ORIGINAL ARTICLE

Clinical utility of blood tests in elite athletes with short term fatigue

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Objective: To determine, in a population of elite athletes at their initial presentation with tiredness or fatigue, whether a set of haematological and biochemical investigations enhances the diagnostic process over and above the information gained from clinical history and examination.
Methods: A sequential series of 50 elite athletes were studied at the initial consultation for a primary complaint of fatigue, tiredness, or a synonym thereof. A standardised clinical history, physical examination, and series of haematological and biochemical test were performed. The effects of the results of the blood tests on the diagnosis made after the clinical history and examination were examined.
Results: In only one case did the test results lead to an alteration in diagnosis. Physical examination did not provide any findings that would not have been suspected from the history, except for a number of incidental findings not relevant to the presenting symptom.
Discussion: In cases of short term fatigue in elite athletes, a thorough clinical history is mandatory. Physical examination is unlikely to reveal any findings not suspected from the history. Routine ordering of a panel of blood tests at the initial consultation should be discouraged. Unless specifically indicated by the history and examination, investigations are not required at the initial consultation.

Fatigue and tiredness are common presentations to both general practitioners and sports physicians. In athletes these symptoms are often a normal consequence of training, and this ''physiological tiredness'' needs to be delineated from fatigue that is perceived by the athlete as unusual and which therefore leads to a medical presentation. Overtraining or over-reaching, infection, nutritional problems, and psychosocial disorders are often discussed as common causes of fatigue in athletes,[1] but little is known about the frequency of the specific diagnoses or contributing factors that explain these symptoms. More is known of those who present with persistent fatigue. For example, in a study of athletes with persistent fatigue and/or chronic infections presenting to a tertiary referral centre, the most often identified conditions ''with the potential to cause'' the presenting symptoms were found to be partial humoral immune deficiency, hypoglycaemia, primary or unresolved infections, and re-activation of the Epstein-Barr virus.[2]

The utility of blood tests in the initial investigation of athletes presenting with fatigue has received scant attention. Although a number of sports medicine texts do not mention the topic, one[1] suggests that, in the athlete presenting with tiredness, ''necessary tests include a full blood count, iron studies and vitamin B12 and folate levels'', and anecdotal evidence suggests that it is not uncommon clinical practice to order a biochemical profile, thyroid function tests, and evaluation of erythrocyte sedimentation rate or C reactive protein concentration in addition to the tests mentioned above. This is in accordance with suggested ''key screening investigations'' for patients presenting to general practitioners with a complaint of fatigue. These included a full blood count, erythrocyte sedimentation rate, urea and electrolytes, blood glucose, liver function tests, and thyroid function tests.[3] A suggested diagnostic pathway that includes blood tests has been published for use in athletes with chronic fatigue.[4]

Preliminary evidence relating to the utility of blood tests was provided in a recent conference abstract in which a retrospective analysis of pathology tests performed in 50 athletes who had presented with fatigue was reported. The authors indicated that only 1.2% of the test results assisted in clinical decisions and concluded that ''a battery of blood tests did not contribute to the diagnosis in fatigued athletes''.[5]

The performance of tests, such as blood tests or radiological procedures, is often seen as an integral component of diagnosis. The expectation, which is, anecdotally, not uncommon among coaches and elite athletes, that a test should be performed, however, often conflicts with one of the basic tenets of clinical medicine—that the vast majority of diagnostic information is derived from the clinical history and, to a lesser degree, from clinical examination.

The primary aim of this prospective study was to determine, in a population of elite athletes at their initial presentation with tiredness or fatigue, whether a set of haematological and biochemical investigations would enhance the diagnostic process over and above the information gained from clinical history and examination. Secondary aims were to document the clinical diagnoses or contributing factors in these athletes and assess whether clinical examination added significant information to the findings of the clinical history in coming to a diagnosis.

METHODS

Approval for this prospective study was obtained from the ethics committee of the Australian Institute of Sport. Between November 2003 and February 2006, a sequential series of 50 elite athletes at the Australian Institute of Sport were recruited at the time of presentation to sports physicians or registrars of the institute, with a primary complaint of fatigue or tiredness. Athletes were not included if they complained initially of other symptoms and later of fatigue or tiredness as an associated symptom.

At the initial consultation, a standardised clinical history (based on a proforma) was taken. Questions on basic characteristics were followed by questions relating to: past and recent medical and surgical history; recent injury and illness; allergies; drugs; supplements; diet; alcohol; smoking; menstrual history; other presenting symptoms and history of

the present problem; psychosocial factors; sleep, appetite, and weight; duration of fatigue; estimated effect on training in percentage terms (full training, 50–100% training, 0–50% training, no training); recent training history and any other aspects of history thought relevant by the athlete or doctor.

This was followed by a standardised clinical examination which included: pulse rate, temperature, blood pressure, an examination of the ear, nose, and throat and the cardiovascular, gastrointestinal, respiratory, and haematological (including lymphoid) systems, and palpation of the thyroid. Further examination was at the discretion of the doctor guided by the findings of the clinical history.

All athletes had 12 ml of blood taken by an experienced phlebotomist from a vein in the cubital fossa, immediately on assumption of the supine position. The blood was taken immediately to an adjacent laboratory where the following were performed: full blood count (haemoglobin, packed cell volume, white cell count and differential, mean red cell volume, mean cell haemoglobin concentration, platelet count), iron studies (serum ferritin, transferrin, iron, percentage transferrin saturation, and, if the serum ferritin was less than 30 μg/ml, soluble transferrin receptor), biochemical profile (electrolytes, urea and creatinine, total protein, albumin, creatine kinase, aspartate aminotransferase (AST), alanine aminotransferase, alkaline phosphatase, γ glutamyl transferase, and total bilirubin), and evaluation of high sensitivity C reactive protein and thyroid stimulating hormone. Additional laboratory investigations were undertaken if clinically indicated.

Measurements of serum iron, transferrin, ferritin, percentage transferrin saturation, and soluble transferrin receptor and the biochemical profile were performed on a Hitachi 911 analyser using Roche reagents. C reactive protein and thyroid stimulating hormone were measured on a DPC Immulite analyser using DPC reagents (DPC, Los Angeles, California, USA), and the full blood count was performed on the Bayer Advia 120 analyser using Bayer reagents (Bayer, Dublin, Ireland).

A diagnosis of medical, nutritional, or psychosocial problems was made on standard clinical grounds. Training related fatigue or tiredness was diagnosed if the onset of fatigue was associated with an unusual increase in the intensity or duration of training, overall training load, or sudden change in mode of training.

Wherever practical, athletes were followed up at clinical consultations or by telephone, not only to assess progress as is normal practice, but to attempt to specifically determine time to resolution of the presenting symptoms.

RESULTS

Fifty elite athletes took part in this study (29 male, 21 female; 52% aged 16–18 years; mean age overall 20 years (range 16–34)).

Fourteen sports were represented: basketball (eight cases), swimming (seven), archery (five), volleyball (five), rowing (five), athletics (four), football (three), water polo (three), gymnastics (two), boxing (two), netball (two), and skating, cycling, and skiing (one case each).

In 86% of cases the duration of fatigue was less than or equal to three weeks, and in 64% fatigue had been present for one to two weeks. Two athletes had fatigue for eight weeks, and one for 10 weeks. Full training was maintained by 52% of the athletes, 44% had modified their training to 50–100% of normal because of fatigue, and 4% had modified their training to 0–50% of normal.

Table 1 details the primary diagnoses and/or contributing factors to fatigue. In 34% of cases, more than one factor contributed to fatigue.

Table 1 Primary diagnoses and/or contributing factors to fatigue

Diagnosis	Percentage of cases
Training related	28
Infection	18
Infection and training related	12
Infection and psychosocial stress	8
Infection, psychosocial stress, and training	8
Psychosocial stress and training	6
Psychosocial stress	8
No clear cause found	12

In thirty nine (78%) of the athletes, at least one test result was outside the normal range. Seventy two individual results were abnormal, which represented 5.3% of all tests performed. In eight cases, AST was slightly above normal (all in the range 41–50 U/l, with normal being less than 38 U/l), with other liver function tests being normal and all returning to normal on follow up. In one patient with a minor increase in AST, the increase persisted at the initial follow up but then returned to normal. Two others had isolated AST activity of 39 U/l, which is within the known coefficients of variation of the pathology laboratory. In both of these cases, other liver function tests were normal. In eight cases, there were minor reductions in haemoglobin, packed cell volume or both, accompanied by normochromic, normocytic red cells and normal iron studies. Six patients showed minor increases in serum bilirubin, with other liver function tests being completely normal. In five cases, there was an isolated, minor increase in mean corpuscular haemoglobin concentration, and in another five there were minor reductions in total serum protein, all of which were associated with normal renal and liver function tests and no evidence of proteinuria. There were three cases of increased serum iron and transferrin saturation, consistent with a history of ingestion of iron containing supplements, and two where the serum ferritin was less than 30 ng/ml. Both were between 25 and 30 ng/ml. Although this was strictly not abnormal, it was below our usual threshold for starting iron supplementation.

In only one case did the test results (raised total white cell count and neutrophilia) lead to an alteration in diagnosis.

Owing to laboratory error, thyroid stimulating hormone was not measured in three cases, and C reactive protein in one.

Additional tests were ordered in six cases. Four of these were latex agglutination tests for infectious mononucleosis. IgG and IgM for Epstein-Barr virus was ordered once, as was the combination of erythrocyte sedimentation rate and anti-gliadin and anti-endomysial antibodies. Each of these tests was negative or within normal limits.

Physical examination did not provide any findings that would not have been suspected from the history, except for a number of incidental findings not relevant to the presenting symptom. Physical examination was completely normal in 56% of athletes. Fourteen athletes (28%) had signs consistent with suspected upper respiratory tract infections (cervical lymphadenopathy, nasal congestion, inflamed throat), and one athlete had signs consistent with a gastrointestinal infection. Six athletes had physical findings that were not related to the cause of the primary symptom.

DISCUSSION

In general medicine, the diagnostic yield from tests in tired patients is remarkably low. In a retrospective Australian

study, only 3% of 342 patients had a significant clinical diagnosis based on an abnormal pathology test,[6] and the yield was 5% in a similar United States study of patients presenting with chronic fatigue.[7] Another United States study in 22 patients with long term fatigue suggested that ''laboratory abnormalities are not useful in guiding evaluation of treatment for their fatigue'',[8] and in a study of 220 patients presenting with fatigue, laboratory results were judged to be clinically important in 9% of cases, but it is not clear if they added information to that obtained from clinical history and examination.[9]

The results of this study, which focused on elite athletes presenting with predominantly short term fatigue, are similar to those found in a general practice population and patients with long term fatigue. In only one case (2% of the sample) did the test results (raised total white cell count and neutrophilia) alter diagnosis. In this case, a 16 year old volleyball player presented with a three to four week history of fatigue. Three weeks before presentation, she had been treated with antibiotics for headache, fever, and a sore throat. At presentation, the initial complaint was fatigue, but she also complained of headache and sore throat accompanied by intermittent fever and mild stress associated with school matters. Clinical examination, particularly of the throat and cervical lymph nodes, was unremarkable, and a diagnosis of viral upper respiratory tract infection was made. Two days later, when note was made of the raised total white cell count and neutrophilia, the patient was recalled. Clinical examination revealed a spot of discharge on the left tonsil and one tender, enlarged cervical lymph node bilaterally. The diagnosis was altered to a bacterial throat infection, and, in view of a history of penicillin allergy, the patient was prescribed erythromycin. Significant improvement was noted three days later.

Although abnormalities were detected in a large number of athletes, on follow up, few were of clinical significance, and this finding probably reflects the problems of performing large numbers of tests in groups when the probability of disease is low. In some cases, the results reflect normal findings in athletes, such as dilutional ''anaemia''. Similar findings were noted in a recent study of haematological and iron related biochemical screening in elite athletes.[10] Those results that were clinically significant, such as a raised white blood cell count in a case of sinusitis or raised iron related variables in a case of previously diagnosed haemochromatosis, added little to clinical decision making.

The nine cases in which increased AST activity was found warrant some discussion. These increases could not be explained by laboratory factors. One athlete had an AST activity of 41 U/l, which at follow up had increased to 54 U/l, and at further follow up had normalised to 30 U/l. Other liver function tests were normal at each follow up. He had been previously diagnosed with iron overload based on heterozygosity for the C282Y and H63D mutations and a peak serum ferritin of 383 ng/ml and peak transferrin saturation of 56%. At the time of presentation, after a series of venesections, his serum ferritin was 104 ng/ml and his transferrin saturation was 37%. On the basis of three previous sets of normal liver function tests in the year of the study, the follow up results, three sets of liver function tests around the time of his initial diagnosis, and noteworthy training factors at the time of presentation, the isolated finding was not felt to be the cause of this athlete's fatigue. The athlete remains under the care of his general practitioner for yearly follow up.

In the other eight cases, all liver function tests were normal at follow up. There was no past or current history suggestive of hepatitis in any of these cases. The concurrent use of omeprasole may explain the increase in one case. This particular athlete and two others had current or recent (within one week in one case) viral upper respiratory infections. In view of the protean manifestations of infections such as that with the Epstein-Barr virus, it is possible that there may be a connection between the upper respiratory tract symptoms and the increased AST activity. Three cases seem to be purely related to training factors. Although increases in ''liver function tests'', with the serum enzymes almost certainly originating in muscle, have been described in relation to some forms of endurance exercise,[11] such changes have not been described in the sports in which these athletes were involved (swimming and rowing). In two cases, there is no, even speculative, reason for the increased AST activity.

This study confirms the pivotal position of the clinical history in the diagnosis of this specific group of fatigued athletes. This is consistent with the findings of others in their studies of consultant medical practice.[12 13] In a study of internists and hospital outpatient clinic patients, in 76% of the cases the history led to the final diagnosis,[12] and, in a general medical clinic, the eventual final diagnosis was determined after the history in 83% of cases.[13]

In this study, physical examination did not reveal any new relevant diagnoses, but served, in 28% of subjects, particularly in cases of infection, to confirm the history based diagnosis. This probably increased the doctor's confidence in the diagnosis.

Haematological and biochemical tests were of little diagnostic use in this clinical scenario, but may be useful in excluding relatively common problems such as iron deficiency and to reassure both athletes and coaches. In the studies noted above,[12 13] laboratory investigation led to the diagnosis in 11%[12] and ''was useful'' in 9%[13] of cases.

In cases of short term fatigue in elite athletes, a thorough clinical history is mandatory. Physical examination is unlikely to reveal findings not suspected from the history, but should be performed as it is a relatively quick and simple procedure, reassures both doctor and athlete, and, in a larger sample, has the potential to reveal an unexpected finding. Routine ordering of a panel of blood tests at the initial consultation should be discouraged. Unless specifically indicated by the history and examination, investigations are not required at the initial consultation. They may become relevant if improvement has not occurred after a number of weeks. Despite these recommendations and the cost savings that may flow from them, issues of athlete and coach reassurance and expectation need to be considered when the question is: to test or not to test?

What is already known on this topic

- There are no published reports of prospective studies of the clinical utility of blood tests in athletes with short term fatigue

What this study adds

- Use of the panel of blood tests studied, at the initial consultation with an athlete with short term fatigue, has very little effect on the diagnosis
- Physical examination in this clinical scenario adds little information, and the clinical history remains the cornerstone of diagnosis

Competing interests: none declared

Ethics approval: Approval for this prospective study was obtained from the ethics committee of the Australian Institute of Sport

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COMMENTARY

This paper highlights an important clinical issue that is often debated in sports medicine circles. The author highlights the complex nature of the symptom of ''fatigue'' in elite athletes and makes appropriate attribution to a combination of pathological and psychosocial factors. A minor omission was the lack of reference to the widespread ''coach driven'' demands for frequent blood testing of athletes both as a ''monitor of aerobic fitness'' and as a predeterminant of overtraining or ''staleness''. This paper provides further evidence supporting the need for a thorough history and clinical examination. It strengthens the core of evidence based research in clinical sports medicine.

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