

# Children, Sports, and Chronic Disease

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## In brief

Chronic disease afflicts several million children in the United States, many of whom face the additional burden of having their physical activities unnecessarily restricted. Yet sports and exercise can alleviate symptoms as well as improve a child's psychosocial development and quality of life. Physicians should consider prescribing exercise programs for children with cystic fibrosis, congenital heart disease, juvenile rheumatoid arthritis, and asthma. They should also strongly advocate these children's right to engage in whatever levels of physical activity will allow them to reach their potential.

**M**ore than 1 million children in the United States are afflicted with severe chronic disease, and an additional 10 million children have less significant chronic disorders.<sup>1</sup> While the incidence of the more serious illnesses, such as cystic fibrosis and congenital heart disease, seems to have remained relatively stable, survival rates have improved and the number of children with chronic illness in the general population has increased. For example, in 1967, 1.1% of all children from

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*Attention must be given to the psychosocial development of chronically ill children as well as to medical management of the primary disease.*

birth to age 16 suffered from chronic medical problems that restricted their activity, compared with 2.0% in 1981, an increase of 0.9% from approximately 700,000 to 1,200,000 children.<sup>23</sup>

Children with chronic medical problems require comprehensive medical care. Most important is the optimal medical management of the primary disease, but attention must also be given to preventive health care and to the child's psychosocial development and general quality of life. The burden of a chronic disease often can isolate a child from peers, and an overprotective family or school can add to this isolation by excessively restricting the child's physical activities.

Several studies<sup>4,9</sup> have found an incidence of psychosocial problems that is two to three times higher among children with chronic disease than

among healthy controls. A poor self-image, a sense of inferiority, insecurity, hostility, excessive use of denial, excessive dependence, a lack of social and interpersonal skills, and excessive concerns about personal appearance and acceptance by peers are common characteristics and issues.

**Exercise may help chronically ill children to control symptoms and succeed in sports.**

Sports and exercise can provide an opportunity for such

children to gain a sense of accomplishment and independence, to experience peer interaction and acceptance, and to vent aggression. They may approach their disease with a greater motivation to control symptoms so that they can be successful in sports. Add the preventive health benefits of exercise and the potential enjoyment of sports, and it becomes apparent that children with chronic disease should not be unduly restricted from physical activity.

Nevertheless, a large percentage of children with a chronic disease are restricted from physical activity. The reasons, in addition to overprotection, include a lack of appropriate information from primary care physicians and the failure of many schools to observe federal legislation that recognizes the rights of these children to an education in the least restrictive environment appropriate to their specific needs.

Passed in 1975 and extended to children and youths aged 3 to 21 in 1980, Pub L No. 94-142 mandates that handicapped children receive an individualized educational program adapted to their specific needs and capabilities. This includes an adapted physical education program. Studies<sup>10-12</sup> have demonstrated that perhaps 75% of children handicapped by a chronic disease are not served by such programs, and only about 30% of parents are even aware of their children's rights.

This article discusses four chronic diseases—cystic fibrosis, congenital heart disease, rheumatoid arthritis, and asthma—for which physical training has been employed as a therapeutic modality. Although results vary, in each case there is objective evidence of benefit.

I hope that after reviewing the issues surrounding physical activity for children with chronic disease, physicians and other health professionals will become strong and forceful advocates for promoting sports and exercise for these children.

### Cystic Fibrosis

Cystic fibrosis, a disease of the mucus-secreting glands of the lungs, pancreas, and all other exocrine glands, occurs in 1 of 2,000 live births among whites and in 1 of 17,000 live births among blacks. It is the most frequent lethal genetic disease affecting white children.

Symptoms result primarily from obstructive pulmonary disease with recurrent infection, pancreatic achylia with malabsorption, biliary cirrhosis, excessive sodium secretion in sweat with heat-related illnesses, and later, sterility.<sup>13,14</sup> The diagnosis is made by a positive sweat test found in 98% of patients.

Death usually results from recurrent pulmonary infection and chronic obstructive pulmonary disease. These conditions create progressive physiologic changes that include decreasing oxygen saturation secondary to abnormal perfusion-to-ventilation distribution, decreasing vital capacity and expiratory flow rates, and increasing total lung capacity. Survival rates have improved progressively over the last several decades and—excluding infant deaths from meconium ileus—half of cystic fibrosis victims survive to 23 years, and more than one third of these indi-

viduals live beyond the age of 30 years.

Children with cystic fibrosis experience psychosocial problems more frequently than do healthy children, though it is arguable whether such problems occur as frequently as the 70% incidence of insecurity, anxiety, and emotional disturbance that Tropauer et al<sup>15</sup> found by analyzing drawings done by children with the disease. Drotar et al<sup>16</sup> did not find the development of anxiety, depression, or maladjustment to be inevitable in children with cystic fibrosis, but rather found that many can cope with their disease and make a psychologically appropriate adaptation.

**Exercise Response.** The exercise response of children with cystic fibrosis is generally abnormal. This seems to be related to a combination of a ventilatory abnormality, poor nutritional status, and chronic infection. Cardiac function appears to be normal until severe disease is present. The most consistent abnormal physiologic response is excessive ventilation for a given work load or oxygen consumption. The hyperventilation is a compensatory response to increased alveolar dead space. As the disease progresses, excess total ventilation cannot compensate for decreased alveolar ventilation, and patients demonstrate elevations in end-tidal carbon dioxide pressure and arteriolar desaturation during exercise. Other physiologic abnormalities that are observed as the disease progresses include an elevated heart rate, an abnormal ventilation-to-perfusion distribution, a high caloric expenditure for ventilation, a low maximum work capacity, and possibly diminished muscular strength.

Cropp et al<sup>17</sup> suggest that patients with cystic fibrosis should not be permitted to exercise at any work level higher than that which produces 5% desaturation. Patients at risk for desaturation may be predicted by a forced expiratory volume in 1 sec (FEV<sub>1</sub>) of less than 60% or by a pulmonary function score of greater than 12. (The pulmonary function score is developed by grading pulmonary function tests that include vital capacity, FEV<sub>1</sub>, forced expiratory flow during the middle half of the forced vital capacity, residual volume, specific airway conductance, and arterial oxygen saturation between normal [0] and severe [3]. (Normative values for the tests can be found in the article by Cropp et al.<sup>17</sup>) Should a low FEV<sub>1</sub> or a

high pulmonary function score exist, an exercise stress test should be performed before exercise recommendations are made.<sup>17-20</sup>

Orenstein et al<sup>21</sup> evaluated a 3-month running program using 31 cystic fibrosis patients aged 10 to 30 years, 10 of whom served as controls. Prior to exercise, the mean maximum oxygen consumption was 33.6 ml·kg<sup>-1</sup>·min<sup>-1</sup>, less than the expected range of 40 to 50 ml·kg<sup>-1</sup>·min<sup>-1</sup>. Maximum heart rate was also diminished. The exercise group showed improvement in exercise tolerance, maximum oxygen consumption, respiratory muscle endurance, and heart rate response at submaximal work loads. Over the course of the study, the FEV<sub>1</sub> diminished in the control group but not in the exercise group. The researchers concluded that the low exercise tolerance of patients with cystic fibrosis may result from a lack of training or may be disease-limited, or both, and that these patients show significant improvement with exercise training. No adverse effects from the program were noted.

Keens et al<sup>22</sup> saw a 57% improvement in ventilatory muscle endurance in seven patients engaged in a swim and exercise program. Orenstein et al<sup>21</sup> and Keens et al<sup>22</sup> both suggest that the work loads for exercise be established at 60% to 85% of peak heart rate.

**Exercise Program.** Physical training seems to improve exercise tolerance in patients with cystic fibrosis, and this improvement should translate into improved function in daily activities and in the capacity to engage in recreational sports. With the added potential benefits of improved respiratory clearing of mucus from deep ventilation and gains in self-image and psychosocial development, physical training should be considered as an adjunct to the care of cystic fibrosis patients.

After appropriate pretesting, an aerobic program of sufficient intensity to produce a heart rate from 60% to 80% of maximum should be performed for 15 to 20 minutes, 3 times a week. High-repetition, low-weight strength exercises can be added to the program, as can exercises to improve

**The generally abnormal exercise response of children with cystic fibrosis seems related in part to poor nutritional status.**

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ventilating muscle endurance. If aerobic endurance permits participation in specific sports, these should be encouraged so that the child can continue physical activity in a recreational setting.

The physician should explain how to prevent heat-related illness. As the disease progresses, care must be taken to diminish the work load to avoid arteriolar desaturation greater than 5%.

### **Congenital Heart Disease**

Congenital heart disease represents a broad variety of anatomic defects, over one third of which are serious and require intervention within the first year of life. The incidence of congenital heart disease is 8 per 1,000 live births. The most common serious defects include ventricular septal defect (15.7% of congenital heart problems, 0.4/1,000 live births); D-transposition of great arteries (9.9%, 0.2/1,000 live births); tetralogy of Fallot (8.9%, 0.2/1,000 live births); coarctation of the aorta (7.5%, 0.2/1,000 live births); and hypoplastic left heart (7.4%, 0.2/1,000 live births).<sup>23,24</sup> Due to improvements in surgical intervention and drug therapy, mortality and morbidity rates have improved significantly.

**Although children with heart disease face potential hazards from intense exercise, they may benefit from specific training programs.**

These children often must be restricted from physical activity prior to corrective surgery, and they frequently do not engage in sports and recreation after repair because of residual disease, overprotection, lack of skills, and poor conditioning for sports activities. Children with congenital heart disease have psychosocial problems similar to those of other children with chronic diseases.<sup>25,26</sup>

**Exercise Response.** The exercise tolerance of children with significant hemodynamic lesions has been found to be abnormal in the preoperative state.<sup>27</sup> This may be due to the intrinsic cardiac defect or to a lack of exercise activities resulting from restrictions placed on the child. Postoperative exercise testing has also revealed a lower than normal maximum work capacity and maximum oxygen consumption, despite an excellent

hemodynamic response.

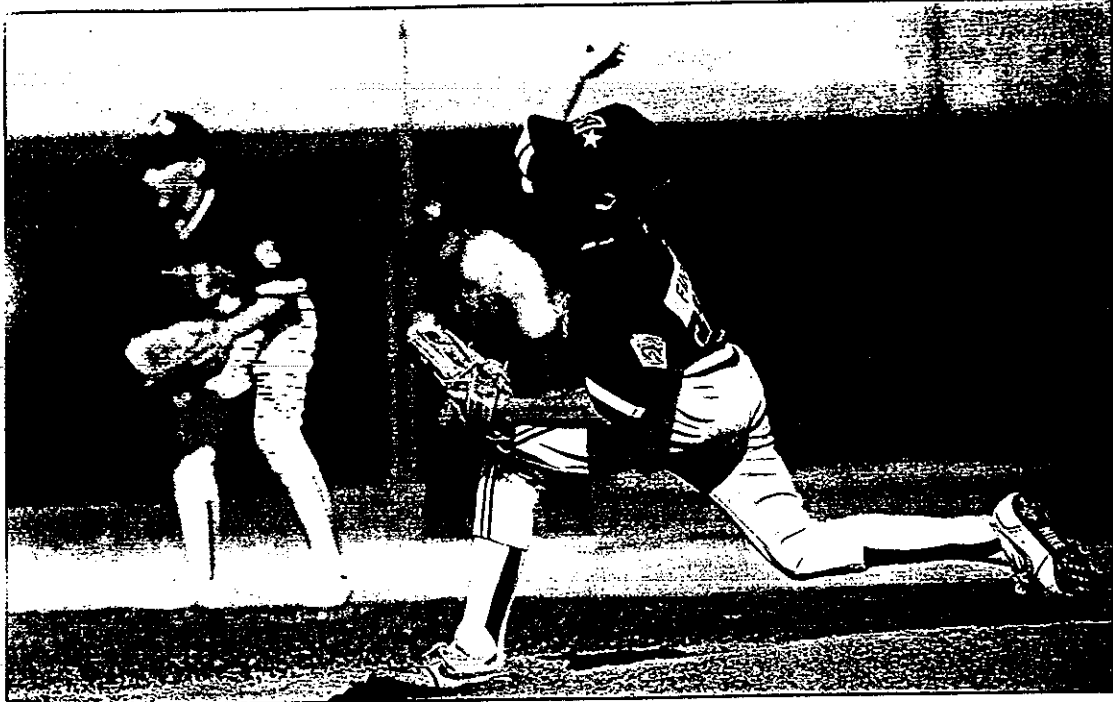
Studies (cited later) have shown not only that children with heart disease face potential hazards from participating in intense physical activity, but also that they may benefit from specific training programs. Tetralogy of Fallot and transposition of the great arteries illustrate these points.

**Tetralogy of Fallot.** Patients who have had a surgical correction for tetralogy of Fallot may have a residual pulmonary stenosis with a gradient of greater than 20 mm Hg (36%), pulmonary insufficiency (70%), ventricular septal defect (20%), and biventricular dysfunction. The latter may be related to the right ventriculotomy and the presence of an outflow patch.<sup>28</sup> Additionally, complete heart block and ventricular arrhythmias may occur.

The response to exercise is often abnormal and includes a reduction in maximum work capacity and maximum oxygen consumption, and a suboptimal heart rate response.<sup>29</sup> The residual pulmonary stenosis gradient may increase during exercise, and there may be biventricular dysfunction, indicated by suboptimal increases in stroke volume and cardiac output in response to increases in end-diastolic pressure in the right and left ventricles.<sup>30,31</sup>

Despite these apparent hemodynamic abnormalities, exercise training of postoperative patients has been beneficial. Bradley et al<sup>32</sup> found significant improvements in peak systolic blood pressure, treadmill time, and maximum oxygen consumption in five patients who trained by walking, running, jumping rope, and engaging in modified aerobic dance at work loads of 60% to 80% of maximum heart rate. While Ruttenberg et al<sup>33</sup> found no significant improvement in three aerobically trained patients, my colleagues and I<sup>34</sup> found a significant increase in maximum work capacity in 16 postoperative tetralogy-of-Fallot patients as well as significant reductions in pulse and oxygen consumption at submaximum work loads. No adverse effects were noted from the programs, some of which were supervised by medical personnel while others were performed at home under parental supervision.

A complete preprogram assessment—including an echocardiogram, Holter monitor, and cardiopulmonary stress test—is essential, and all our



*In determining which sports activities are safe for a child with congenital heart disease, the physician must consider the child's exercise capacity and existing or potential residual abnormalities.*

patients had postoperative cardiac catheterization. These tests are necessary to detect residual abnormalities and ventricular rhythm disturbances. A 5% overall mortality rate occurs among postoperative tetralogy-of-Fallot patients and a 33% mortality rate among patients with proven ventricular dysrhythmia. Those patients who develop a ventricular arrhythmia are usually older at the time of initial evaluation and subsequent surgery, and they show ventricular extrasystole on standard electrocardiograms.<sup>35,36</sup>

**Transposition of the Great Arteries.** Advances in the surgical correction of transposition of the great arteries has significantly improved the morbidity and mortality of children with this lesion. Tests of the exercise tolerance of postoperative patients have demonstrated reductions in work capacity, maximum oxygen consumption, systolic blood pressure, and right and left ventricular compliance.<sup>37-38</sup> When Vaccaro et al<sup>39</sup> tested five postoperative patients using a medically supervised aerobic training program, they found a de-

crease in body fat and an increase in maximum oxygen consumption and treadmill time. Ruttenberg et al<sup>39</sup> found that three postoperative patients improved their treadmill time after training.

Like patients who have tetralogy of Fallot, these children require complete cardiopulmonary assessment before beginning any training program; pretraining assessments have found such problems as sick sinus syndrome, atrial tachyarrhythmias, and exercise-induced supraventricular tachycardia and atrial and supraventricular premature beats. Additional abnormalities that can limit exercise tolerance include residual tricuspid regurgitation, atrial septal defect, and obstruction of systemic or pulmonary venous return, as well as the requirement of the right ventricle to function as the systemic ventricle.<sup>40,41</sup>

**Exercise Program.** The preceding discussion of two congenital cardiac lesions stresses both the potential benefits of training and the caution that must be exercised to ensure safety. While further studies are needed to more fully delineate the ex-

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ercise potential of children with these and other congenital heart diseases, improvement in exercise tolerance also has been demonstrated following surgery in patients with aortic stenosis<sup>33</sup> and ventricular septal defect.<sup>34</sup> Exercise-induced abnormalities have been noted postoperatively in children with aortic stenosis<sup>32</sup> and coarctation of the aorta.<sup>35</sup> Thus, consideration should be given to physical training programs for children with congenital heart disease to allow them to reach their maximum functional potential. However, a full diagnostic evaluation should precede the program, and the program must be specifically prescribed and supervised. In some cases, the patient's parents may eventually supervise the program.

**Physicians cannot assume that schools will provide physically stimulating recreational activities for children with rheumatoid arthritis.**

Aerobic training activities should be designed to produce 60% to 75% of maximum heart rate for 10 to 20 minutes three times per week, and the program should incorporate activities that will improve body composition, flexibility, and muscular strength. After aerobic training, the child's exercise capacity, the original lesion, and existing or potential residual abnormalities should all be considered in determining which recreational activities and sports are safe for a given child.<sup>44</sup> While it is important to delineate what a child should *not* do, it is equally important to carefully instruct both the child and the parents in what the child *can* do.

### Juvenile Rheumatoid Arthritis

Juvenile rheumatoid arthritis afflicts approximately 250,000 children in the United States, occurring in 2.2 cases per 1,000 live births. The disease is characterized by intermittent exacerbations and remissions of polyarticular arthritis (25% to 50%), pauciarticular arthritis (36% to 45%), or systemic arthritis (10% to 30%), and by an eventual resolution with minimal residual deformity in 75% of the cases. Twenty-five percent of children with juvenile rheumatoid arthritis will develop residual deformity, and 10% will have significant disabilities.<sup>45,46</sup>

Children who have rheumatoid arthritis share the problems of other children with chronic medical problems: They need frequent medical attention, they must comply with prescribed therapy and prescriptions, they have to learn to adapt to functional limitations, and they develop psychosocial problems from living with their disease.

The psychosocial problems of childhood rheumatoid arthritis have been well described, and probably result from feelings of inferiority and being different. They can result in a low self-image, depression, behavior problems, disturbed relationships, anxiety, social withdrawal, excessive denial, overdependence, and subconscious hostility. These problems may not be related to the severity of the disease; males appear to be affected more often than females, and the longer the disease and the more stable its course, the more able the child is to develop coping skills.<sup>47-50</sup>

**Exercise Response.** It is apparent that these children require a broad range of professional services. However, current data seem to indicate that the potential benefits of sports and exercise-related recreational activities tend to be overlooked.

Because juvenile rheumatoid arthritis has a remitting course, and because its victims frequently show no obvious deformity or cognitive impairment, these children often are not served by Pub L No. 94-142. Parents may sacrifice special services available in alternative schools to keep their children in a mainstream school setting.

For example, Stoff et al<sup>51</sup> found that of 64 school-age children with rheumatoid arthritis, 25% had problems with handwriting, 41% with standing in line, 48% with climbing stairs, and 36% with participating in physical education; yet only 18% of these children received school-based physical therapy, and only 13% received an adaptive physical education program. Whitehouse et al<sup>52</sup> found that of 135 children with rheumatoid arthritis, 19% received no physical education, 8% attended irregularly, and only 15% had individual educational programs designed for their special needs. Interestingly, only 29% of the parents knew of Pub L No. 94-142.

These studies make it clear that physicians cannot assume that schools will provide either physical therapy or physically stimulating recre-

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recreational activities for children with rheumatoid arthritis, and that they must help educate parents regarding the right of children with chronic diseases to a complete educational experience.

While further studies are needed, it seems reasonable to think that exercise and recreational activities could benefit children with rheumatoid arthritis. If appropriately designed and implemented when the disease is not acute, such activities should enhance the children's psychosocial development and improve their general health and quality of life.

**Exercise Program.** Further studies also are required to determine the effect of various forms of exercise and sports on pathologic joint inflammation. Currently, physical therapy programs for arthritic children include increasing or maintaining range of motion to prevent deformity, increasing or maintaining strength to avoid atrophy, improving independence in daily activities, increasing cardiovascular and muscle endurance, and correcting posture.<sup>53</sup> Physical therapists are available to implement these programs, which should then be performed daily for optimal results. For this reason, most physical therapy programs encourage recreational activities that will keep the arthritic child active and that promise high compliance.

While physicians must carefully admonish these children to avoid pain, obtain appropriate rest, and avoid activities that will load acutely inflamed joints, they should also provide children and their parents with instructions for engaging in controlled exercise and sports activities that can support the multiple goals of a rehabilitation program. They should also act as advocates to ensure that schools provide these children with appropriate exercise opportunities.

### Asthma

Asthma is a common chronic childhood disease that affects up to 8 million children episodically and 2 million children chronically. It is characterized by bronchospasm and excessive mucus production that results in airway obstruction. When asthma is severe, hypercapnia and oxygen desaturation can occur. The latter is caused by a ventilation-to-perfusion imbalance. Asthma can be classified as:

- intermittent (characterized by episodes of less than 5 days per month);
- chronic (characterized by lack of extended symptom-free periods and by pathologic changes that include smooth muscle hypertrophy, cellular infiltration, and impaired mucociliary clearance);
- seasonal (provoked by inhalants at specific times of the year).<sup>54-58</sup>

Children with asthma commonly have psychosocial problems that appear to be related to the severity of the disease.<sup>59</sup>

**Exercise Response.** The exercise tolerance of asthmatic children varies greatly. Using a bicycle ergometer, Strunk et al<sup>60</sup> demonstrated that the work capacity of 90 children with moderate to severe asthma was between 15% and 120% of normal, with 45% of the children below normal and 5% borderline. Surprisingly, exercise tolerance was not related to the severity of the disease, hospitalizations, steroid use, the presence of exercise-induced asthma, or a history of respiratory failure. Psychosocial maladjustment was the single variable that accounted for the variations in cardiopulmonary fitness. The authors hypothesized that poor psychological adaptation can inhibit children from participating in exercise-related recreational activities, which can further increase maladjustment and diminish cardiovascular fitness. This study associates psychosocial maladjustment with functional disability in a child with a chronic disease. It also emphasizes the need for comprehensive medical care to permit children to reach their optimal functional potential.

The response of asthmatic children to physical fitness programs has been encouraging. Petersen et al<sup>61</sup> trained 20 boys aged 8 to 13 for 18 months, 1 hour per day, 3 days per week, with calisthenics, relay games, sports skills, and gymnastic stunts. The researchers found improvement in all physical fitness parameters and in vital capacity; a decrease in school absences; and improved sociabil-

**Poor psychological adaptation can inhibit asthmatic children from participating in exercise-related recreational activities and thus lead to further maladjustment and diminished cardiovascular fitness.**

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ity, self-assertion, and acceptance by peers. Orenstein et al<sup>62</sup> employed a running program to train 23 children aged 6 to 16 for 4 months, 30 minutes per day, 3 days per week. They found a 9% improvement in work capacity, a 15% improvement in maximum oxygen consumption, and a decrease in heart rate for submaximal work. The authors found no change in the severity of the disease or in pulmonary function studies.

Ludwick et al<sup>63</sup> trained a group of 65 severely asthmatic children aged 8 to 17 years for 5 days per week with a 12-minute workout on a bicycle ergometer. Only children whose work capacity was less than 85% of normal were included in the study. Of those children who were less than two standard deviations below their expected work capacity, 84% were able to reach normal levels. Five of the patients were tested for maximum oxygen consumption, and all showed improvement. The severity of the disease did not predict which children would initially be below the expected work ability, nor did it predict those who would improve. No changes were noted in spirometry or pulmonary function tests, and the most important variable for predicting improvement was remaining in the program for more than 6 weeks. Bundgaard et al<sup>64</sup> found a decreased use of medication after training, and Sly et al<sup>65</sup> noted a reduction in the number of days of wheezing, but improvement of the clinical course of asthma has not been observed consistently.

Breathing exercises to help asthmatic children voluntarily use the abdominal muscles, the accessory muscles of respiration, and the extensors and flexors of the vertebral column, and to properly position the shoulder girdle have produced some benefits. However, this may result more from a sense of psychological control and relaxation than from physiologic improvement.<sup>66</sup> Isocapnic hyperventilation with increased minute ventilation volumes and breathing against inspiratory resistance can increase the endurance and strength of the ventilatory muscles.<sup>67</sup>

Physical fitness training for asthmatic children has often raised the concern that the program would be complicated by the development of exercised-induced asthma. This common problem arises in 70% to 90% of known asthmatics and in

35% to 45% of nonasthmatic children with atopic problems. The characteristics of bronchospasm induced by exercise have been well described, as have therapeutic modalities for controlling this problem.<sup>68,69</sup> Activities that are thought to be most asthmogenic include (in decreasing order) running, cycling, walking, and swimming,<sup>70,71</sup> though the level of ventilation and not the specific activity may be the critical factor.<sup>72</sup>

In studies of physical training programs for asthmatics (cited earlier), the problem of exercise-induced bronchospasm was well controlled. Studies that have attempted to evaluate an improvement in exercise-induced asthma as a result of training have revealed conflicting results. Henriksen and Nielson<sup>73</sup> trained 42 children 90 minutes per day, 2 days per week for 6 weeks, and found that the exercise-induced reduction in peak expiratory flow rate fell from 44% to 30%. Fitch et al<sup>74</sup> found no change in children engaged in a swim program, and Bundgaard et al<sup>75</sup> found no improvement in adults doing calisthenics.

**Exercise Program.** Physical training programs appear to be beneficial for children with asthma. It is yet to be fully determined if these programs modify the severity of the disease, improve exercise-induced asthma, decrease medication requirements, or improve pulmonary function tests, but they do seem to improve the psychosocial status of the child and reestablish normal levels of physical work capacity.

Ideal programming should incorporate all the components of health-related physical fitness and provide an appropriate aerobic stimulus. Activities to increase thoracic mobility, such as throwing, should be included in the program, and exercises to improve ventilatory muscle endurance should be considered.

The exercise environment should be warm, humid, and free of known allergens. In cold, dry environments, exercisers should wear a face mask or scarf. If exercise-induced bronchospasm becomes a problem, appropriate medication should be prescribed, and activities of moderate intensity but short duration should be recommended. The child may take advantage of the 40-minute refractory period after a bout of exercise-induced asthma.<sup>76,77</sup> During this time, he or she could perform

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# TOLECTIN<sup>®</sup> (tolmetin sodium) 200 (200 mg tablets) / DS (400 mg capsules) / 600 (600 mg tablets)

The following is a brief summary only. Before prescribing, see complete prescribing information in TOLECTIN product labeling.

**Contraindications:** Anaphylactoid reactions have been reported with TOLECTIN as with other nonsteroidal anti-inflammatory drugs. Because of the possibility for cross-sensitivity, TOLECTIN should not be given to patients in whom aspirin and other nonsteroidal anti-inflammatory drugs (particularly zomepirac sodium) induce symptoms of asthma, rhinitis, urticaria, or other symptoms of allergic or anaphylactoid reactions. Patients experiencing anaphylactoid reactions on TOLECTIN should be treated with conventional therapy, such as epinephrine, antihistamine and/or steroids.

**Warnings:** *Risk of GI Ulceration, Bleeding and Perforation with NSAID Therapy:* Serious gastrointestinal toxicity such as bleeding, ulceration, and perforation, can occur at any time, with or without warning symptoms, in patients treated chronically with NSAID (Nonsteroidal Anti-inflammatory Drug) therapy. Although minor upper gastrointestinal problems, such as dyspepsia, are common, usually developing early in therapy, physicians should remain alert for ulceration and bleeding in patients treated chronically with NSAIDs even in the absence of previous GI tract symptoms. In patients observed in clinical trials of several months to 2 years duration, symptomatic upper GI ulcers, gross bleeding, or perforation appear to occur in approximately 1% of patients treated for 3 to 6 months, and in about 2% to 4% of patients treated for 1 year. Physicians should inform patients about the signs and/or symptoms of serious GI toxicity and what steps to take if they occur.

Studies to date have not identified any subset of patients not at risk of developing peptic ulceration and bleeding. Except for a prior history of serious GI events and other risk factors known to be associated with peptic ulcer disease, such as alcoholism, smoking, etc., no risk factors (eg, age, sex) have been associated with increased risk. Elderly or debilitated patients seem to tolerate ulceration or bleeding less well than other individuals and most spontaneous reports of fatal GI events are in this population. Studies to date are inconclusive concerning the relative risk of various NSAIDs in causing such reactions. High doses of any NSAID probably carry a greater risk of these reactions, although controlled clinical trials showing this do not exist in most cases. In considering the use of relatively large doses (within the recommended dosage range), sufficient benefit should be anticipated to offset the potential increased risk of GI toxicity.

**Precautions:** Patients who develop visual disturbances during treatment with TOLECTIN should have ophthalmologic evaluations and follow-up.

Cases of acute interstitial nephritis with hematuria, proteinuria, and occasionally nephrotic syndrome have been reported. Closely monitor patients with impaired renal function; they may require lower doses.

In patients with prerenal conditions leading to a reduction of renal blood flow or blood volume, administration of an NSAID may precipitate overt renal decompensation. Patients at greatest risk are those with heart failure, liver dysfunction, those taking diuretics, and the elderly.

TOLECTIN prolongs bleeding time. Patients who may be adversely affected by prolongation of bleeding time should be carefully observed when TOLECTIN is administered.

In patients receiving concomitant TOLECTIN-steroid therapy, any reduction in steroid dosage should be gradual to avoid the possible complications of sudden steroid withdrawal.

TOLECTIN should be used with caution in patients with compromised cardiac function, hypertension, or other conditions predisposing to fluid retention.

The antipyretic and anti-inflammatory activities of the drug may reduce fever and inflammation, thus diminishing their utility as diagnostic signs in detecting complications of presumed noninfectious, noninflammatory painful conditions.

A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be evaluated for evidence of the development of more severe hepatic reactions while on therapy with TOLECTIN. Severe hepatic reactions, including jaundice and fatal hepatitis, have been reported with TOLECTIN as with other nonsteroidal anti-inflammatory drugs. Although such reactions are rare, if abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (eg, eosinophilia, rash), discontinue TOLECTIN.

**Carcinogenesis, Mutagenesis, Impairment of Fertility—**Tolmetin sodium did not possess any carcinogenic, mutagenic potential, or impairment of fertility in standard *in vitro* tests and/or *in vivo* tests in animals. Effects on parturition (including increased incidences of dystocia and delayed parturition) have been shown, however, as with other prostaglandin inhibitors.

**Pregnancy—**TOLECTIN has not been studied in pregnant women. Drugs in this class have known effects on the fetal cardiovascular system which may cause constriction of the ductus arteriosus in utero during the third trimester of pregnancy, which may result in persistent pulmonary hypertension of the newborn. Therefore, TOLECTIN should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Nursing Mothers—**Because TOLECTIN is secreted in human milk, nursing should not be undertaken while a patient is on this drug.

**Pediatric Use—**The safety and effectiveness of TOLECTIN for children under 2 years of age have not been established.

**Drug Interactions—**Increased prothrombin time and bleeding have been reported in patients on concomitant TOLECTIN and warfarin therapy; caution should be exercised when administering TOLECTIN to patients on anticoagulants.

Caution should be used if TOLECTIN is administered concomitantly with methotrexate. TOLECTIN and other nonsteroidal anti-inflammatory drugs have been reported to reduce the tubular secretion of methotrexate in an animal model, possibly enhancing the toxicity of methotrexate.

**Laboratory Tests—**Because serious GI tract ulceration and bleeding can occur without warning symptoms, physicians should follow chronically treated patients for the signs and symptoms of ulceration and bleeding and should inform them of the importance of this follow-up (see Warnings—Risk of GI Ulceration, Bleeding and Perforation with NSAID Therapy).

**Drug/Laboratory Test Interaction—**Metabolites of tolmetin in urine have been found to give positive tests for proteinuria using tests which rely on acid precipitation as their endpoint. No interference is seen in the tests for proteinuria using dye-impregnated commercially available reagent strips.

**Drug-Food Interaction—**In a controlled single dose study, administration of TOLECTIN with milk had no effect on peak plasma tolmetin concentration, but decreased total tolmetin bioavailability by 16%. When TOLECTIN was taken immediately after a meal, peak plasma tolmetin concentration and total bioavailability were reduced by 50% and 16%, respectively.

**Information for Patients—**TOLECTIN, like other drugs of its class, is not free of side effects. The side effects of these drugs can cause discomfort and, rarely there are more serious side effects, such as gastrointestinal bleeding, which may result in hospitalization and even fatal outcomes.

NSAIDs (Nonsteroidal Anti-inflammatory Drugs) are often essential agents in the management of arthritis, but they also may be commonly employed for conditions which are less serious.

Physicians may wish to discuss with their patients the potential risks (see Warnings, Precautions, and Adverse Reactions sections) and likely benefits of NSAID treatment, particularly when the drugs are used for less serious conditions where treatment without NSAIDs may represent an acceptable alternative to both the patient and physician.

**Adverse Reactions: Incidence Greater Than 1%—**The following adverse reactions which occurred more frequently than 1 in 100 were reported in controlled clinical trials.

**Gastrointestinal:** Nausea (11%), dyspepsia, gastrointestinal distress, abdominal pain, diarrhea, flatulence, vomiting, constipation, gastritis, and peptic ulcer.

**Body as a Whole:** Headache, asthenia, chest pain

**Cardiovascular:** Elevated blood pressure, edema

**Central Nervous System:** Dizziness, drowsiness, depression

**Metabolic/Nutritional:** Weight gain, weight loss

**Dermatologic:** Skin irritation

**Special Senses:** Tinnitus, visual disturbance

**Hematologic:** Small and transient decreases in hemoglobin and hematocrit not associated with gastrointestinal bleeding have occurred.

**Urogenital:** Elevated SGU, urinary tract infection

\*Reactions occurring in 3% to 9% of patients treated with TOLECTIN. Reactions occurring in fewer than 3% of the patients are unmarked.

**Incidence Less Than 1% (Causal Relationship Probable)—**

**Gastrointestinal:** Gastrointestinal bleeding with or without evidence of peptic ulcer, glossitis, stomatitis, hepatitis, liver function abnormalities

**Body as a Whole:** Anaphylactoid reactions, fever, lymphadenopathy, serum sickness

**Hematologic:** Hemolytic anemia, thrombocytopenia, granulocytopenia, agranulocytosis

**Cardiovascular:** Congestive heart failure in patients with marginal cardiac function

**Dermatologic:** Urticaria, purpura, erythema multiforme, toxic epidermal necrolysis

**Urogenital:** Hematuria, proteinuria, dysuria, renal failure

**Incidence Less Than 1% (Causal Relationship Unknown)—**

**Body as a Whole:** Epistaxis

**Special Senses:** Optic neuropathy, retinal and macular changes

Full directions for use should be read before administering or prescribing.

For information on symptoms and treatment of overdose, see full prescribing information.

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## chronic disease continued

high-intensity exercise while potentially avoiding the precipitation of bronchospasm. Careful instruction may be required to help the child with asthma plan a physical training program or choose a sport, but the potential benefits can allow the child to reach his or her full functional ability.

### Implications for Quality of Life

A chronic disease represents a significant burden for a child. Health professionals must make every effort to control the disease process and permit the child to reach his or her full functional potential. The first priority of care is to intervene optimally in the disease process, but attention must also be given to preventive health care and to the child's psychosocial development and quality of life. Exercise, sports, and recreation can potentially help achieve all of these goals and should be considered in the overall care of the child.

After an appropriate preassessment, a structured and supervised training program should be provided for physically inactive children. Specific recommendations can then be made for sport participation to enhance the recreational component of the activity. Sport selection should take into account aerobic demands, collision potential, dynamic and static components of movement, and the areas of the body most stressed by the activity (ie, throwing vs running sports).<sup>78</sup> A safe competitive level should then be selected; for example, only learning and performing the skills of the sport, recreational participation (nonorganized or organized), or full interscholastic competition.

The American Academy of Pediatrics is currently developing a manual to assist school teachers in providing sports and physical activities for children with chronic diseases. In addition, primary care physicians must assume an aggressive role in promoting physical activity for children with chronic diseases to help ensure that they are not unfairly excluded from health-promoting exercise and sports activities. **FSM**

References cited in this article are available on request from the author at the address below.

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