Rheuma Facts[®] A Quarterly Magazine

Serving physicians with interest in Rheumatology

16th Issue

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Current News

Allopurinol Found Safe in Patients with Concomitant Gout, CKD

Allopurinol treatment is not associated with increased mortality in patients with gout and chronic kidney disease even at 5 years after starting treatment, a study has found.

Around 1 in 5 patients with gout also have chronic kidney disease, and previous research suggests that hyperuricemia is itself a contributor to renal disease, which is why there has been interest in the use of serum urate-lowering medication in patients with both conditions.

Since the publication of two earlier randomized controlled trials suggested a twofold increase in mortality among patients with renal disease who were treated with allopurinol in an attempt to slow progression, there has been wariness about the drug in patients with compromised renal function. At 5 years after the patients started allopurinol, the study found that mortality was a statistically significant 15% lower (hazard ratio, 0.85; 95% CI, 0.77 – 0.93) among those on allopurinol, compared with those not taking the drug. The rate was 4.9 deaths per 100 person-years among those on allopurinol, compared with 5.8 among those not taking it.

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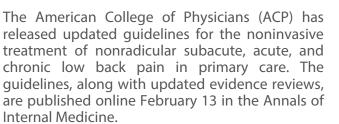
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New ACP Guidelines for Non-radicular Low Back Pain

Compiled and summarized by: Dr. Ahmed Iqbal Mirza Consultant Rheumatologist Aga Khan University Hospital, Karachi



Overall, the new guidelines emphasize conservative treatment. First-line therapy should incorporate nondrug therapies. Nonsteroidal anti-inflammatories (NSAIDs) or muscle relaxants should be considered when nondrug therapy fails. The guidelines strongly discourage the use of opioids.

"For treatment of chronic low back pain, clinicians should select therapies that have the fewest harms and lowest costs because there were no clear comparative advantages for most treatments compared with one another. Clinicians should avoid prescribing costly therapies; those with substantial potential harms, such as long-term opioids (which can be associated with addiction and accidental overdose); and pharmacologic therapies that were not shown to be effective, such as [tricyclic antidepressants] and [selective serotonin reuptake inhibitors]," write Amir Qaseem, MD, PhD, MHA, chair of the ACP guidelines committee, and colleagues.

Lower back pain is one of the most common reasons for clinic visits in the United States. It is associated with increased healthcare costs as well as lost wages and decreased work productivity.

Acute back pain generally lasts less than 4 weeks and usually resolves on its own. Subacute low back pain is defined as lasting 4 to 12 weeks, while chronic back pain lasts over 12 weeks. Up to 30% of patients report persistent low back pain up to 1 year after experiencing an acute episode. One in five report substantial limitations in activity, according to background information in the article.

To develop the guideline, the ACP reviewed randomized controlled trials and systematic

reviews of studies evaluating noninvasive, nondrug, and drug therapy for low back pain in adults. To be included, studies had to be published in English between January 2008 and November 2016. The authors identified earlier studies using the 2007 ACP/American Pain Society systematic reviews. The guidelines and evidence reviews also underwent peer review and a public comment period.

While no therapy was clearly better than any other, new evidence supports mindfulness-based stress reduction and tai chi in chronic low back pain and acupuncture in acute low back pain.

Also, new research suggests lack of benefit for acetaminophen in acute low back pain and supports use of duloxetine in chronic low back pain. By contrast, tricyclic antidepressants appear to be no better than placebo in this setting.

The ACP made the following strong recommendations:

- •Most patients with acute or subacute low back pain improve over time regardless of treatment and can avoid potentially harmful and costly treatments and tests. First-line therapy should include nondrug therapy, such as superficial heat (moderate-quality evidence), massage, acupuncture, or spinal manipulation (low-quality evidence). When nondrug therapy fails, consider NSAIDs skeletal muscle relaxants or (moderate-quality evidence).
- •For chronic low back pain, consider nondrug therapy, such as exercise, multidisciplinary rehabilitation, acupuncture, mindfulness-based stress reduction (moderate-quality evidence), tai chi, yoga, motor control exercise, progressive relaxation, electromyography biofeedback, low-level laser therapy, operant therapy, cognitive-behavioral therapy, or spinal manipulation (low-quality evidence).
- •For chronic low back pain that does not respond to nondrug therapy, consider NSAIDs



as first-line therapy. For second-line, consider tramadol or duloxetine. Consider opioids only in patients in whom first- and second-line therapy has failed, in whom the risk outweigh the benefits, and only after full discussion of the potential risks and benefits.

The recommendations stress that clinicians should reassure patients that acute and subacute back pain usually resolves on its own, and they should provide patients with relevant information for self-care. They also note that, overall, studies poorly report harms. The guideline does not address topical drugs, epidural injections, or cyclo-oxygenase-2 selective NSAIDs.

In a linked editorial, Steven J. Atlas, MD, MPH, from Massachusetts General Hospital in Boston, points out that the initial focus on nondrug therapy may be "reasonable" but represents a "major change for primary care clinicians" because research in real-world settings is lacking.

"This change in emphasis partly reflects the limited pharmacologic choices nonsteroidal anti-inflammatory drugs and skeletal muscle relaxants, with acetaminophen no longer being recommended. It also may represent a shift toward efforts to prevent progression to chronic low back pain by identifying patients at increased risk for persistent pain," he writes.

The main problem with nondrug therapies lies in insurance coverage issues, he stresses, and whether such treatments are available and affordable for patients.

He also casts doubt on whether these new recommendations are enough to improve guideline-oriented care. "Likely what is needed is an 'all of the above' approach: more pragmatic trials to evaluate proven therapies and their combinations in real-world settings; efforts to reduce the use of low-value services, such as payer coverage policies based on guideline recommendations; patient engagement through shared decision making; and pressure on insurers to cover nonpharmacologic, noninvasive therapies that have shown benefit," he writes.

Nevertheless, he concludes that evidence reviews and guidelines like these can "drive efforts" to decrease use of therapies with no clear benefit and improve outcomes in low back pain.

Ann Intern Med. Published online February 13, 2017

Sjögren's Syndrome

Compiled and summarized by: Dr. Ahmed Iqbal Mirza Consultant Rheumatologist Aga Khan University Hospital, Karachi

- Sjögren's syndrome is an autoimmune condition that can occur at any age, but is most common in older women. Many patients develop Sjögren's syndrome as a complication of another autoimmune disease, such as rheumatoid arthritis or lupus.
- Sjögren's syndrome is an inflammatory disease that can affect many different parts of the body, but most often affects the tear and saliva glands. Patients with this condition may notice irritation, a gritty feeling, or painful burning in the eyes. Dry mouth (or difficulty eating dry foods) and swelling of the glands around the face and neck are also common. Some patients experience dryness in the nasal passages, throat, vagina and skin. Swallowing difficulty and symptoms of acid reflux are also common.
- "Primary" Sjögren's syndrome occurs in people with no other rheumatic disease. "Secondary" Sjögren's occurs in people who have another rheumatologic disease, most often systemic lupus erythematosus and rheumatoid arthritis. It can occasionally be confused with a newly described syndrome call IGG4 disease.
- Most of the complications of Sjögren's syndrome occur because of decreased tears and saliva. Patients with dry eyes are at increased risk for infections around the eye and may have damage to the cornea. Dry mouth may cause an increase in dental decay, gingivitis (gum inflammation), and oral yeast infections (thrush) that may cause pain and burning. Some patients have episodes of painful swelling in the saliva glands around the face.
- Complications in other parts of the body can occur. Pain and stiffness in the joints with mild swelling may occur in some patients, even in those without rheumatoid arthritis or lupus. Rashes on the arms and legs related to inflammation in small blood vessels (vasculitis) and inflammation in the lungs, liver, and kidney may occur rarely and be difficult to diagnose. Numbness, tingling, and weakness also have

been described in some patients. The parotid gland is at the edge of the jaw and can become swollen and inflamed in some people with Sjögren's Syndrome.

The cause of Siggren's syndrome is not known, but it is an autoimmune disorder. People with this

disease have abnormal proteins in their blood. This suggests that the immune system, which normally functions to protect the body against cancers and infections, is reacting against its own tissue. The decrease in tears and saliva seen in Sjögren's syndrome occurs when the glands that produce these fluids are damaged by inflammation. Research suggests that genetic factors and possibly viral infections may predispose people to developing this condition.

Diagnosis depends on a combination of

sometimes special studies. Dry eyes and mouth may be early signs of the condition but require further investigation, because these symptoms can be caused by many other conditions or medications. Special tests may assess any decrease in tear or saliva production. An eye examination is helpful in detecting any eye changes seen in Sjögren's. Blood tests can determine the presence of antibodies (immune system proteins that help destroy foreign invaders) typical of the disease. Typical antibodies include anti-nuclear antibodies (ANA), anti-SSA and SSB antibodies or rheumatoid factor, but these are not always present. Biopsies of saliva glands around the face or under the surface of the inner lip also may be used to make a diagnosis.

Treatment is designed to lessen the most



respond to artificial tears applied regularly during the day or to gels applied at night. Other measures, such as plugging or blocking tear ducts, can be used in more severe cases. Eye drops that reduce inflammation in the glands around the eyes, such as cyclosporine, may be used to increase tear production. Drinking water, chewing gum, or using saliva substitutes may relieve dry mouth. Some patients benefit from using prescription medications that stimulate saliva flow, such as pilocarpine or cevimuline . If patients develop yeast infections, anti-fungal therapies may be used. Humidifiers and nasal saline irrigation may improve nasal dryness. Medications that reduce gastric acid (such as proton-pump inhibitors and H2 blockers) may lessen symptoms of acid reflux. Treatments may help relieve some of the dryness, but usually some dryness persists.

All patients should receive regular dental care to prevent cavities and tooth loss that may occur as a complication of Sjögren's. Patients with dry eyes should see an ophthalmologist (eye doctor) regularly for signs of damage to the cornea. Patients with excessive redness and pain in the eyes should be evaluated for infections.

Hydroxychloroguine an antimalarial drug used in lupus and rheumatoid arthritis, may be helpful in some patients with Sjögren's syndrome by reducing joint pain and rash experienced by some patients. Patients with rare but serious systemic symptoms, such as fever, rashes, abdominal pain, or lung or kidney problems, may require treatment with corticosteroids such as prednisone and/or immunosuppressive agents like methotrexate, mycophenolate azathioprine or cyclophosphamide . In addition, researchers are evaluating rituximab and other biological therapies to treat cases of Sjögren's that affect the entire body.

A vast majority of patients with Sjögren's syndrome remain very healthy, without any serious complications. Patients should know that they face an increased risk for infections in and around the eyes and an increased risk for dental problems due to the long-term decrease in tears and saliva.

Rarely, patients muy have complications related to inflammation in other body systems, including:

Lung problems that may mimic pneumonia

- Abnormal liver and kidney function tests
- Skin rashes related to inflammation of small blood vessels
- Neurologic problems causing weakness and numbness

In a small number of people, Sjögren's syndrome may be associated with lymphoma, a cancer of the lymph glands.

Sjögron's syndromo cannot be cured, but in many

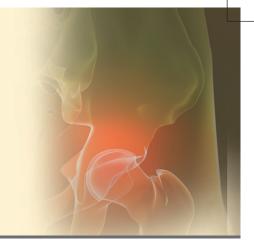
symptoms. Rheumatologists are specialists in musculoskeletal disorders and, therefore, are more likely to make a proper diagnosis. They also can advise patients about the best treatment options available.

People with Sjögren's syndrome usually are able to live normal lives with very few adjustments. When a diagnosis is made, many patients must focus a great deal of attention dealing with dry eyes and dry mouth, but these symptoms tend to subside with time. Any pain or redness in the eyes should be evaluated promptly, as this may signal an infection. To reduce risk for cavities and other dental problems, patients must pay close attention to proper oral hygiene and regular dental care.

Patients should see their physician regularly for general health screening. They also should pay close attention to any abnormal swelling in the glands around the face or neck, under the arms, or in the groin areas, as this may be a sign of lymphoma.

Hot Topics in Rheumatology Key questions and answers

Compiled and summarized by: Dr. Ahmed Iqbal Mirza Consultant Rheumatologist Aga Khan University Hospital, Karachi



Question 1: How important is light, sun light and the ingestion of vitamin D from food and drugs?

Answer: The majority of vitamin D in our bodies is made by our bodies when we are exposed to natural sunlight. We also obtain a very small amount of vitamin D from some of the foods we eat. Vitamin D is a precursor and is converted into a hormone which actually carries out the work in our bodies, called Hormone D. One of the main roles of hormone D is to increase absorption of calcium and phosphorus in the intestines. (Cortisone and Hormone D share the same chemical structure, as they are both cholesterol derivatives). Having the correct concentration of vitamin D in our blood stream allows our immune system to protect us from infections, inflammatory and autoimmune diseases and also some types of cancer. Therefore it is important to have healthy levels of levels of vitamin D in our blood, especially in winter and in Northern countries, when daylight is limited. Vitamin D supplements should be taken daily and not as a single, weekly, monthly or annual mega-dose. Vitamin D helps us absorb calcium, a vital component of bones. In older people, taking Vitamin D supplements in winter is the most effective and safest way to help prevent and treat osteoporosis.

Question 2: Why, for a long time, have low doses of cortisone derivatives been used to treat chronic rheumatic inflammatory, autoimmune diseases?

Answer: Every night our bodies produce cortisone that is mainly used to protect us from infections, excessive immune responses, cancer cells and the effects of stress. Some people who have chronic stress from conditions such as depression/anxiety, chronic infections or severe chronic diseases will use all the cortisone their bodies produce during the night time, which results in deficient cortisone levels. How do we overcome this cortisone deficiency? By administering small doses of cortisone derivatives (i.e. prednisone) every night or very early in the morning. Modulating the immune system in this way, by re-introducing cortisone, will ensure the body is better protected against infections, excessive immune responses, cancer cells and the effects of stress.

Question 3: Why are women more frequently affected by rheumatic immune/inflammatory diseases?

Answer: Women are more frequently affected by rheumatic immune/inflammatory diseases because they have higher blood concentrations of oestrogens, and oestrogens normally increase the immune response. Oestrogens produce early antibodies, which protect the body from infections and other antigens. However, in conditions where the immune system is activated or when oestrogens, such as contraceptives, are administered the body produces an excess of antibodies, which leads to an increased risk of immune/inflammatory disease. One of the reasons that men are also affected by rheumatic immune/inflammatory diseases is that peripheral fat tissues, found in both men and women, produces oestrogens, which can lead to an increased production of antibodies.

Question 4: What is the best approach to managing the first appearance of joint or musculoskeletal pain?

Answer: Chronic pain is a neurological/ biochemical alarm signal which is almost always the first sign of disease. Pain must never be masked with pain killers before the doctor has diagnosed the cause of the pain. The best way to treat acute and chronic pain is to target the cause of the pain. In cases of joint or musculoskeletal pain "the first step" is referral to a rheumatologist.

Question 5: Why do some people get cold hands or feet and what is the treatment for cold hands or feet?

Answer: Cold hands reflect an altered microcirculation, which is particularly common

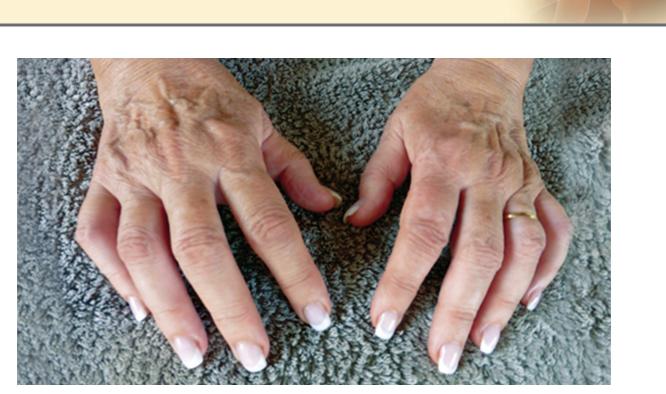
during winter and in women who are under emotional stress (Raynaud's phenomenon). However, in almost 20% of people who have cold hands, the cause isn't just functional and benign, but is the sign of connective tissue disease. In particular, systemic lupus erythematosus and systemic sclerosis might be clinically characterized, even in very early phases, by Raynaud's phenomenon. How is the cause of cold hands or feet diagnosed? The best method is to test the levels of specific antibodies in the blood or to use nailfold capillaroscopy, which is a safe and inexpensive technique which uses a tiny microscope to examine the microvascular nail bed. After more than 30 years of intensive investigation, capillaroscopy is now officially considered by the EULAR and ACR guidelines as both an essential mandatory diagnostic tool for the and classification criteria of systemic sclerosis.

Question 6: Is chronic low back pain almost always related to postural conditions or is it due to intervertebral disc prolapse?

Answer: In large populations of primary care patients who had been experiencing chronic lower back pain symptoms for an average of 7-9 years, in at least 20-25% of cases (40-50% of which were men), the cause was related to axial inflammatory spondyloarthritis. To be able to diagnose early and correctly treat chronic back pain in men and women, it is important to consider that almost 60-70% of patients are diagnosed with an MRI scan, 25-30% with an X-ray and the presence of one other spondyloarthritis symptom, and 10-15% with a positive HLAB27 test. To optimize treatment and reduce disease progression, targeted available. therapies are However, axial inflammatory spondyloarthritis is only one cause of chronic lower back pain and almost 80% of cases of chronic low back pain are caused by postural conditions or intervertebral body disk conflict.

Post-Chikungunya Rheumatoid Arthritis

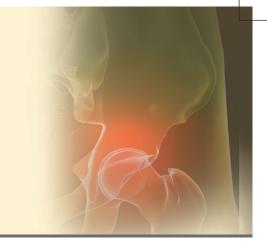
Compiled and summarized by: Dr. Ahmed Iqbal Mirza Consultant Rheumatologist Aga Khan University Hospital, Karachi



A 70-year-old woman sought treatment in Jan, 2017 for joint pain and disabilities persisting after chikungunya. Her medical history included high blood pressure, hypothyroidism, and dengue infections. During September 2016, the patient had high-grade fever, intense fatigue, and a maculopapular troncular exanthema without lymphadenopathy. Five days later, she had distal polyarthritis (joint pain and swelling) in interphalangeal joints, wrists, and ankles without plantar involvement. Recent infection with chikungunya virus was confirmed (IgM and IgG against chikungunya virus was detected in 2 blood samples), and recent dengue was excluded.

Despite initial brief improvement, the patient never totally recovered and subsequently chronic polyarthritis developed, which involved >10 joints, including interphalangeal joints, wrists, and knees. Non-steroidal anti-inflammatory drugs did not relieve the diffuse pain, stiffness, and swelling. She was given oral steroids (20mg/day) in the beginning. She was referred to another hospital in Karachi later because of treatment failure. She reported continuous pain in the left knee and wrists and multiple tenosynovitis on flexors and extensors of the fingers. She did not report any fever or axial, shoulder, or hip pain. Radiographs of the involved joints showed no abnormalities.

The patient had mild inflammation (C-reactive protein level 13 mg/L, fibrinogen level 3.4 g/L) but no specific autoimmunity (results were negative for anticitrullinated peptide antibodies, rheumatoid factor, antineutrophil cytoplasmic and antinuclear antibodies). antibodies, Serologic results for viruses other than chikungunya virus were negative or indicated past vaccination. The patient's condition met the 2010 American College of Rheumatology/European League against Rheumatism criteria for rheumatoid arthritis.



For this corticosteroid-resistant, seronegative, and non-destructive post-chikungunya rheumatoid arthritis, methotrexate was prescribed at a weekly low dose after exclusion of contraindications.

The reported case was caused by chikungunya virus infection during an epidemic in Karachi. This unfavorable post-chikungunya outcome of chronic inflammatory rheumatism 8 months later indicates a probable course of post-chikungunya disorders.

The spectrum of post-chikungunya rheumatic and musculoskeletal disorders includes multiple tendinitis and tenosynovitis, plantar fasciitis, mechanical disbalance in susceptible joints, syndromes, edematous polyarthralgia, tunnel rheumatoid arthritis, and psoriatic arthritis. Although the proportion of patients with chronic disease has decreased, postchikungunya chronic inflammatory rheumatism, mostly rheumatoid arthritis, develops in \approx 5% of these patients. These patients had a poor prognosis and were given disease-modifying anti-rheumatic drugs (DMARDs), despite the postinfectious origin of rheumatism. Patients with post-chikungunya rheumatoid arthritis should benefit from methotrexate, which is recommended for treatment of classic rheumatoid arthritis.

In our experience, resistance to or dependence on corticosteroids beyond the third month after disease onset is hiahlv evocative of post-chikungunya chronic inflammatory rheumatism. This finding requires early treatment with DMARDs to control the inflammatory process, prevent bone erosions, and prevent inevitable side effects of prolonged corticotherapy. To date, the efficacy of different

DMARDs for treatment of post- chikungunya chronic inflammatory rheumatism has not been evaluated. Therefore, physicians should follow the international guidelines for treatment of classic rheumatoid arthritis and psoriatic polyarthritis, which recommend methotrexate as first-line treatment for patients fulfilling chronic inflammatory rheumatism criteria after 3 months of evolution.

Thus, a possible increase in post-chikungunya rheumatoid arthritis should not be overlooked. Physicians and public health authorities should prepare a response to the patients' postchikungunya stage in the epidemic areas. Clinical vigilance is recommended to identify patients with unfavorable outcomes 3 months after disease onset and for those in whom post-chikungunya chronic inflammatory rheumatism develops and who require specific treatment.

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PATIENT FACT SHEET

Amplified Musculoskeletal Pain Syndrome (AMPS)

CONDITION DESCRIPTION

Amplified musculoskeletal pain syndrome (AMPS) is an umbrella term for non-inflammatory musculoskeletal pain

Other names you might hear are: juvenile fibromyalgia syndrome, chronic musculoskeletal pain (CMP), chronic widespread pain (CWP), reflex sympathetic dystrophy (RSD), reflex neurovascular dystrophy (RND) or myofascial pain. AMPS is most commonly seen in childhood and adolescence, and most commonly affects pre-adolescent and adolescent girls. Several studies have noted an average age ranging from 11.5 to 15 years. AMPS is thought to be almost nonexistent in children under 4 years of age. The exact cause of AMPS is not well understood; however, the most current research suggest that this chronic non-inflammatory pain condition is the result of malfunction or disordered response and over amplification of the pain signal by the central nervous system and peripheral nervous system.



Common symptoms may include, but are not limited to, headaches, abdominal pain, dizziness, arthralgias and tachycardia.

About 70% of patients with AMPS may have allodynia, a painful sensation in response to non-painful touch. Patients may also face disproportional physical dysfunction, which may include the inability to bear weight or handle the touch of other people, clothing or bedding. Patients may feel fatigued, and may have difficulty falling asleep, or staying asleep, and wake up without any feeling of refreshment.

Anxiety and/or depression may be common, and should be considered in all newly diagnosed patients. Stress plays a role in triggering AMPS and stressors should be routinely evaluated. Some neurologic symptoms involving the brain, spine or nerves) that are not explained by a physical disorder may occur. This can include shaking, paralysis, blindness, non-epileptic seizures and conversion gait.



The goal of AMPS treatment is to return the child to normal daily function.

By minimizing pain, restoring normal sleep and mood and decreasing any negative impact that the pain syndrome may have on health-related quality of life. In order to do this, diagnosis of the primary and secondary causes is important and may involve referral to other specialists, such as psychologists, and physical and occupational therapists. This team approach to pain management is an important part of AMPS treatment.

Treatment of AMPS consists of pain management without medications. Treatments may involve cognitive behavioral

therapy, physical and occupational therapy, regular aerobic (cardio) exercise and focusing on stress reduction. Since AMPS can often affect the entire family, family counseling is frequently recommended. As a pain management recommendation, gradually increase exercise programs, regular daily activity in the form of functional aerobic training, desensitization for allodynia and psychotherapy. There are in-patient and out-patient treatment centers around the country who work daily with patients who have severely debilitating AMPS; these therapy sessions can be up to six hours in duration.



Once a diagnosis of AMPS has been made, the child is recommended to participate in normal activities, attend therapy sessions and gradually return to a normal schedule.

If your child is missing large amounts of school, work with your medical provider and the administration of your school to make sure that catch up material is provided and set up a plan for the return to a full day of school. Often, even if your child is not able to absorb every word that is being taught, going to school, interacting with friends and gradually building endurance is a key component of returning to school.

Lastly, it is important to recognize that the pain that your child is experiencing, while not dangerous, it is very real. Validation of the pain is an important part of working to eliminate it and the child must recognize that he is an important part of the treatment team.

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Question

What is the Diagnosis?