# The Myocarditis Foundation

## - *Help Us* End Suffering and Sudden Death From Myocarditis

Myocarditis is a medical condition that many people have never heard of, until it strikes them or someone they know - then it can be devastating!

The Myocarditis Foundation, a 501(c)(3) nonprofit organization, was formed in 2005 in response to the dire need for more information about myocarditis, an inflammatory response that attacks the heart muscle leading to cardiac dysfunction and heart failure. The Foundation:

- Founded and led by volunteer, world-renown physicians and patients
- Develops and maintains an array of awareness and educational programs for physicians, researchers, patients, and the public
- Provides the ONLY fellowship-mentor research program funding innovative basic, clinical, and translational myocarditis research studies
- Strives to spark the interests of medical professionals and the public in hopes of advancing the development of accurate, rapid diagnostic methods and safe, effective therapies that minimize or eliminate myocarditis progression to heart dysfunction, failure, and sudden death.

The Myocarditis Foundation is the only nonprofit organization devoting ALL of its resources to saving the lives of those who will be touched by myocarditis. We rely on community support, corporate sponsorships, foundation grants, individual gifts, and countless volunteer hours.

YOUR tax-deductible contribution keeps our *HEARTBEATS* strong …. PLEASE support our work and join us in ending the death and suffering caused by myocarditis!

## What Physicians Know Today (excerpts from published references)

- Myocarditis is an underdiagnosed cause of acute heart failure, sudden death, and chronic dilated cardiomyopathy (2).
- Acute myocarditis is a rare but potentially devastating condition that is most commonly caused by viruses (5).
- Myocarditis is present in 10–50% of heart biopsy samples taken from patients with acute dilated cardiomyopathy (DCM), which is an important cause of heart failure and heart transplantation, with a prevalence of 36.5 per 100 000 in the USA (1).
- The extreme diversity of clinical manifestations has made the true incidence of myocarditis difficult to determine. Recent prospective postmortem data have implicated myocarditis in sudden cardiac death of young adults at rates of 8.6% to 12% (3).
- Myocarditis has been linked to sudden infant death syndrome, because inflammatory infiltrates have been found on autopsies of some victims (6).
- In one study myocarditis was present in 15 of the 90 (17%) of sudden, unexpected deaths of children, suggesting that the prevalence of "silent" myocarditis may be higher in the pediatric population than is generally suspected and may contribute to a significant number of sudden and unexpected deaths in children (4).
- There are approximately 75 deaths per year in athletes between 13-25 years. 89% occur in males, 64% occur in females. Most deaths occur during or immediately after exercise, with causes including Hypertrophic cardiomyopathy: 36%, Coronary anomalies: 17%, Myocarditis: 6%, Arrhythmogenic Right Ventricular Dysplasia: 4%, Long QT Syndrome: 4% (7).
- Myocarditis is the reason for sudden cardiac death in 5-22% of athletes < 35 years of age. For prevention of myocarditis and sudden cardiac death it is recommended to stop elite sport for 4 weeks after an unspecific infection. Whether moderate sport can be started earlier is unclear. When myocarditis is verified, athletes have to withdraw from sport for at least 6 months (8).

## What Still Needs To Be Understood

- Why do some people contract myocarditis when exposed to viruses and other stimuli, and others do not?
- How can myocarditis be detected before developing life-threatening symptoms such as heart failure and dilated cardiomyopathy?

- Why does myocarditis exhibit dramatically different symptoms in different patients?
- How can primary-care and emergency physicians distinguish myocarditis from other more benign conditions that exhibit the same symptoms?
- What is the link between myocarditis and exercise that makes it a contributing factor in sudden death?

## References


**1) The heat is off: immunosuppression for myocarditis revisited**
Leslie T. Cooper*
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Online publish-ahead-of-print 26 June 2009

Non-ischaemic, dilated cardiomyopathy (DCM) is an important cause of heart failure and heart transplantation, with a prevalence of 36.5 per 100 000 in the USA. Depending on the histological or immunohistological criteria employed, myocarditis is present in 10–50% of heart biopsy samples taken from patients with acute non-ischaemic DCM.

When T cell and macrophage number are quantified by immunohistological methods or the definition of myocarditis is broadened to include expression of class II major histocompatability complex antigens and adhesion molecules, myocarditis is present in 40 – 50% of patients with chronic DCM. Of the many known causes of myocarditis, viral infection is perhaps the most important. From 25 to 40% of myocardial samples from patients with chronic, unexplained DCM contain viral genomes. Although a host of viruses have been implicated in myocarditis and DCM, viral infection is not always accompanied by inflammation.

**2) Myocarditis**
Sandeep Sagar MD [a], Prof Peter P Liu MD [b], Prof Leslie T Cooper MD
The Lancet, Volume 379, Issue 9817, Pages 738 - 747, 25 February 2012

Myocarditis is an underdiagnosed cause of acute heart failure, sudden death, and chronic dilated cardiomyopathy. In developed countries, viral infections commonly cause myocarditis; however, in the developing world, rheumatic carditis, *Trypanosoma cruzi*, and bacterial infections such as diphtheria still contribute to the global burden of the disease. The short-term prognosis of acute myocarditis is usually good, but varies widely by cause. Those patients who initially recover might develop recurrent dilated cardiomyopathy and heart failure, sometimes years later. Because myocarditis presents with non-specific symptoms including chest pain, dyspnoea, and palpitations, it often mimics more common disorders such as coronary artery disease. In some patients, cardiac MRI and endomyocardial biopsy can help identify myocarditis, predict risk of cardiovascular events, and guide treatment. Finding effective therapies has been challenging because the pathogenesis of chronic dilated cardiomyopathy after viral myocarditis is complex and determined by host and viral genetics as well as environmental factors. Findings from recent clinical trials suggest that some patients with chronic inflammatory cardiomyopathy have a progressive clinical course despite standard medical care and might improve with a short course of immunosuppression.

**3) Myocarditis - Current Trends in Diagnosis and Treatment**
Jared W. Magnani, MD; G. William Dec, MD

Myocarditis is the end result of both myocardial infection and autoimmunity that results in active inflammatory destruction of myocytes. Its precise characterization and natural history have been limited by the extraordinary variability of its clinical presentations, laboratory findings, and the diversity of etiologies. The relatively low incidence and difficulties in unequivocally establishing a diagnosis have limited the conduct of large-scale, randomized clinical trials to evaluate treatment strategies.

The extreme diversity of clinical manifestations has made the true incidence of myocarditis difficult to determine. Recent prospective postmortem data have implicated myocarditis in sudden cardiac death of young adults at rates of 8.6% to 12%. Furthermore, it has been identified as a cause of dilated cardiomyopathy in 9% of cases in a large prospective series.

In another series of 34 patients with known normal coronary anatomy presenting with symptoms and ECG changes consistent with an acute coronary syndrome, 11 (32%) of the patients were found to have myocarditis on biopsy.

**4) Occurrence of Myocarditis in Sudden Death in Children**
G.R. Noren, 1M.D.; N. A. Stale),, 2M.D.; C. M. Bandt, 3M.D.; and E. L. Kaplan, 1M.D.

Of particular interest is that myocarditis was present in 15 of the 90 (17%) of sudden, unexpected deaths and in only 2 of the 48 violent deaths examined (4%).

One cannot assume that death was the result of the myocarditis in all children who died suddenly and unexpectedly with the findings of an interstitial myocarditis. However, a 17% incidence of myocarditis in this group seems inordinately high and suggests that interstitial myocarditis is present much more frequently than commonly appreciated and may be the primary cause of death resulting from either a fatal arrythmia or cardiac failure secondary to myocardial dysfunction.

This study suggests that the prevalence of "silent" myocarditis may be higher in the pediatric population than is generally suspected and may contribute to a significant number of sudden and unexpected deaths in children, particularly those older than one year of age. The incidence of histologic myocarditis in children dying a violent death is similar to that reported as an incidental finding in adults.

5) **Sudden Death in Young Athletes: Screening for the Needle in a Haystack**
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*Am Fam Physician.* 1998 Jun 1;57(11):2763-2770.

Acute myocarditis is a rare but potentially devastating condition that is most commonly caused by viruses. Coxsackie B virus has been implicated in 50 percent of cases.[15] Early symptoms, if present, may include exercise intolerance and congestive heart failure symptoms with dyspnea, cough and orthopnea. Subtle clinical signs include tachycardia in the absence of fever, pulsus alternans and other clinical signs of heart failure (e.g., $S_3$ gallop, soft apical murmur, distended neck veins, peripheral edema). Most patients with myocarditis present with sudden death secondary to a ventricular arrhythmia and had few, if any, prodromal signs or symptoms. In addition, inflammatory coronary artery aneurysms associated with Kawasaki's disease have also been reported as a cause of sudden death.[16]

Attempts have been made[20] to put screening strategies for the prevention of sudden death into perspective by estimating disease prevalence. It has been estimated that 200,000 competitive asymptomatic athletes would need to be screened to potentially identify one athlete who would die as a result of competition. [corrected] If we had a tool to screen for sudden death with a sensitivity and specificity of 99 percent, the low prevalence of disease would yield a positive predictive value of only 0.05 percent. In other words, only one positive test out of every 2,000 would be correctly positive, and 1,999 would be falsely positive.

TABLE 4
**Screening for Sudden Death in Young Athletes**

| *Condition* | *Historical features* | *Physical examination* |
|---|---|---|
| Hypertrophic cardiomyopathy | Family history of hypertrophic cardiomyopathy, premature sudden death, recurrent syncope and/or lethal arrhythmias requiring urgent management. Personal history of exertional chest pain and/or syncope. | Wide range of ausculatory findings, from normal examination to harsh midsystolic murmur that accentuates with Valsalva maneuver and/or with standing. |
| Coronary artery diseases, congenital and acquired | Family history of early coronary artery disease, premature death and/or coronary anomalies. Personal history of exercise-induced chest pain, syncope and/or fatigue. | Physical examination is anticipated to be normal. |
| Myocarditis | Personal history of fatigue, exertional dyspnea, syncope, | Examination may be normal. Palpable or auscultated extra |

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| | palpitations, arrhythmias and/or acute congestive heart failure. | systoles, $S_3$ and/or $S_4$ gallops and other clinical signs of failure should arouse suspicion. |
| Aortic stenosis | Personal history of exercise-induced chest pain, breathlessness, light-headedness, syncope or dizziness. | Constant apical ejection click. Harsh systolic ejection murmur heard maximally at the upper right sternal border, crescendo/decrescendo profile, normally ≥ grade 3. |
| Marfan's syndrome | Family history of Marfan's syndrome or unexpected premature sudden death. | Arachnodactyly, tall stature, pectus excavatum, kyphoscoliosis and lenticular dislocation. Murmur of mitral valve prolapse and/or aortic regurgitation. |

NOTE: *These conditions may be asymptomatic and may present without any clues on physical examination. The history and physical examination are complementary and not mutually exclusive*.

Myocarditis appears to be more common in children than in adults.[8] Its true incidence, however, is unknown; it is thought that subclinical cases ("silent" myocarditis) occur much more often than do severe cases. Many cases are unrecognized because of the wide range of signs and symptoms and, in some patients, the complete lack of clinical findings.[8,9] In a postmortem study of children who died without a history suggestive of myocarditis, researchers found evidence of active or healed myocarditis in 17 of 138 cases (12.3%).[8,10] Of the 17 cases, 15 occurred in children who died suddenly. In postmortem studies in adults, myocardial inflammation occurred in 1% to 9%.[8]

**6) Viral Myocarditis in Children**

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Age plays a marked role in prevalence. During the neonatal period, myocarditis is usually abrupt, severe, and often fatal, with mortality as high as 75%.[11,12] Infants infected with coxsackievirus B during the first year of life have a high incidence of myocarditis. Myocarditis has been linked to sudden infant death syndrome, because inflammatory infiltrates have been found on autopsies of some victims.[2] Incidence increases again during late childhood and adolescence; the myocarditis usually has a delayed onset and patients recover.[7]

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**7) INCIDENCE, MECHANISM AND CARDIAC CAUSES OF DEATH**

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. *Incidence* - There are approximately 75 deaths per year in athletes between 13-25 years. 89% occur in males, 64% occur in females. Most deaths occur during or immediately after exercise.
. *Mechanism of Death* - Certain heart conditions react adversely to exercise. Exercise causes the heart to fibrillate, usually ventricular fibrillation and then stop. The athlete collapses suddenly and if not resuscitated immediately dies within minutes.
. *Cardiac Causes of Sudden Death* - Hypertrophic cardiomyopathy: 36% Coronary anomalies: 17% Myocarditis: 6% Arrhythmogenic Right Ventricular Dysplasia: 4% Long QT Syndrome: 4%

**8) Myocarditis and sudden cardiac death in athletes. Diagnosis, treatment, and prevention**

[Article in German], Frick M, Pachinger O, Pölzl G.
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Myocarditis is the reason for sudden cardiac death in 5-22% of athletes < 35 years of age. Actually, parvovirus B19 and human herpes virus 6 are the most important pathogens. Clinical presentation of myocarditis is heterogeneous, with all courses between asymptomatic and fulminant reported.

Especially in athletes it is important to take subtle discomforts seriously and initiate further evaluation. Electrocardiogram, laboratory parameters, serologic markers, and echocardiography are helpful in diagnosis of myocarditis, but are not specific. Magnetic resonance imaging (MRI) of the heart has

become an important tool in the evaluation of patients with myocarditis and allows noninvasive appraisal of myocardial inflammation using late enhancement. However, MRI is not able to assess viral persistence. Therefore, endomyocardial biopsy (EMB) remains the gold standard in diagnosis of myocarditis. When considering EMB in these athletes one should not ignore spontaneous healing in 50% of patients with myocarditis. Contrariwise, specific therapy (e.g., immunosuppression, interferon, immunoglobulins) for myocarditis is only feasible after getting results of EMB.

When myocarditis is verified, athletes have to withdraw from sport for at least 6 months. Before restarting physical activity, a detailed examination is necessary and most of the patients will undergo another EMB. For prevention of myocarditis and sudden cardiac death it is recommended to stop elite sport for 4 weeks after an unspecific infection. Whether moderate sport can be started earlier is unclear.

## For More Information

You can learn more about myocarditis and what you can do to help at www.MyocarditisFoundation.org.