebral infarction (0.1 to <0.5%), cerebral hemorrhage (<0.1%), gastrointestinal hemorrhage (<0.1%), impaired liver function (<0.1%), rash and other allergic reactions (<0.1%) etc.	Additive effect with heparin, warfarin, aspirin, dipyridamole, ticlopidine hydrochloride, and other t-PA medications, leading to increased risk of hemorrhage When given with aprotinin medications, urokinase may have weakened capacity for fibrinolysis
Alteplase	Degrades fibrin and enhances activation of plasmin	290 000–435 000 units/kg; first administer 10% of total volume of medication i.v. for 1–2 min, and the remaining volume by i.v. drip over 60 min	Tendency to bleed, including cerebral hemorrhage (0.4%), gastrointestinal hemorrhage (0.6%), pulmonary hemorrhage (0.08%). After reperfusion, arrhythmias such as premature ventricular contraction, ventricular tachycardia, and ventricular fibrillation (incidence unknown), shock/anaphylactic symptoms (0.1%), abnormal hepatic function (0.1 to <0.5%) etc.	Increased risk of hemorrhage when given with other thrombolytics, anticoagulants, antiplatelet medications etc.
Monteplase	Its half-life, affinity for fibrin, and plasminogen activator activity are greater than those of alteplase	27 500 units/kg, i.v. over 2–3 min	Cerebral and gastrointestinal hemorrhage (0.1 to <5%), tendency to bleed including pulmonary hemorrhage (incidence unknown), cardiac rupture/perforation of intraventricular septum (0.1 to <5%). After reperfusion, arrhythmias such as premature ventricular contraction, ventricular tachycardia, and ventricular fibrillation (incidence unknown), shock/anaphylactic symptoms (0.1%), abnormal hepatic function (0.1 to <0.5%) etc.	Same as above
Pamiteplase	Same as above	65 000 units/kg, i.v. over 1 min	Severe bleeding, including cerebral hemorrhage, retroperitoneal hemorrhage, gastrointestinal hemorrhage etc (0.1 to <5%), cardiac rupture/cardiac tamponade (0.1 to <5%), ventricular tachycardia/ventricular fibrillation (0.1 to <5%), shock (<0.1%).	Same as above

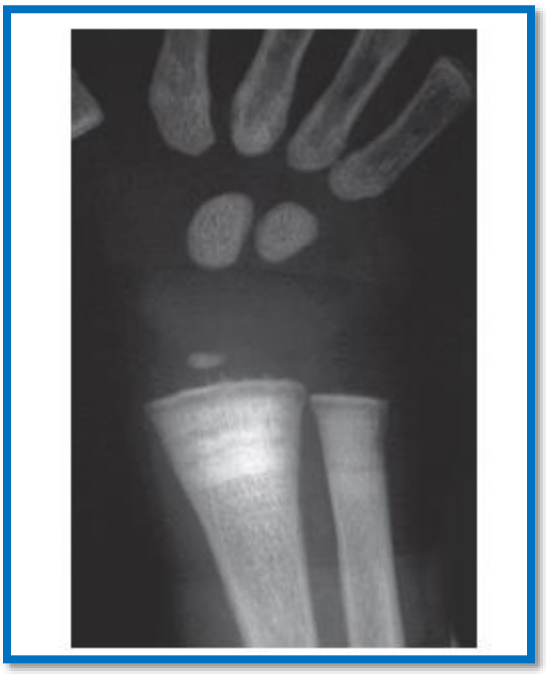
APTT, activated partial thromboplastin time; AT-III, anti-thrombin III; HIT, heparin-induced thrombocytopenia; IVIG, i.v. immunoglobulin; LMWH, low-molecular-weight heparin; PT-INR, prothrombin time international normalized ratio; TTP, thrombotic thrombocytopenic purpura.

Anti-anginals and coronary vasodilators

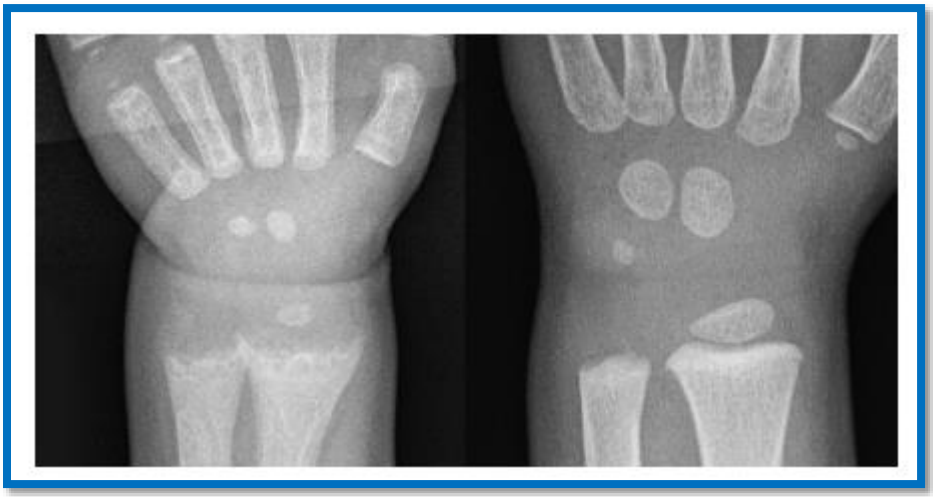
- Angina symptoms are extremely rare during the acute phase of KD, and patients with such symptoms are typically aged 1–2 years and thus cannot easily explain their symptoms to caregivers. In adult patients, the characteristics of angina symptoms may allow classification of angina as stable or unstable. The principal therapeutic goal for angina is to reduce heart rate (thereby reducing cardiac workload), decrease preload and afterload, and increase coronary artery flow. For these reasons, beta-blockers, calcium antagonists and nitrovasodilators may be useful.
- **(1)** Beta-blockers are the first choice for stable effort angina. To avoid side-effects in other body organs, beta-blockers that selectively block β-1 are recommended. As well as reducing myocardial workload and suppressing oxygen consumption, beta-blockers increase coronary blood flow accompanying bradydiastole, thereby preventing development of myocardial ischemia. Although atenolol, bisoprolol, and metoprolol have all been found to be effective,114 beta-blockers may worsen prognosis in patients with coronary vasospasm, because upregulated α-receptor function may induce exacerbation of coronary tonus and symptoms of coronary spastic angina.115 Carvedilol is a non-selective beta-blocker that also blocks α-1, and it increases coronary flow by lowering peripheral resistance in coronary arteries. **(2)** Calcium antagonists suppress the flow of Ca^{2+} into vascular smooth muscle cells. They are therefore extremely useful in preventing coronary vasospasm and are the first choice in treating coronary spastic angina.117 KD-related myocardial infarction often occurs during sleep and may be induced by coronary spasms.118 The ability of calcium antagonists to protect cardiovascular function seems to be due to stimulation of NO production. Because diltiazem blocks the L-type Ca^{2+} channel in cardiac myocytes, however, it is contraindicated for use in newborns up to early infancy.
- **(3)** Nitrates exert their effect by dilating coronary arteries and reducing preload. Nitrates increase coronary blood flow and reduce both preload and afterload, which reduces the workload of the left ventricle, thereby relieving myocardial ischemia. Acute KD, however, is characterized by persistent damage to endothelial cells. Therefore, nitrates may not be effective in dilating impaired coronary arteries. A sublingual tablet of nitroglycerine or an oral spray of nitroglycerine or isosorbide dinitrate may alleviate angina symptoms. Nitrovasodilators are contraindicated in patients with glaucoma, in those taking phosphodiesterase inhibitors, and in those with cardiogenic shock, severe hypotension, or severe anemia.
- **(4)** Nicorandil is a hybrid medication (a nitrovasodilator that opens the ATP-sensitive potassium channel) and can selectively dilate coronary arteries and inhibit coronary vasospasm. 119 It is therefore useful in preventing angina. Nicorandil also affects mitochondria, resulting in pharmacological preconditioning that protects against myocardial ischemia.
- The use of the aforementioned medications, both in cases of KD and in pediatric patients in general, is off-label. This article is based on a study first reported in *PediatricCardiology and Cardiac Surgery*, 2012; 28 (Suppl. 3): 1–s28.120

REFERENCE: *Pediatrics International* (2014) **56**, 135–158 doi: 10.1111/ped.12317

RADIOLOGY OF WRIST NORMAL/ABNORMAL



1.COMMENTS:



2.COMMENTS

COMMENTS

1. **Iatrogenic vitamin D intoxication**
In a child with physiological bowlegs who mistakenly was thought to have X-linked hypophosphatemia. Multiple opaque bands are present in the distal radialmetaphysis.

2. **Vitamin D deficiency rickets**.
A 14-month-old child withgrowth failure and severe rickets who responded well to vitamin D therapy. **The initial image (*left*) shows loss of definition of the zones of provisional calcification** for the distal radial and ulnar metaphyses along with metaphyseal fraying and concavity ("cupping") and physeal widening with an increased distance between the epiphysis and visualized portion of the metaphysis. Periosteal new bone also is present that is seen best along the metacarpals but also is present along the distal radius. **With healing (*right*), the zone of provisional calcification is well mineralized and the other findings have resolved**.

CLINICAL KEY POINTS FOR CLINICIAN

Key Points The initial radiographic finding in rickets is loss of mineralization of the zone of provisional calcification. .
Isolated distal ulnar metaphyseal cupping is a normal variant in an infant and should not be confused with rickets

REFERENCE: Caffey's Pediatric Diagnostic Imaging edition Twelfth Edition pp:1523-1544

CLINICAL SCENARIOS

- **A 6 yr old girl is having nocturnal enuresis. Anxious parents have tried remedies for enuresis. They deny any h/o uti. They are not sure about the frequency of micturition. There is no h/o constipation.There is no family history of nocturnal enuresis. No other contributory history available**

How do you define this girl's problem?

- Nocturnal enuresis (NE) is defined in accordance with the International Children's Continence Society (ICCS) as "intermittent nocturnal incontinence." (1) Primary monosymptomatic nocturnal enuresis (PMNE) is defined as lifelong continuous "enuresis without any other history of lower urinary tract symptoms and without a history of bladder dysfunction." (1)

- For all other children who do not fit these criteria, the broad term nonmonosymptomatic nocturnal enuresis (NMNE) is used. Children with NMNE may have a variety of different reasons for their enuresis, which should not be thought of as homogenous in cause or treatment. Reasons can include urinary tract infections, diurnal enuresis, and known anatomical or neurologic bladder dysfunction.

- A subset of children with NE who previously have had a dry period for 6 months or longer are characterized as having secondary NE .

- **8 yr girls mother whose child is suffering from nocturnal enuresis.Mother says that she has changed three diapers and maximum approximate urine volume was 120 ml Mother was suffering from nocturnal enuresis till 12 yrs. This child has no uti. She is not drinking more than 200 ml after 6 o'clock**

What inference can be made from her observation?

- The EBC(estimated bladder capacity) is defined using the following equation: EBC =30 mL + (age in years× 30 mL). Some children with PMNE will have small bladder capacities.Bladder capacity can be determined by using the voiding diary and maximum voided volume to look for a pattern of frequent small volume voids during the day and should be considered especially likely when the maximum voided volume on the voiding diary is less than 50% of the EBC.

- Another group of children with PMNE will have nocturnal polyuria (NP) as part of their condition. This condition is defined as urine production greater than 130% of the child's expected bladder capacity (EBC).

- Although sleep arousal abnormalities, NP, sleep disordered breathing, small bladder capacity, and overactive bladder can be independent causes of PMNE, in most children these factors can occur in combination, with many children having 2 or even 3 of these

factors. In many cases, there is a strong genetic or familial cause that can further complicate this and can be elicited by taking a thorough family history

-

My daughter Nandhana has nocturnal enuresis. I try to wake up three of my daughters at 5 o'clock in the morning. But I find it difficult to wake up Nandhana eventhough she obeys with reluctance saying ." I have to sleep a little more". She has no snoring or day time sleepiness

What inference I should have about her behaviour?

- Children with PMNE can have a variety of different and overlapping physiologic variants that cause them to have incontinence.

- Central to PMNE is an inability of the child to awaken to the stimulation to void. Nearly every family will tell you that their child is a very heavy sleeper and that they do not wake to many types of physical or audible stimulation at night.

- Although sleep studies have been conflicting at finding a single type of sleep problem in these children, the lack of arousal is what characterizes these children and separates them from children with nocturia in which the child awakens to void.

- It is therefore important to understand that difficulty with sleep arousal is central to virtually all children with all types of NE.

How long should I wait?

- NE is a common condition in early childhood that decreases in prevalence as children approach adolescence. NE is ubiquitous in the newborn and is part of the infantile voiding pattern.

- A total of 10%to 15%of children will still wet the bed by age 6 years. Up to 15% of children will outgrow the condition annually in the teenage years so that only 1% to 2% of people will still have PMNE into adulthood. (2)(3) The condition is more common among boys and in children with a first-degree relative with a history of PMNE.

- If one parent has a history of PMNE, then up to half of their children will have it. If both parents hadPMNE, then up to three-fourths of the children will have it. PMNE is seen more commonly in children with attention-deficit/hyperactivity disorder, which frequently represent challenging cases for treatment

How to make rapid screen in our practice?

Rapid Screen to Determine Type of Enuresis	
QUESTION	IF RESPONSE IS POSITIVE, THEN CONSIDER
Previously dry for 6 months	NMNE or SNE
Associated with daytime urine control issues	NMNE
Constipation or fecal soiling	NMNE
Severe recent stress	SNE
If responses to all above questions are negative, then consider	MNE
MNE=monosymptomatic nocturnal enuresis; NMNE=nonmonosymptomatic nocturnal enuresis; SNE=secondary nocturnal enuresis	

7 yr old has started voiding during nighttime. He had been dry for an year. Child has started skipping family events and is not willing ro play with his friends. What points you specifically note during your examination?

genital examination	labial adhesions in girls and meatal stenosis in boys.
continuous leaking of fluid from the vagina or perineum	an ectopic ureter as the source of the enuresis.
identify the anus, vaginal opening, and urethral opening.	Vaginal and/or urethral opening is not seen, then labial adhesions might be present.
the skin of the genital area	skin changes from chronic wetness or irritation
to check the underwear of the child	to assess for wetness and stool streaking. Stool around the anus may be a product of poor wiping but might be indicative of encopresis or constipation
perineum	Perianal tears or fissures may suggest longstanding constipation.
perineal sensation	underlying spinal cord disease
examine the sacrum and lumbar spine.	Sacral dimples, tufts of hair over the midline, and abnormal or asymmetric gluteal cleft should raise the examiner's suspicion of an underlying spinal cord problem, such as tethered cord, cord lipoma, or persistent dural sinus.
abdominal examination	to check for a palpable bladder and for significant palpable stool in the left lower quadrant should be performed.
Oropharynx	to determine the location and size of the tonsils.

What all tests are to be done initially?

- In all children with NE, according to the International Continence Society (ICS), the only mandatory screening laboratory should be urinalysis. (4) This is useful to identify renal disease in cases where proteinuria or hematuria is present and to rule out urinary infection as the cause of the NE. Occult cystitis may not be elicited by a history or physical examination, and a urinalysis should be able to detect this.

- If the child has a low specific gravity, then diabetes insipidus or other causes of polyuria should be considered.

- In most cases, it is appropriate for the pediatrician to have the family complete an elimination diary. This diary should consist of a stool and bladder diary that documents the timing and volume of voids, number and type of stools during the day, and characterization This should be mandatory for all specialist evaluations of children with NE and especially those who have had treatment failure because this helps identify children who have small bladder capacity or excessive urine production. The fluid intake will help identify children with increased solute or fluid intake.

- Although not mandatory, recording the type of fluids the child is drinking can be important, especially if the child is consuming large volumes of caffeinated beverages because these may have a diuretic effect and create overactivity in the bladder. These types of beverages should be reduced or eliminated from the child's diet and especially eliminated before bed.

What are the option left for me in managing three scenarios described?

Possible Treatment Protocols in MNE	
TYPE OF MNE	**TREATMENT**
All cases	Limit fluids before bed (<200 mL)
	Void before bed
	Regular sleep and wake schedule
Classic PMNE	Alarm (first)
	Desmopressin (second)
Nocturnal polyuria	Desmopressin
Sleep disordered breathing	Sleep study or referral
Small bladder capacity	Alarm
Overactive bladder (suspected)	Desmopressin and oxybutynin
	Alarm and oxybutynin
Small bladder and nocturnal polyuria	Desmopressin and alarm (consider oxybutynin as well)
MNE=monosymptomatic nocturnal enuresis; PMNE=primary monosymptomatic nocturnal enuresis	

What am I to look if I fail with these measures?

CAUSE	NEXT STEP
Constipation or retained fecal burden	Bowel regimen
Occult voiding dysfunction	Behavioral therapy, postvoid residual volume, uroflowmetry
Treatment compliance failure	Family goal discussion and assessment of child's interest in participation
Neurologic condition	Detailed neurologic examination and consider lumbar magnetic resonance imaging
Psychological stressors	Psychological evaluation and counseling as needed
Metabolic concerns	Laboratory evaluation and consider endocrine referral
Sleep disorders	Sleep laboratory referral with polysomnography
Sleep disordered breathing	Sleep specialist referral

REFERENCE: **Nocturnal Enuresis: An Approach to Assessment and Treatment** Aaron P. Bayne and Steven J. Skoog. *Pediatrics in Review* 2014;35;327 DOI: 10.1542/pir.35-8-327

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