

A longitudinal study of exercise metabolism during recovery from viral illness

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An elite athlete engaged in a longitudinal programme of physiological assessment suffered a loss of performance that was later ascribed to an asymptomatic viral illness. In this 15-month, single subject, repeated measures study it was possible to demonstrate a severe decrease of exercise performance following viral illness. The oxygen uptake equivalent to the onset of blood lactate accumulation of 4 mmol l^{-1} (OBLA) decreased by 17% following viral illness, then recovered slowly, but had not returned to pre-viral levels 50 weeks later. Steady state exercise metabolism was also affected. During prolonged exercise at 70% of $\dot{V}O_{2\text{max}}$ the proportion of energy derived from carbohydrate metabolism increased and an inability to maintain euglycaemia was observed. In both the graded and prolonged exercise tests, a pronounced tachycardia was evident after viral illness, possibly as a result of a febrile response to the infection, or, a direct effect of the virus upon myocardial performance. These data provide some preliminary and unique findings of the effects of viral illness upon the physiological and metabolic responses to exercise in an elite athlete. The data also demonstrate the sensitivity of currently used laboratory measures of exercise performance to monitor the changes in physiological function during recovery from viral illness.

Keywords: Viral illness, metabolism, cycling, performance

High-intensity or high-volume training has been reported to increase the incidence of viral and other infectious illnesses among many athletes engaged in training and competition¹⁻³ which may lead to a serious and long-term reduction in athletic performance. The symptoms of a protracted illness in some athletes can resemble those of 'chronic fatigue'⁴ or 'post-viral fatigue syndrome'⁵. Though no reduction in muscle strength or fatigability has been found in patients with post-viral fatigue⁶ subtle changes in hypothalamic function⁷ and skeletal muscle metabolism^{8,9} may persist for several months after the initial infection subsides.

Rarely is there an opportunity to study the physiological changes that result from viral infection

in an elite athlete. Most often the athlete will attend for physiological assessment only after he or she develops an unexplained lack of form. In these cases there is often a lack of detailed physiological data pertaining to the athlete's 'in form' condition with which to compare the effects of the infectious illness. This approach rarely provides adequate evidence of a reduction in physiological function and/or exercise performance resulting directly from the onset of viral infection.

The focus of this report is the physiological and metabolic data obtained from an elite road cyclist who contracted a viral infection (unknown to both athlete and scientist) while engaged in a longitudinal programme of physiological investigation. Detailed data regarding the physiological response to maximal and submaximal exercise were therefore available before, during and after infection. All post-infection trials were performed after a thorough clinical examination had been performed.

Methods

The subject of this report is a 24-year-old male elite road cyclist engaged in training for national and international competition. The competitive event is the 100-km road race requiring the ability to sustain a power output in excess of 300 W for up to 4 h depending upon the prevailing conditions. These data were obtained over a 15-month period beginning in March. The training load at this phase of the training cycle was not considered to be high by the athlete or coach.

Experimental protocol

Maximal oxygen uptake ($\dot{V}O_{2\text{max}}$; protocol A) and the onset of blood lactate accumulation (OBLA; protocol B) were last measured 4 weeks before the recognition of viral illness. Steady state submaximal tests (protocol C) were performed before and during the infectious illness with 7 days intervening between these two tests. The results of the second of these two tests prompted clinical examination and viral antibody studies. Though clinical examination was singularly unrewarding, raised antibodies to Cox-sackie (titres > 300) were subsequently confirmed. OBLA was then reassessed 1, 10, 20 and 50 weeks after the toxic phase of the illness had passed. In the

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absence of any elevation of body temperature or resting heart rate, the subject resumed light training after 1 week and had returned to full training after 4 weeks of recovery.

All exercise tests were performed by the subjects riding their own racing bike on a motorized treadmill (Woodway, XEGL2, Weil-am-Rhein, Germany) at 17 m.p.h. with a fixed incline of 3%. The pedal cadence was maintained at 88 r.p.m. by selection of appropriate gearing. A linear increase in exercise intensity was obtained by the addition of weights to a pulley system attached to the rear of the bike (Figure 1). A 20-min warm-up at 17 m.p.h. at 3% incline with a 1.0 kg weight attached to the pulley, requiring 60% of $\dot{V}O_{2\max}$ was performed before each exercise test. The subject also undertook a 7-day weighed food intake before the start of the study and maintained the same food intake for 3 days before each exercise test which was performed in the morning after an overnight fast.

Protocol A – measurement of maximal oxygen uptake ($\dot{V}O_{2\max}$)

This test consisted of successive 3-min stages in which the weight added to the pulley was increased by 0.5 kg per stage until exhaustion. Expired gas samples were collected during the last minute of each stage and for the last minute of exercise. Capillary blood samples ($2 \times 20 \mu\text{l}$) were obtained within the last 30 s of each stage and at 3 and 5 min after exercise. Heart rate and rate of perceived exertion (RPE) were recorded at the end of each stage and at exhaustion.

Protocol B – graded incremental exercise test

This test consisted of six 10-min stages (1 to 6) in which the weight added to the pulley was increased by 0.3 kg per stage calculated to increase the energy expenditure by 5% of $\dot{V}O_{2\max}$ per stage. Expired gas samples were collected over the last 2–3 min of each stage, capillary blood samples ($2 \times 20 \mu\text{l}$) obtained during the last 30 s of each stage, and heart rate and RPE recorded at the end of each stage.

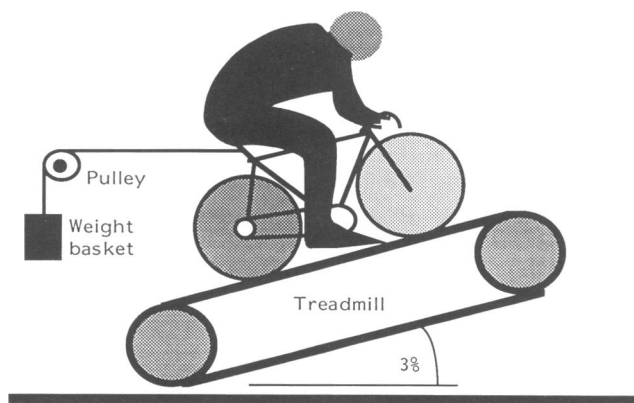


Figure 1. Treadmill cycle ergometry

Protocol C – steady state submaximal exercise test

This test consisted of 3 h at 17 m.p.h. at 3% incline with a 1.0 kg weight attached to the pulley. The relative exercise intensity for this test was calculated to be 70% of maximal oxygen uptake ($\dot{V}O_{2\max}$). Expired gas samples were collected during the last 2–3 min of each 15-min period of exercise, capillary blood samples ($2 \times 20 \mu\text{l}$) were obtained during the last 30 s of each 15-min period and heart rate and RPE recorded at the end of each 15-min period.

Indirect calorimetry

The measurement of oxygen uptake and carbon dioxide excretion was performed using the Douglas Bag (Plysu, Milton Keynes, UK) technique according to the WHO recommendations¹⁰. The total energy expenditure was calculated by summation of the values obtained for each 15-min expired gas sample – the percentage contribution of carbohydrate and fat to the metabolic mixture was calculated from the respiratory exchange ratio (RER).

Analytical method

Capillary blood samples were taken into heparinized capillary tubes, deproteinized in perchloric acid (0.4 M), centrifuged at 5°C and the supernatant stored at -20°C before enzymatic analysis of lactate and glucose¹¹.

OBLA interpolation from lactic acid curves

The blood lactate data from the graded exercise tests (protocol B) were plotted against oxygen uptake as the independent variable. The oxygen uptake equivalent to a reference blood lactate concentration of 4 mmol l^{-1} was interpolated from the fitted curve (Figure 2).

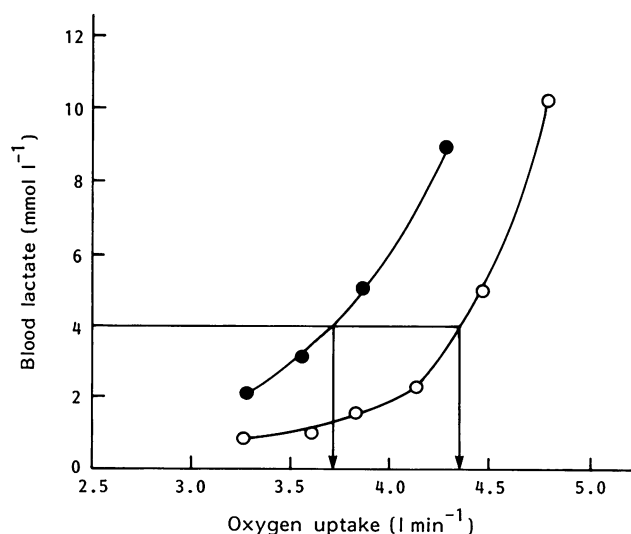


Figure 2. Interpolation of onset of blood lactate accumulation (OBLA) from blood lactate data before (○—○) and after (●—●) viral illness (for details see text)

Table 1. Cardiovascular and metabolic responses to prolonged submaximal exercise at 70% of $\dot{V}O_{2\max}$ before and after viral illness

Sample time (min)	$\dot{V}O_2$ ($l\ min^{-1}$)		RER (units)		Heart rate (beats min^{-1})		RPE (units)		Glucose ($mmol\ l^{-1}$)	
	Before	After	Before	After	Before	After	Before	After	Before	After
15	3.24	3.33	0.92	0.93	140	155	10	11	4.12	3.85
30	3.24	3.40	0.93	0.92	140	159	11	12	3.90	3.95
45	3.25	3.26	0.91	0.93	142	157	11	12	3.90	3.87
60	3.31	3.33	0.89	0.95	140	161	11	12	3.94	3.70
75	3.33	3.33	0.88	0.93	144	162	11	12	4.01	3.53
90	3.24	3.36	0.86	0.91	142	163	11	13	4.03	3.11
105	3.29	3.46	0.85	0.89	146	165	11	13	3.95	3.11
120	3.41	3.43	0.84	0.88	150	171	12	13	3.78	3.03
135	3.45	3.51	0.84	0.86	152	174	12	14	3.62	2.79
150	3.43	3.55	0.82	0.86	155	176	12	17	3.50	2.59
180	3.46	—	0.79	—	158	—	13	—	3.45	—

RER, respiratory exchange ratio; RPE, rate of perceived exertion

Results

Subject data. The following data were recorded 4 weeks before the viral illness. Height 176.4 cm; weight 64.1 kg; estimated body fat, 13.4%; maximal oxygen uptake, 4.78 $l\ min^{-1}$; maximal heart rate 192 beats min^{-1} .

Prolonged submaximal exercise. A pronounced increase in heart rate and perceived exertion ratings in the post-viral trial led to the test being terminated by the experimenter after 150 min (Table 1). As indicated by the change in RER, prolonged submaximal exercise produced a shift in substrate utilization towards a higher percentage of fat oxidation with time. The contribution of fat as a metabolic fuel in the pre-exercise trial increased from 27% after 15 min of exercise to 70% after completion of 3 h. Fat oxidation during the post-viral trial was increased from 23% after 15 min to 47% after 150 min of exercise. Over an equivalent time period (i.e. 150 min) fat oxidation in the pre-viral trial accounted for 60% of the total oxidative metabolism. Resting blood glucose was slightly higher at rest (4.42 versus 4.61 $mmol\ l^{-1}$) in the post-viral trial but, whereas euglycaemia was effectively maintained in the pre-viral trial, the blood glucose concentration decreased markedly after 60 min of exercise after viral illness.

Graded exercise tests. Compared to the pre-viral test, the subject was unable to complete the graded exercise protocol after the infectious illness managing to complete only four of the six stages of the test 1 week post-infection and five of the six stages thereafter. There was a pronounced increase in heart rate at all levels of exercise after 1 week and 10 weeks of recovery which was less evident during stages 1 to 6 after 50 weeks' recovery (Table 2). Near maximal heart rates were attained during the final stage of the graded exercise test at all days of measurement. The blood lactate values were also significantly higher at all stages of the graded exercise test after infection,

the interpolated values revealing a 17% change 1 week after the illness and gradually returning to normal after 50 weeks of recovery (Table 3).

Table 2. Heart rate and blood lactate during graded incremental exercise measured before and during recovery from viral illness

Time (weeks)	Heart rate					
	1*	2*	3*	4*	5*	6*
Pre-viral - 4	150	158	166	174	183	189
Post-viral + 1	159	174	181	187	—	—
Post-viral + 10	156	166	174	183	189	—
Post-viral + 20	150	157	174	181	187	—
Post-viral + 50	149	158	167	177	189	—

Time (weeks)	Blood lactate					
	1*	2*	3*	4*	5*	6*
Pre-viral - 4	0.91	1.10	1.62	2.34	5.10	10.3
Post-viral + 1	2.15	3.18	5.05	8.95	—	—
Post-viral + 10	1.20	1.82	2.45	4.48	9.44	—
Post-viral + 20	1.29	1.60	2.70	4.45	9.20	—
Post-viral + 50	0.89	1.30	2.14	5.32	7.99	—

*Exercise stage

Table 3. Maximal oxygen uptake and onset of blood lactate accumulation (OBLA) before and during recovery from viral illness

Time (weeks)	Performance data	
	$\dot{V}O_{2\max}$ ($l\ min^{-1}$)	OBLA (% $\dot{V}O_{2\max}$)
Pre-viral - 4	4.78	94
Post-viral + 1	4.28*	77
Post-viral + 10	4.30*	81
Post-viral + 20	4.57*	84
Post-viral + 50	4.65*	88

* $\dot{V}O_{2\text{peak}}$

Discussion

The post-viral cardiovascular response to exercise shows a marked tachycardia which could have been the result of an increased cardiac output to satisfy thermoregulatory requirements to an elevated body temperature. Though tenable, this explanation could not account for the non-linear heart rate response (HRR) to increasing exercise intensity observed after viral illness (Figure 3). This abnormal response could be indicative of a decrease in myocardial performance, possibly caused by the preference of the Coxsackie virus for the heart muscle and possibly leading to myocarditis or pericarditis. Clinical electrocardiographic studies during exercise did not however reveal any abnormality in this subject.

The post-viral pattern of metabolic response to exercise in this study indicates a pronounced effect upon carbohydrate metabolism characterized by a greater use of carbohydrate as a metabolic fuel – a failure to maintain euglycaemia and an increase in anaerobic glycolysis resulting in higher blood lactate. Infectious illness can initiate a broad and complex array of metabolic responses¹² some of which are directly related to the specific host defense mechanisms while others contribute to the maintenance of body homeostasis, the provision of metabolizable energy and the synthesis of acute phase proteins. Hormones that regulate carbohydrate metabolism are intimately involved in the host defence response to infectious illness. Decreased carbohydrate tolerance and hyperinsulinaemia often result after viral illness¹³ – findings that are consistent with recent reports of severe and long lasting insulin resistance¹⁴, possibly as a result of elevated levels of hormones antagonistic to insulin such as cortisol, glucagon and growth hormone. The combined effect of these hormonal responses to viral illness would be to increase the availability of glucose at the expense of glucose storage. The observation that insulin resistance has no effect upon oxidative disposal of glucose but effects an apparent block on glucose storage would support this view¹⁵. The resultant hyperglycaemia and glucose intolerance during the early

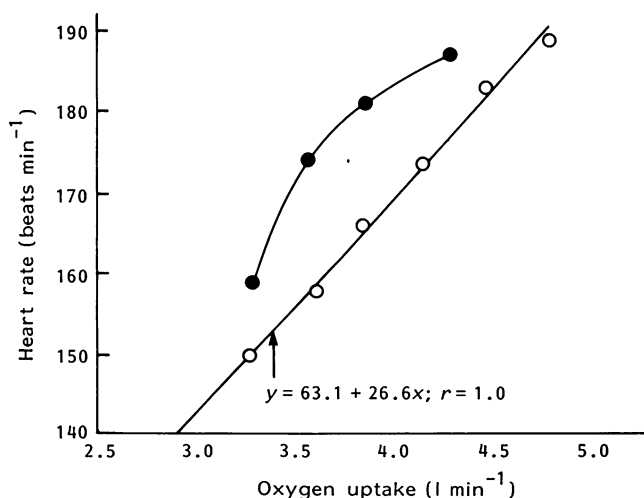


Figure 3. Heart rate relationship to oxygen uptake before (○—○) and after (●—●) viral illness

stages of an infectious illness can reverse to hypoglycaemia and depletion of tissue carbohydrate during persistent infectious illness. The combined effect of viral illness and exercise, which is known to have an insulin-like effect, would accelerate the uptake and oxidation of blood glucose. Failure to maintain euglycaemia during exercise, as was observed in this study, could therefore result from lower basal levels of liver glycogen and increased demand for glucose as an oxidizable fuel.

An alternative explanation for the increased carbohydrate oxidation during prolonged exercise could be a failure in the relative contribution of fat oxidation to overall energy metabolism. Lipolysis of triglycerides stored in adipose tissue is accelerated during exercise by an increase in the activity of adipose cell, or hormone sensitive lipase (HSL), resulting in up to a five-fold increase in the circulating level of free fatty acids. This rise in free fatty acids is mediated by the combined effects of an increasing β -adrenergic stimulus to the adipocyte and a decline in the circulating insulin during prolonged exercise¹⁵. Though little is known about the actual process by which free fatty acids are taken up by skeletal muscle, the increase in the presentation of free fatty acids to the muscle (i.e. flow \times concentration) during exercise is known to produce a corresponding increase in their uptake and oxidation¹⁶. The shift in substrate for exercising muscle to a higher percentage of fat oxidation reduces the rate of muscle glycogen utilization and increases the duration for which exercise can be performed¹⁷. Though the circulating glycerol and fatty acid concentrations were not measured in this study and the exercise response of fatty acid mobilization after viral illness is unknown, the resting levels of serum fatty acids are known to be lowered in severe acute and chronic viral infections¹⁸, and may remain low for some time after the acute phase of the infection has passed¹⁹.

The onset of blood lactate accumulation is frequently used as a determinant of endurance performance in well-trained cyclists²⁰. Recent reports of a high correlation between muscle and blood lactate concentration during incremental exercise has been interpreted to indicate that the blood lactate threshold corresponds to the muscle lactate threshold²¹. The increased production of lactate for the same absolute exercise intensity after viral illness implies either an accelerated flux through glycolysis or decrease in the rate of entry of pyruvate for mitochondrial oxidation. The short time period of detraining after viral illness (10 days) is unlikely to account for the observed changes in OBLA and, although there is insufficient evidence from the present study to support the hypothesis that the increase in blood lactate is linked to abnormal metabolism of muscle *per se*, it is possible that the oxidative capacity of muscle could be affected after viral illness²² thereby requiring a greater contribution from anaerobic glycolysis to maintain the rate of adenosine triphosphate resynthesis and causing an increase in muscle acidosis⁸. Alternatively, diversion of glucose away from carbohydrate oxidation could lead to an increased blood lactate concentration. The mechanism of action for such an effect could be

similar to that induced by septicaemia²³ and mediated via a change in activity of the pyruvate dehydrogenase complex thereby limiting the rate of pyruvate oxidation.

In summary, the data from this study show a pronounced change in physiological correlates of endurance performance following viral infection. The data also provide a warning to both athletes and their coaches of the potential damage that could occur if athletes attempt to 'run off a cold' or other infectious illness. Though limited in number these data warrant a more detailed investigation of the mechanism by which viral illness affects sporting performance and the time course of recovery from viral illness.

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