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The Differential Diagnosis and Clinical Approach to the Athlete With Chronic Fatigue

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Chronic fatigue in the athletic population is a common but difficult diagnostic challenge for the sports physician. While a degree of fatigue may be normal for any athlete during periods of high volume training, the clinician must be able to differentiate between this physiological fatigue and more prolonged, severe fatigue, which may be due to a pathological medical condition. Once the clinician has excluded all medical conditions causing chronic fatigue in athletes, a significant proportion of fatigued athletes remain without a diagnosis. Novel data indicate that skeletal muscle disorders may play a role in the development of symptoms experienced by the athlete with chronic fatigue. The histological findings from muscle biopsies of athletes suffering from the "fatigued athlete myopathic syndrome" (FAMS) are presented. The mechanisms of the relationship between these histological muscle changes and the symptoms of fatigue in these athletes are also described.

Key Words: chronic fatigue, skeletal muscle, myopathy, exercise, skeletal muscle function

Key Points:

• Chronic fatigue in the athletic population is a common but difficult diagnostic challenge for the sports physician.

• The clinician must be able to differentiate between physiological fatigue and more prolonged, severe fatigue, which may be due to a pathological medical condition.

• A stepwise evaluation of the fatigued athlete is suggested.

• The histological findings from muscle biopsies of athletes suffering from the "fatigued athlete myopathic syndrome" (FAMS) are described.

Introduction

Previous research has examined fatigue related to the athlete's nutritional, fluid ingestion and training regimens, which when altered, could result in fatigue. This review will concentrate on the medical aspects related to the athlete presenting with chronic fatigue.

Nutritional, fluid, and training factors can be easily measured. Therefore, many issues regarding these variables have been well studied. Chronic fatigue in the athlete cannot be quantified as easily, and therefore remains an under researched area of sports medicine. Sports physicians therefore have to make recommendations to athletes with chronic fatigue based on the "art" rather than the "science" of medicine. However, recent research has increased knowledge of the aetiology of chronic fatigue in athletes, which will be described in this review.

Possible reasons for difficulty in the diagnosis and subsequent management of the athlete with chronic fatigue are that: (i) There is uncertainty of the terminology used to define chronic fatigue. Terms including *overtraining, overreaching, overtraining syndrome,* and *chronic fatigue syndrome* are often incorrectly used; (ii) the current diagnostic criteria for these conditions are often inadequate or incorrect; and (iii) the aetiology, and therefore the diagnosis and management of chonic fatigue in athletes, is still not currently well understood.

In an attempt to address some of these issues, a clinical diagnostic approach is proposed to evaluate athletes presenting with chronic fatigue. The causes of chronic fatigue in the athlete are outlined in Table 1. These fit into one of two major groups, classified as either physiological or pathological fatigue.

Physiological Fatigue

Physiological fatigue or training-induced fatigue refers to the symptoms of tiredness that develop when the athlete undertakes a high volume of training. Indeed, athletes commonly use the process of overload, or gradually increased workload, as a stimulus for adaptation (22). During this process, an imbalance between exercise and recovery occurs, which leads to the symptoms of fatigue.

Table 1 Aetiology of Chronic Fatigue in the Athlete

1. Physiological fatigue
    - a) training induced fatigue
        - i) overreaching (increased intensity, duration or frequency of training)
        - ii) excessive competition
    - b) nutritional deficiency
        - i) carbohydrate
        - ii) protein
        - iii) fluid
        - iv) vitamins and anti-oxidants
        - v) micronutrients
    - c) insufficient sleep
    - d) travel across time zones
    - e) pregnancy
2. Pathological fatigue
    - a) medical conditions
        - i) chronic infective conditions: viral, bacterial or paracytic (including hepatitis, infectious mononucleosis, HIV, malaria, tuberculosis, brucellosis)
        - ii) haematologic conditions (including iron deficiency anaemia)
        - iii) neoplastic conditions
        - iv) cardio-respiratory conditions (including coronary artery disease, cardiac failure, bacterial endocarditis asthma, exercise induced asthma)
        - v) neurogenic-neuromuscular (including post -concussive syndromes, multiple sclerosis, myasthenia, myotonia, paramyotonia)
        - vi) endocrine-metabolic conditions (including diabetes, hypothyroidism, hyperthyroidism Addison's disease, Simmond's disease, hyperparathyroidism, hypophosphataemia, kalaemic periodic paralases, Cushing's syndrome, hypogonadism)
        - vii) Psychiatric-psychological conditions (including anxiety, depression, psychoneuroses, eating disorders)
        - viii) Drug induced (including beta-blockers, other anti-hypertensive agents, agents acting on the central nervous system, antihistamines, lipid lowering agents, alcohol, antibiotic agents)
        - ix) Other (including malabsorption syndromes, allergic conditions, spondyloarthropathies)
    - b) Overtraining Syndrome
    - c) Chronic Fatigue Syndrome
    - d) "Fatigued Athlete Myopathic Syndrome"

Training overload and *overreaching* are terms describing the process of undergoing training loads that are greater than the accustomed training load of the athlete (22). These are caused by

altering training intensity, frequency, and duration, or by reducing the recovery period between training sessions. Physiological fatigue may arise from this form of training. The characteristic feature of fatigue arising from overreaching is that it is reversed by reduction in training or a few days of rest (30, 45).

Minor and transient changes in immune function after an acute bout of exercise may be a marker of overreaching (48). However, the Profile Of Mood States (POMS) questionnaire was the single best marker to indicate imminent fatigue during a period of overreaching (48). Snyder (45) found that during a period of intense training, a decrease in the blood lactate concentration:relative perceived exertion ratio was a sensitive marker preceding the manifestation of symptoms of training induced fatigue.

It is important that sufficient quantities of carbohydrate are ingested, particularly when rapid recovery from a prior exercise bout is required (19). Furthermore, dietary carbohydrate is also important in maintaining exercise performance during periods of chronic exercise training (43). More glycogen is stored in the muscle if the athlete's diet is high in carbohydrate (12). Skeletal muscle glycogen resynthesis is impaired for up to 10 days following certain forms of exercise, particularly those causing delayed onset muscle soreness (DOMS; 8, 42). Indeed, it appears that inadequate ingestion of carbohydrate, skeletal muscle damage (42), and symptoms of overreaching are related (12). The role of amino acids, vitamins, micronutrients, and anti-oxidants in the prevention and treatment of the symptoms of overreaching are currently under study (1, 11).

Interestingly, Scharf and Barr (39) have proposed that abnormal eating patterns, including bingeing, in athletes who are overreaching, may be caused by decreased concentrations of circulating tryptophan, which is thought to lead to deficiencies in brain serotonin concentrations. This theory remains to be explored.

Other causes of physiological fatigue include inadequate quality and quantity of sleep, international travel across time zones and, occasionally, undiagnosed pregnancy (6, 29, 35, 37).

Pathological Fatigue

Pathological fatigue may be defined as fatigue and tiredness that cannot be attributed to physiological adaptations (34). Pathological causes of fatigue are outlined in Table 1. These include infections, neoplasias, and disorders of the haematological, cardio-respiratory, neuromuscular, or endocrine systems (36, 46, 40, 41, 49, 50). Psychological or psychiatric disorders including depression, excessive anxiety related to sporting performance or other problems, bulimia, and anorexia nervosa could also present as chronic fatigue in the athlete (23).

Commonly prescribed medications listed in Table 1 have the potential to cause chronic fatigue in athletes. These medications include beta-adrenergic blockers, other anti-hypertensive agents, agents acting on the central nervous system, antibiotics, anti-histamines, and lipid lowering agents (15, 16).

The Overtraining Syndrome

The overtraining syndrome refers to a symptom complex characterised by non-adaptation to training, decreased physical performance and chronic fatigue following high volume and/or high intensity training and inadequate recovery (18, 22). The overtraining syndrome requires weeks or months of rest or greatly reduced training for complete recovery (28). While decreased physical performance together with chronic fatigue have been used most commonly to diagnose the overtraining syndrome, there is still little consensus about how to diagnose this disorder.

Clinical features of the overtraining syndrome vary greatly (18, 22). However, the symptoms of "heavy legs," increased waking pulse rate, lack of motivation, decreased enjoyment of exercise, sleep disorders, painful skeletal muscles, dizziness upon standing, frequent infections, weight loss, depression, decreased libido, and increased effort during exercise training without improvement in performance, are commonly described features of the overtraining syndrome (18, 28).

Changes in body mass, and heart rate, blood pressure, serum or urine glucose, urea, glutamine, and various enzymes and hormone concentrations, increased concentrations of serum creatinine kinase (CK), low erythrocyte count, and decreased haemoglobin and serum ferritin concentrations have been documented in some studies of overtrained athletes (4, 20, 21, 44, 47) but not in others (28, 32, 48).

Table 2 Diagnostic Criteria for the Chronic Fatigue Syndrome (Adapted from ref. 27)

The patient must have both major criteria plus either (a) 6 minor symptoms and at least 2 physical criteria, or (b) at least 8 minor symptoms:

Major Criteria

(i) New onset of persistent or relapsing debilitating fatigue, of at least 6 month duration, that does not resolve with bed rest and is severe enough to impair daily activity below 50% of normal.

(ii) Exclusion of other clinical conditions that may produce similar symptoms

Minor Symptom Criteria

Symptoms must have coincided with onset of chronic fatigue and have persisted or recurred for at least 6 months

(i) Low grade fever, 37.5 °C-38.6 °C or chills
(ii) Sore throat
(iii) Painful cervical or axillary adenopathy
(iv) Generalised weakness
(v) Skeletal muscle discomfort or myalgia
(vi) Prolonged fatigue (24hr or longer) after moderate exercise
(vii) Generalised headaches
(viii) Migratory arthralgia
(ix) Neuropsychologic symptoms (one symptom or more; photophobia, transient visual scotoma, forgetfulness, irritability, confusion, difficulty thinking, inability to concentrate, depression)
(x) Sleep disorders (insomnia or hypersomnia)
(xi) Main symptom complex developed within a few days

Physical Criteria

As documented by a physician on at least two occasions, at least 1 month apart

(i) Low grade fever (37.5 °C-38.6 °C)
(ii) Nonexudative pharyngitis
(iii) Palpable or tender anterior or posterior cervical or axillary lymph nodes (<2 cm)

Effective monitoring of the overtrained athlete has recently been reviewed (9, 28). While the most appropriate medical tests for monitoring the overtraining syndrome are still unclear, it appears that performance during standardized exercise testing, including serial measurement of heart rate, oxygen consumption and blood lactate concentration during a submaximal exercise test, the POMS inventory and a training and symptom log are possibly the best tools for monitoring the overtraining syndrome (18, 28, 48). An example of the Sport Science Institute of South Africa's training diary for monitoring the symptoms and signs of the overtraining syndrome, described previously (31), is listed in Table 2.

The Chronic Fatigue Syndrome

Criteria for the diagnosis of the chronic fatigue syndrome have been previously well described and are listed in Table 3 (27). Symptoms include chronic fatigue of at least 6 months duration that does not resolve with bed rest and is severe enough to reduce average daily activity to below 50% of normal (27). Our experience is that while these diagnostic criteria may be appropriate for the general population, very few fatigued athletes fulfil these criteria. The clinical picture of the chronic fatigue syndrome is also one which can mimic diseases of insidious onset including cancer, tuberculosis, depression, and AIDS. When making the diagnosis of chronic fatigue syndrome, it is always important not to overlook serious and potentially curable diseases.

To address this challenge, we have we have designed a clinical diagnostic approach to athletes presenting with chronic fatigue. The outline of our diagnostic approach and investigation of the athlete is shown in Figure 1. Our approach includes a minimum of two visits before the aetiology of chronic fatigue can be established. However, it is more likely that the athlete with chronic fatigue will have to visit on several occasions to the clinic and exercise laboratory before a diagnosis is made.

Table 3 Checklist of Factors to Establish During History Taking in the Evaluation of the Athlete With Chronic Fatigue

Duration and severity of fatigue
Onset of fatigue marked by a particular event, infection of trave
Fatigue constant or intermittent
Extent of impairment of exercise performance or activities of daily living
Fatigue associated with particular venues or climate
Quality and quantity of sleep
Classic symptoms of the overtraining syndrome
Medications
Nutritional supplements
Presence of systemic symptoms of disorders of cardiovascular, gastrointestinal, neuromuscular, endocrine, ear nose & throat, urogenital systems.
Menstrual history
Brief training history
Present training status
Rest periods between training sessions
Initial 24 hour dietary recall
Initial psychological assessment

Visit 1

At this consultation, a detailed history is taken and a thorough physical examination is performed.

History. A checklist of important factors to establish during the history taking are listed in Table 3. It is important to determine the duration and severity of the fatigue, whether the onset of the fatigue was marked by a particular event (infection or overseas travel), whether the fatigue is constant or intermittent, the extent of impairment of exercise performance or activities of daily living, and if the fatigue is associated with particular environmental conditions (venue or climate). Does the athlete have sufficient quantity and quality of sleep? Does the athlete have any of the classic symptoms of the overtraining syndrome? Is the athlete presently ingesting any medications or nutritional supplements? Does the athlete have any systemic symptoms indicative of abnormalities of the cardiorespiratory, gastrointestinal, neuromuscular, endocrine, ear nose and throat (ENT), and urogenital systems? In the female athlete, a menstrual history should be taken to exclude either pregnancy or possible anemia from excessive blood loss from heavy menstrual bleeding.

It is helpful to know at what stage of the training cycle the athlete is in and what the athlete's intended future training program entails. The volume, intensity, frequency of training as well as the quantity and quality of rest between training sessions and competitions should be established. If the athlete keeps a log book, the weekly training volumes over the previous few months should be determined and any large changes to the athlete's program should be noted.

The athlete is asked to recall all food eaten in a typical 24-hour period (including both training and competition), and the athlete's attitudes and practices with respect to nutrition and fluid intake before, during, and after competition are determined. This brief screening procedure is performed only to alert the clinician to possible eating disorders and insufficient or incorrect nutritional practices. If these are suspected, the athlete is referred to a dietician for a more detailed dietary analysis.

Possible psychological contributions to the athlete's fatigue should be determined. In young athletes, the HEADS questions (designed to determine stress from the Home, Education, Activities, Alcohol, Drugs, Depression, Sex, and Sport) may be particularly useful to indicate problem areas that would necessitate referral to a sport psychologist (17).

Physical Examination. A general medical examination to exclude signs of jaundice, anaemia, oedema, and lymphadenopathy should be performed, followed by a detailed medical examination of the cardiorespiratory, gastrointestinal, neuromuscular, and ENT systems. The athlete's temperature, resting heart rate, and blood pressure are measured and noted.

Special Investigations. While the history and physical examination are the most important components of the first

visit to enable the clinician to establish a diagnosis, it is helpful to conduct a number of baseline special investigations, the results of which could indicate specific pathology. We suggest that the athlete's hemoglobin concentration, white cell count, erythrocyte sedimentation rate, and serum ferritin concentration are measured. A urine dipstick test is performed to exclude renal abnormalities and determine hydration status by measurement of urine osmolality.

The athlete is given a daily training diary (Table 5) and asked to complete it for the following 2-3 week period. During this time, the baseline blood test results are reviewed. It is essential that the athlete continues with their normal pattern of training during this time so that the symptomatology can be reviewed.

Table 4 Clinical Diagnostic Approach to the Athlete With Chronic Fatigue

Visit 1 • History • Physical examination • Initial dietary evaluation • Training diary • Baseline special investigations: Hb, WCC, ESR/Visc, s-glucose, s-ferritin, urine dipstick 2–3 weeks Visit 2 • Review of training diary • Review of test results	
Pathological fatigue	Physiological fatigue
Further special investigations might include: • FBC and differential count • Renal function & electrolytes • Liver functions • Thyroid functions • Glucose tolerance test • Creatinine kinase • Urinary myoglobin • Viral studies • Chest X-ray • Cardio-respiratory exercise test • Lung functions • Dietary recall • POMS questionnaire • Training log	Appropriate Rx No response Monitoring overtraining: repeated submaximal exercise tests, repeated POMS, dietary intervention, training log
Visit 3 Review of the test results • Overtraining syndrom • Review daignostic criteria: Chronic Fatigue Syndrome • Unable to make diagnosis	
FAMS	Other
Tests of skeletal muscle function EMG studies Neuromuscular stimulation studies NMR spectroscopy Skeletal muscle biopsies	
Note. Hb = haemoglobin; WCC = white cell count; ESR = erythrocyte sedimentation rate; visc = plasma viscosity; s = serum; FBC = full blood count; POMS = profile of mood states; FAMS = fatigued athlete myopathic syndrome; EMG = electromyography; NMR = nuclear magnetic resonance.	

Table 5 Example of the Sport Science Institute of South Africa: Training Diary to Monitor Signs and Symptoms of Overtraining

Date	Waking heart rate	Hours sleep	Sleep rating	Postural diziness score	Body mass	Symptom score	Muscle stiffness score	Training detail	Training rating	General depression rating
Mon 1										
Tue 2										
Wed 3										
Thu 4										
Fri 5										
Sat 6										
Sun 7										
Average										

Instructions to the athlete:

1. Complete all aspects of your training diary on a daily basis.
2. Waking heart rate: should be measured each morning before getting out of bed. After waking, continue to lie in bed, relaxed for 5 min, then count your pulse rate for 30 s. Multiply that number by 2 and record that figure in your diary.
3. Sleep rating: document the quality of the previous nights sleep according to the following scale: Gr 1-uninterrupted sleep, feeling refreshed; Gr 2-Interrupted sleep, not requiring more sleep; Gr 3-interrupted sleep, requiring more sleep; Gr 4-interrupted sleep, feeling terrible.
4. Postural dizziness score: this refers to dizziness experienced when getting up suddenly from a lying or sitting position. Monitor this each day as you get out of bed by standing up suddenly; Gr 1-no dizziness; Gr 2-some dizziness but disappears within 2 s; Gr 3-marked dizziness, having to lie down again.
5. Body mass: measure your body mass with a calibrated scale each second morning after getting out of bed.
6. Symptom score: record number if you have suffered from any of the following symptoms in the past 24 hr; 1-sore throat; 2-cough; 3-nausea or vomiting; 4-diarrhoea; 5-stomach ache; 6-headache; 7-fatigue; 8-other.
7. Muscle stiffness score: record any skeletal muscle stiffness or pain which you experience as a result of your training; Gr 1-no stiffness or pain; Gr 2-mild stiffness and pain, not affecting workout; Gr 3-moderate muscle stiffness or pain, able to complete workout with difficulty; Gr 4- severe muscle stiffness or pain, unable to complete workout.
8. Training detail: record i) the duration and type of exercise and ii) your training effort; Gr 1-felt good during the entire workout; Gr 2-neither hard nor easy, felt good during some parts of the workout; Gr 3-somewhat difficult, felt a little tired; Gr 4-very difficult, had difficulty completing the workout.
9. General depression rating: Gr 1-no depression, good mood; Gr 2-mild depression, feeling down or sad only at times; Gr 3-moderate depression, feeling down or sad most times; Gr 4-severe depression, feeling down or sad all of the time.

Visit 2

At this visit, the completed training diary and results of the baseline tests are reviewed with the athlete. The clinician should, at this stage, be able to distinguish between physiological and pathological fatigue.

If the clinician suspects that the chronic fatigue is physiological in origin, the appropriate management is employed and may include rest, dietary, and psychological intervention. Referral of the athlete to a dietician or sport psychologist for further assessment, intervention, and monitoring is essential.

Further special investigations should be conducted if: (i) the athlete does not respond to rest, dietary, or psychological intervention; (ii) the cause of the chronic fatigue is not directly apparent; or (iii) indicated by abnormalities of the baseline investigations. These include a full blood and differential count, serum electrolyte (including sodium, potassium, magnesium, and chloride) determination, liver functions, thyroid functions, viral serology studies, serum creatinine kinase concentration, and a glucose tolerance test. A chest x-ray, lung function

test, and cardio-respiratory exercise test could also be conducted if the athlete has signs and symptoms of cardio-respiratory disease, as indicated by the results of the initial clinical examination.

Visit 3

The results of these tests are reviewed at visit 3, and the clinician should now be in a position to i) exclude medical conditions which could cause fatigue; ii) review the criteria and possibly exclude the chronic fatigue syndrome; or iii) make the diagnosis of the overtraining syndrome and institute a monitoring programme as discussed previously.

It is our experience that after all of the above mentioned tests have been conducted, there are some athletes where no diagnosis can be made and there are athletes who do not respond to long periods of rest and adequate nutritional and psychological support. These athletes do not fulfil the criteria of the Chronic Fatigue Syndrome (23; 27), and are clearly also not overtrained. In this group of athletes the aetiology of chronic fatigue is still unknown and further investigations are warranted.

The Fatigued Athlete Myopathic Syndrome (FAMS)

A trend has been recently recognized in some athletes suffering from chronic fatigue and decreased exercise performance. These athletes: (i) have a history of a high volume of exercise training over many years; (ii) present with chronic fatigue, but also have a clinical picture that is dominated by skeletal muscle symptoms including excessive DOMS, stiffness, muscle tenderness, and skeletal muscle cramps; (iii) do not fit the clinical picture of the disease states outlined in Table 1; (iv) do not fulfil the criteria for the chronic fatigue syndrome; and (vi) often have consulted many clinicians unsuccessfully in search of a diagnosis (14).

Table 6 Histological Features of Skeletal Muscle Biopsies From Athletes With Fatigue Associated Myopathic Syndrome (FAMS)

Athlete	Sport	Age	Presenting symptoms	Skeletal muscle biopsy findings
1	Runner	44	Prolonged muscle pain after exercise, fatigue	Increased subsarcolemmal glycogen, thickened basement membrane
2	Ultramarathon runner	50	“Heavy legs”, dyspnea, fatigue	atrophic fibres, abnormal lipid deposition displacing mitochondria, abnormal NADH
3	Marathon runner	39	“Heavy legs”, chronic fatigue, muscle stiffness	abnormal mitochondrial morphology and distribution
4	Runner	28	Decreased performance, fatigue, muscle discomfort	Type II hypertrophy, abnormal mitochondrial morphology
5	Runner	31	Prolonged DOMS, cramps, chronic fatigue	Subsarcolemmal mitochondrial aggregation, myelin body and crystal inclusions within mitochondria
6	Runner	20	Exercise intolerance, muscle pain, chronic fatigue	Focal degenerative fibre changes, non-specific mitochandrial abnormalities
7	Cyclist	43	“Heavy legs”, exercise intolerance, chronic fatigue	Abnormal mitochondrial cristae, areas of myofibrillar loss
8	Swimmer	36	Exercise intolerance, chronic fatigue, symptoms reversed with alcohol ingestion	Fibre atrophy, internal nuclei, fibre grouping, abnormal mitochondria
9	Cyclist	35	Decreased performance, cramps, chronic fatigue	Abnormal mitochondrial cristae, central nuclei, necrotic fibres, increased lipid

Analysis of skeletal muscle biopsies have been used for over three decades to study muscle composition and morphology (5). We have found that histological and electron microscopic analysis of skeletal muscle biopsies before and after exercise is useful to gauge the effect of the exercise bout on the skeletal muscle structure. Nuclear Magnetic Resonance spectroscopy (P131 NMR) is also a useful non-invasive method to study metabolic changes within active skeletal muscle in health and disease (50).

Skeletal muscle biopsies of the vastus lateralis from athletes who present with the above symptom complex were recently performed. The athlete's characteristics and muscle biopsy findings are presented in Table 6. Of these 9 athletes, 5 had performed at international, national, or provincial level. Structural abnormalities of the skeletal muscle were found in all 9 subjects. These abnormalities were not specific to any previously recognized disease of the skeletal muscle and included (i) irregular muscle fiber size and distribution, (ii) alterations in mitochondrial structure (Figure 1), (iii) abnormal lipid inclusions, and (iv) mitochondrial inclusions.

While these changes are nonspecific, they appear to be common to this group of athletes. It is difficult to determine if these changes are indeed pathological or represent a form of physiological adaptation to long term exercise training. Similarly, it is difficult to determine if these changes are the cause or the effect of the exercise intolerance experienced by these athletes.

While the aetiology of these changes is not directly apparent, it is well known that acute bouts of strenuous exercise, particularly long distance running, can damage skeletal muscle structure and that the changes in the muscle and regeneration can be seen as late as 12 weeks after the event (2, 26). One hypothesis explaining these abnormalities is that repeated bouts of high volume exercise training over many years cause repeated and chronic damage to skeletal muscle structure, which finally presents with exercise intolerance and skeletal muscle symptoms. An alternative hypothesis explaining this phenomenon is that chronic oxidative stress during high-intensity exercise directly or indirectly

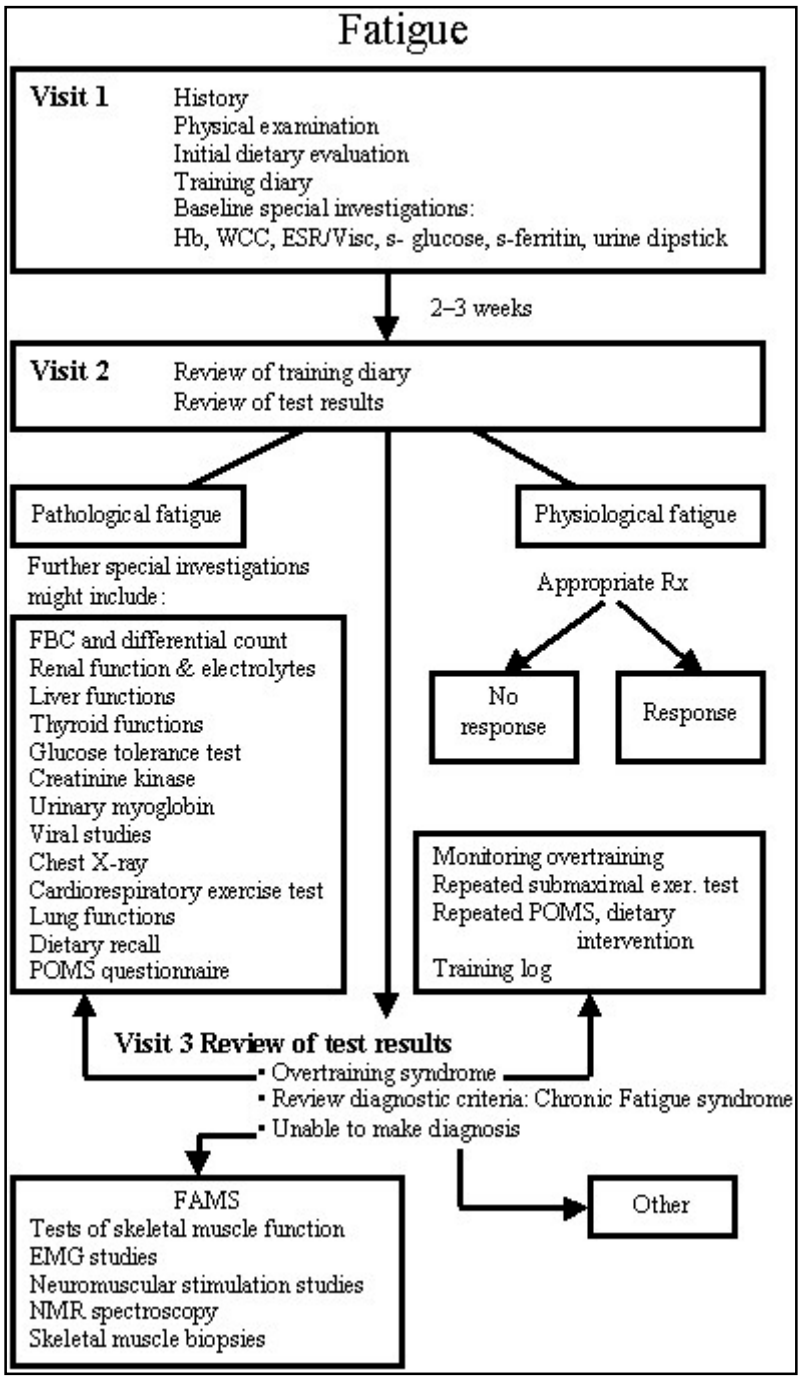

Figure 1 — Clinical diagnostic approach to the athlete with chronic fatigue. Abbreviations: Hb = haemoglobin; WCC = white cell count; ESR = erythrocyte sedimentation rate; visc = plasma viscosity; s = serum; FBC = full blood count; POMS = profile of mood states; FAMS = fatigued athlete myopathic syndrome; EMG = electromyography; NMR = nuclear magnetic resonance.

causes cellular organelle damage (1). It must be noted, however, that not all studies have found muscle pathology in athletes diagnosed with chronic fatigue syndrome (38). These authors concluded that the physical deterioration in performance was related to detraining rather than muscular pathology. Further work is needed to assess the reason for these different findings.

Analysis of serological tests conducted on these patients revealed that 6 of the 8 athletes previously had Ebstein Barr virus infection. It is possible that these athletes had what has previously been termed the "post viral fatigue syndrome" (3). Recently, it has been suggested that in chronic fatigue there is dysregulation of antiviral responses to Ebstein Barr and other viruses (13).

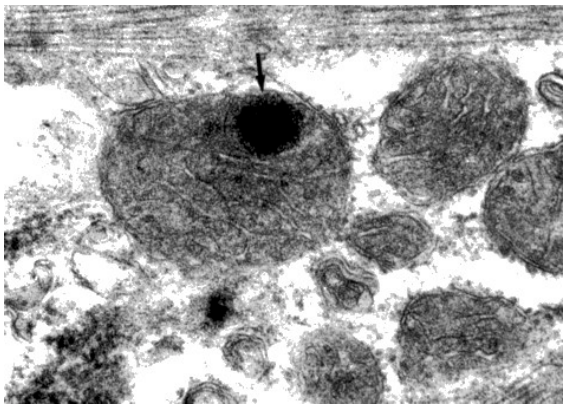

Figure 2(a) — An electron micrograph showing a mitochondrion containing a large electron dense inclusion (arrow; x72,900).

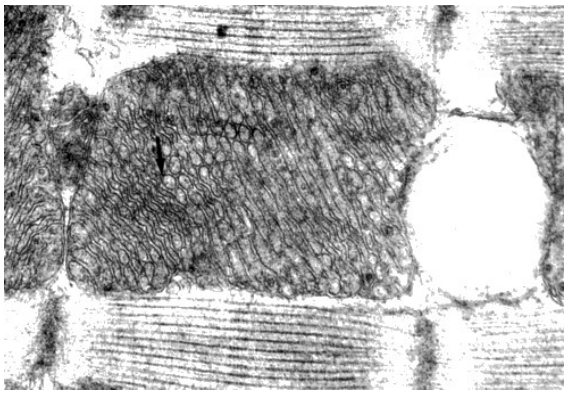

Figure 2(b) — An electron micrograph of a large mitochondrion packed with intricate cristae formation (arrow; x72,900).

Fatigued Athlete Myopathic Syndrome and Central Symptoms of Fatigue

The relationship between chronic fatigue syndrome, the fatigued athlete myopathic syndrome, and the central symptoms of fatigue have not been clearly identified. For example, isokinetic and isometric tests including measurement of peak torque, total work done in a 30-s test, maximal voluntary contraction, and time to fatigue can be performed as indicators of skeletal muscle contractile function and to measure the resistance of the skeletal muscle to the onset of fatigue (10). However, recent research has shown that individuals with chronic fatigue or fatigued athlete myopathic syndromes are able to generate similar force output to sedentary controls despite symptoms of fatigue at rest prior to testing and a reluctance to initiate the testing protocol for force output testing (St Clair Gibson et al., unpublished data). These findings indicate that the symptoms of fatigue in these individuals are central in origan. Recent work has suggested central motor mechanisms accompanying motor response preparation may be impaired in chronic fatigue syndrome subjects (24).

To assess the central component of fatigue in these subjects, muscle compound action potential (M wave) and electromyographic analyses (25) and transcutaneous skeletal muscle stimulation by means of an interpolated twitch are useful tools to differentiate between central and peripheral mechanisms of fatigue (7). Further research is required to assess the relationship between the muscle pathology and central changes described previously. Hypothesis regarding the relationship between the central and peripheral pathology include: (i) Afferent signals from the damaged muscle may be chronically activated and induce symptoms of fatigue as a protective mechanism, (ii) changes in the hypothalamic-pituitary-adrenal axis may have both peripheral and central affects, (iii) the changes in the brain structures may be completely unrelated to the muscle pathology, (iv) the symptoms of fatigue may be part of a clinical depression in the fatigued athletes caused by the change in lifestyle or psychological makeup induced by the deterioration of athletic performance, or (v) the central symptoms of fatigue may be caused by Ebstein Barr virus infection or other pathogens reacting directly with both muscle and brain tissue.

Overview

Chronic fatigue in the athlete is a complex and challenging diagnostic problem, which requires the clinician to follow a systematic approach so that a diagnosis can be established. The skeletal muscle abnormalities which exist

in athletes with chronic fatigue who present predominantly symptoms indicative of skeletal muscle pathology have been described. It is important that research continues, to determine the cause of the chronic fatigue in athletes and, in particular, the cause of skeletal muscle changes seen in these athletes. Only through understanding the mechanisms whereby these changes occur, could appropriate treatments and preventative measures be employed.

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