

# Spondyloarthropathy: A Common Familial Form of Arthritis

Harold A. Williamson, Jr., MD, and Bernhard H. Singsen, MD  
Columbia, Missouri

Ankylosing spondylitis is the most common of a group of related seronegative rheumatic diseases known collectively as the spondyloarthropathies. Other illnesses in this group include Reiter's syndrome, psoriatic arthritis, and the arthropathies of ulcerative colitis and regional enteritis.<sup>1</sup> Recent epidemiologic evidence suggests that these conditions are often concentrated in families, are frequently associated with the HLA-B27 tissue-typing antigen, are more common than previously recognized, and are easily confused with other diseases.<sup>2</sup> A case report of a young boy with spondyloarthropathy will serve to highlight the clinical features at onset, diagnostic problems, family involvement, and the clinical course.

## CASE REPORT

A 12-year-old boy was seen at the University of Missouri Family Medical Care Center in December 1980 because of left hip pain. The pain worsened with exercise, awakened him at night, and was associated with morning stiffness. There was no personal or family history of tendonitis, rash, fever, ocular complaints, gastrointestinal symptoms, or involvement of other joints. Two years previously he had a similar complaint, diagnosed as "toxic synovitis," which resolved spontaneously. Three weeks previously, an orthopedist diagnosed "traumatic sacroiliitis."

The general physical examination was normal, except that his height and weight were below the third percentile. The ranges of motion of all joints, including the left hip, were normal. No effusion, synovial thickening, or warmth were found. Tenderness to percussion over the left sacroiliac joint was elicited.

Upon referral, a pediatric orthopedist found a normal sedimentation rate, white blood cell count, and hemoglobin level; antinuclear antibodies and rheumatoid factor were absent. Roentgenograms of the spine, sacroiliac joints, and hips were normal, as was a left hip arthrogram. A pediatric rheumatologist then saw the boy and made a presumptive diagnosis of spondyloarthropathy on the basis of recurrent arthritis in the lower extremities in a male patient with associated sacroiliitis; a test for HLA-B27 was positive. The boy was begun on aspirin, 10 grain four times a day, with marked improvement. He was instructed in posture and physical therapy. History from the father revealed long-standing problems with his shoulders, low back, and parasternal joints. A maternal aunt and grandmother were also both subsequently found to have psoriasis.

Over the next year the boy experienced severe, transient arthritis in the left third and fourth metacarpophalangeal joints and left third metatarsophalangeal joint; however, back pain did not recur. Tolmetin, 200 mg four times a day, was added to his treatment, with good response. During the second year of illness he developed ankle arthritis, fingernail pitting, onycholysis, and a scaly, erythematous eruption over his knees; a diagnosis of psoriasis was confirmed. Indomethacin, 25 mg half strength, was added to ameliorate worsening morning stiffness. The boy's height progressively rose to the 25th percentile. He has remained active in sports and is mostly pain-free.

The patient's father developed multifocal costochondritis in 1981 and was also found to be HLA-B27 positive. The patient's younger brother has been

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From the Departments of Family and Community Medicine, and Child Health and Medicine, Division of Pediatric Rheumatology, University of Missouri-Columbia, Columbia Missouri. Requests for reprints should be addressed to Dr. Harold A. Williamson, Jr., University of Missouri Health Sciences Center, One Hospital Drive, Columbia MO 65212.

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evaluated twice for plantar fasciitis and recurrent neck pain.

## DISCUSSION

The spondyloarthropathies are a group of chronic inflammatory diseases affecting primarily the axial skeleton and lower extremities, most frequently becoming evident in older children or young adults.<sup>1,2</sup> Ankylosing spondylitis is the prototype; other rheumatoid factor-negative spondyloarthropathies include Reiter's syndrome, psoriatic arthritis, the enteropathic arthropathies, and various reactive arthritides—all of which are associated to varying degrees (40 to 90 percent) with the HLA-B27 antigen.

Ankylosing spondylitis is the most common cause of arthritis in boys and young men and has a prevalence equal to rheumatoid arthritis.<sup>1</sup> HLA-B27 is present in 6 to 8 percent of white populations and in 4 percent of blacks. Twenty percent of the HLA-B27-positive male population will eventually develop symptomatic spondylitis,<sup>2,3</sup> and a similar percentage of the female population will have distinctive radiologic changes but less specific physical complaints. The sex distribution is therefore equal, although spondyloarthropathy is diagnosed less frequently in women. Spondyloarthropathies thus have a prevalence of 1 to 1.5 percent in the general population; however, they are diagnosed much less frequently, probably because of under-recognition, the mild nature of the illnesses in many patients, and the apparent nonspecificity of complaints. A family history of spondyloarthropathy, related symptoms, or associated illnesses may be elicited in nearly one half of affected children.<sup>4</sup>

The pathologic hallmark of the spondyloarthropathies in children and adults is enthesopathy—inflammation of the bony attachments of ligaments and tendons.<sup>4</sup> In more severely affected persons, erosive osteitis and periostitis may develop; associated rapid and extensive healing of these lesions often causes new bone formation along ligaments, which may result in bony spurs such as at the heel. Ultimately this process in the spinal ligaments results in the so-called "bamboo spine."

Diagnostic criteria for ankylosing spondylitis often have limited utility, especially in the early stages of illness. Decreased mobility of the lumbar spine, low back pain, reduced chest expansion, and radiographic changes in the sacroiliac joints confirm the diagnosis in adults according to the "Rome" and "New York" criteria, but these findings may not be evident in the early years of disease, particularly in children.<sup>4</sup> Hence, many experts rely on the simple evidence of symptomatic sacroiliitis. Testing for HLA-B27 is positive in 70 to 80 percent of children and adults with ankylosing spondylitis and thus may be useful for an early,

presumptive diagnosis. However, the test is not needed if the diagnosis is clinically evident.<sup>5</sup> The frequency of HLA-B27 in other spondyloarthropathies correlates with the presence of arthritis, and ranges from 40 percent in psoriasis and the enteropathic arthropathies to 75 to 90 percent in Reiter's syndrome.

In a preselected population the insidious onset of back pain in a patient younger than 40 years, persisting for at least three months, associated with morning stiffness, and improving with exercise was 95 percent sensitive and 85 percent specific for inflammatory spinal disease.<sup>6</sup> In contrast, about one third of patients with spondyloarthropathies experience peripheral arthritis first, usually as asymmetric pauciarticular involvement of the lower extremities.<sup>7</sup> Enthesopathy and arthritis of the first metatarsal-phalangeal joint is a common presentation, but must be carefully sought.<sup>8</sup> Heel pain, plantar fasciitis, sausage digits, inflammation at the anterior tibial tubercle, costochondritis, and other forms of periostitis also occur frequently. Uveitis, aortitis, and pulmonary fibrosis are nonarticular manifestations that should be looked for. It is also essential, particularly in children, to search for the conjunctivitis and urethritis of Reiter's syndrome; the diarrhea, weight loss, and bloody stools of the enteric arthropathies; and the skin and fingernail changes of psoriasis, as demonstrated in this teenage patient.

The prognosis for the spondyloarthropathies is highly variable. The most severe cases develop spinal ankylosis and become susceptible to vertebral fracture. Severe kyphosis may also occur as a result of chronic poor posture, and peripheral arthritis or enthesitis may be severe enough to limit mobility and function. One half of all patients with ankylosing spondylitis, Reiter's syndrome, psoriatic arthropathy, or the enteric arthropathies become significantly and permanently disabled.

The objective of treatment is to relieve pain, decrease inflammation, and to maintain good posture and function. Nonsteroidal anti-inflammatory agents, beginning with aspirin or tolmetin, adding indomethacin and phenylbutazone as indicated, are useful in diminishing symptoms and altering the disease progression. Salicylates seem to work less well but should be tried first. A firm mattress and thin pillow, along with extension exercises, may ameliorate cervical and thoracolumbar deformities. Swimming is also an excellent form of physical therapy.

Family physicians have an excellent opportunity to diagnose the spondyloarthropathies at an early stage and in different family generations. Ankylosing spondylitis, as well as the other less common spondyloarthropathies, should be considered in persons with low back pain and morning stiffness, or in seronegative asymmetric, pauciarticular arthritis when occurring in boys and young men and in patients with enthesopathy. Often a presumptive diagnosis based on

clinical findings and family history must be made and treatment initiated, as other confirmatory features often occur only late in the disease.

## References

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BRIEF SUMMARY  
**DIABINESE®** (chlorpropamide)  
 TABLETS, USP

## CONTRAINDICATIONS

DIABINESE is contraindicated in patients with:

1. Known hypersensitivity to the drug.
2. Diabetic ketoacidosis, with or without coma. This condition should be treated with insulin.

## WARNINGS

### SPECIAL WARNING ON INCREASED RISK OF CARDIOVASCULAR MORTALITY

The administration of oral hypoglycemic drugs has been reported to be associated with increased cardiovascular mortality as compared to treatment with diet alone or diet plus insulin. This warning is based on the study conducted by the University Group Diabetes Program (UGDP), a long-term prospective clinical trial designed to evaluate the effectiveness of glucose-lowering drugs in preventing or delaying vascular complications in patients with non-insulin-dependent diabetes. The study involved 823 patients who were randomly assigned to one of four treatment groups (*Diabetes*, 19 [supp. 2]:747-830, 1970).

UGDP reported that patients treated for 5 to 8 years with diet plus a fixed dose of tolbutamide (1.5 grams per day) had a rate of cardiovascular mortality approximately 2 1/2 times that of patients treated with diet alone. A significant increase in total mortality was not observed, but the use of tolbutamide was discontinued based on the increase in cardiovascular mortality, thus limiting the opportunity for the study to show an increase in over-all mortality. Despite controversy regarding the interpretation of these results, the findings of the UGDP study provide an adequate basis for this warning. The patient should be informed of the potential risks and advantages of DIABINESE and of alternative modes of therapy.

Although only one drug in the sulfonylurea class (tolbutamide) was included in this study, it is prudent from a safety standpoint to consider that this warning may also apply to other oral hypoglycemic drugs in this class, in view of their close similarities in mode of action and chemical structure.

## PRECAUTIONS

### General

**Hypoglycemia:** All sulfonylurea drugs are capable of producing severe hypoglycemia. Proper patient selection, dosage, and instructions are important to avoid hypoglycemic episodes. Renal or hepatic insufficiency may cause elevated blood levels of DIABINESE and the latter may also diminish glucose tolerance capacity, both of which increase the risk of serious hypoglycemic reactions. Elderly, debilitated or malnourished patients, and those with adrenal or pituitary insufficiency are particularly susceptible to the hypoglycemic action of glucose-lowering drugs. Hypoglycemia may be difficult to recognize in the elderly, and in people who are taking beta-adrenergic blocking drugs. Hypoglycemia is more likely to occur when caloric intake is deficient, after severe or prolonged exercise, when alcohol is ingested, or when more than one glucose-lowering drug is used.

Because of the long half-life of chlorpropamide, patients who become hypoglycemic during therapy require careful supervision of the dose and frequent feedings for at least 3 to 5 days. Hospitalization and intravenous glucose may be necessary.

**Loss of control of blood glucose:** When a patient stabilized on any diabetic regimen is exposed to stress such as fever, trauma, infection, or surgery, a loss of control may occur. At such times, it may be necessary to discontinue DIABINESE and administer insulin.

The effectiveness of any oral hypoglycemic drug, including DIABINESE, in lowering blood glucose to a desired level decreases in many patients over a period of time, which may be due to progression of the severity of the diabetes or to diminished responsiveness to the drug. This phenomenon is known as secondary failure, to distinguish it from primary failure in which the drug is ineffective in an individual patient when first given.

## ADVERSE REACTIONS

**Hypoglycemia:** See PRECAUTIONS section.

**Gastrointestinal Reactions:** Cholestatic jaundice may occur rarely. DIABINESE should be discontinued if this occurs. Gastrointestinal disturbances are the most common reactions, nausea has been reported in less than 5% of patients, and diarrhea, vomiting, anorexia, and hunger in less than 2%. Other gastrointestinal disturbances have occurred in less than 1% of patients including proctocolitis. They tend to be dose related and may disappear when dosage is reduced.

**Dermatologic Reactions:** Pruritus has been reported in less than 3% of patients. Other allergic skin reactions, e.g., urticaria and maculopapular eruptions have been reported in approximately 1% or less of patients. These may be transient and may disappear despite continued use of DIABINESE; if skin reactions persist the drug should be discontinued.

Porphyria cutanea tarda and photosensitivity reactions have been reported with sulfonylureas. Skin eruptions rarely progressing to erythema multiforme and exfoliative dermatitis have also been reported.

**Hematologic Reactions:** Leukopenia, agranulocytosis, thrombocytopenia, hemolytic anemia, aplastic anemia, pancytopenia and eosinophilia have been reported with sulfonylureas.

**Metabolic Reactions:** Hepatic porphyria and disulfiram-like reactions have been reported with DIABINESE.

**Endocrine Reactions:** On rare occasions, chlorpropamide has caused a reaction identical to the syndrome of inappropriate antidiuretic hormone (ADH) secretion. The features of this syndrome result from excessive water retention and include hyponatremia, low serum osmolality, and high urine osmolality.

## DOSE AND ADMINISTRATION

There is no fixed dosage regimen for the management of diabetes mellitus with DIABINESE or any other hypoglycemic agent. In addition to the usual monitoring of urinary glucose, the patient's blood glucose must also be monitored periodically to determine the minimum effective dose for the patient, to detect primary failure, and to detect secondary failure. Glycosylated hemoglobin levels may also be of value in monitoring the patient's response to therapy.

The total daily dosage is generally taken at a single time each morning with breakfast. Occasionally cases of gastrointestinal intolerance may be relieved by dividing the daily dosage. A LOADING OR PRIMING DOSE IS NOT NECESSARY AND SHOULD NOT BE USED.

**Initial Therapy:** 1. The mild to moderately severe, middle-aged, stable, non-insulin-dependent diabetic patient should be started on 250 mg daily. Older patients should be started on smaller amounts of DIABINESE, in the range of 100 to 125 mg daily.

2. No transition period is necessary when transferring patients from other oral hypoglycemic agents to DIABINESE. The other agent may be discontinued abruptly and chlorpropamide started at once. In prescribing chlorpropamide, due consideration must be given to its greater potency.

Many mild to moderately severe, middle-aged, stable non-insulin-dependent diabetic patients receiving insulin can be placed directly on the oral drug and their insulin abruptly discontinued. For patients requiring more than 40 units of insulin daily, therapy with DIABINESE may be initiated with a 50 per cent reduction in insulin for the first few days, with subsequent further reductions dependent upon the response.

Five to seven days after the initial therapy, the blood level of chlorpropamide reaches a plateau. Dosage may subsequently be adjusted upward or downward by increments of not more than 50 to 125 mg at intervals of three to five days to obtain optimal control. More frequent adjustments are usually undesirable.

**Maintenance Therapy:** Most moderately severe, middle-aged, stable non-insulin-dependent diabetic patients are controlled by approximately 250 mg daily. Many investigators have found that some milder diabetics do well on daily doses of 100 mg or less. Many of the more severe diabetics may require 500 mg daily for adequate control. PATIENTS WHO DO NOT RESPOND COMPLETELY TO 500 MG DAILY WILL USUALLY NOT RESPOND TO HIGHER DOSES. MAINTENANCE DOSES ABOVE 750 MG DAILY SHOULD BE AVOIDED.

## HOW SUPPLIED

Blue, D'-shaped, scored tablets in strengths of 100 mg, tablet code 393; (100's, NDC # 0663-3930-66; 500's, NDC # 0663-3930-73; and 100 unit dose of 10 x 10, NDC # 0663-3930-41) and 250 mg, tablet code 394; (100's, NDC # 0663-3940-66; 250's, NDC # 0663-3940-71; 1000's, NDC # 0663-3940-82; 100 unit dose of 10 x 10, NDC # 0663-3940-41; and 30's D-Pak, NDC # 0663-3940-30).

**RECOMMENDED STORAGE:** Store below 86°F (30°C).

**CAUTION:** Federal law prohibits dispensing without prescription.

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