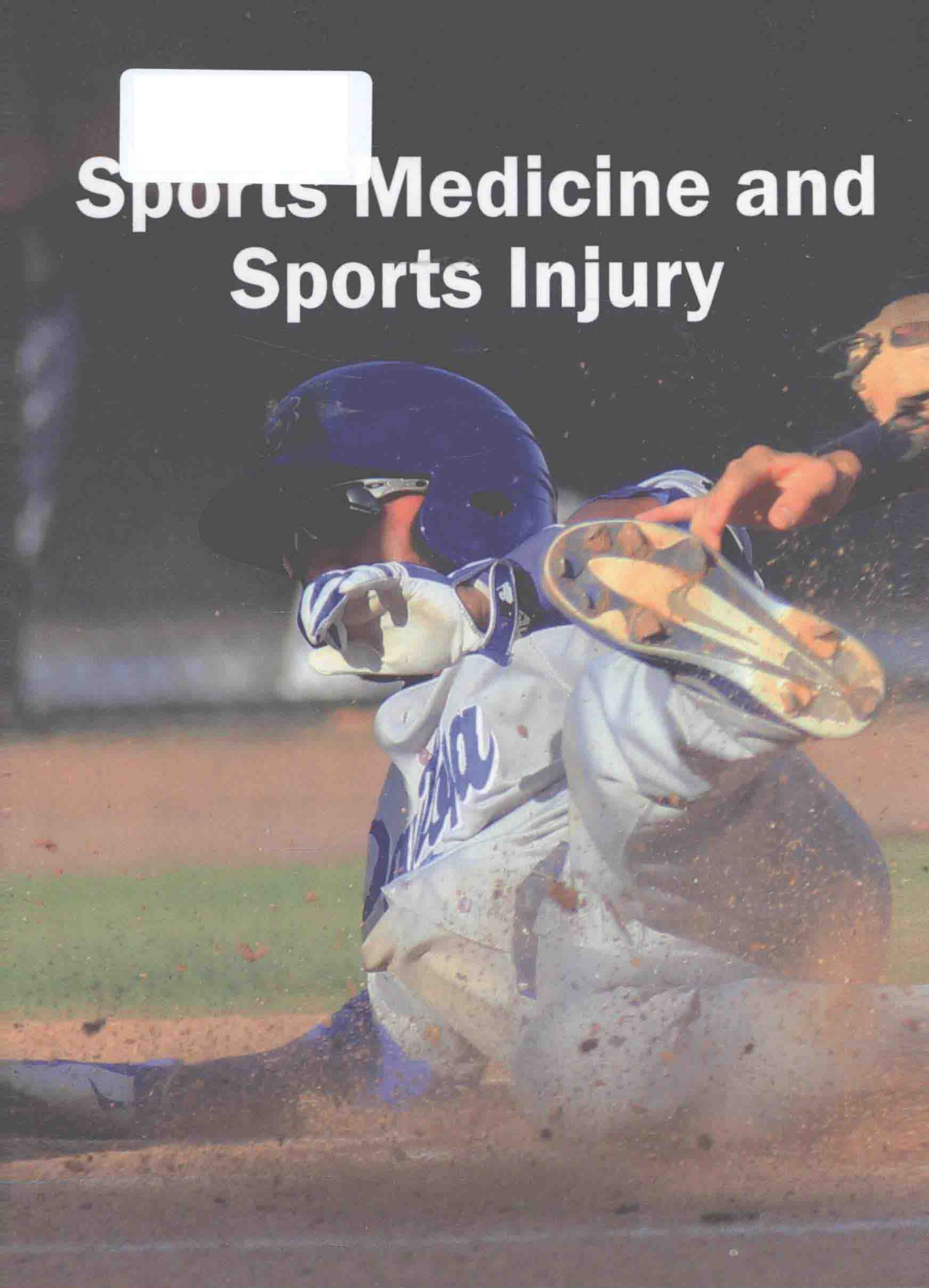
Sports Medicine and Sports Injury



Pablo De Souza

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Edited by **Pablo De Souza**

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Preface

I am honored to present to you this unique book which encompasses the most up-to-date data in the field. I was extremely pleased to get this opportunity of editing the work of experts from across the globe. I have also written papers in this field and researched the various aspects revolving around the progress of the discipline. I have tried to unify my knowledge along with that of stalwarts from every corner of the world, to produce a text which not only benefits the readers but also facilitates the growth of the field.

This book is dedicated to the recent findings and emerging concepts of sports medicine. For the last several years, sports medication has been a growing discipline in USA and Western Europe. Immense strides have been made in comprehending the fundamental functioning of work outs, power utilization and the mechanisms of sports damage. Furthermore, a development in minimally invasive surgeries and physical rehabilitation has led to athletes returning to their respective sport quickly after injuries. This book presents some latest information from experts on the physiology of work out and sports routine, and updates on medical disorders treated in athletes.

Finally, I would like to thank all the contributing authors for their valuable time and contributions. This book would not have been possible without their efforts. I would also like to thank my friends and family for their constant support.

Editor

Contents

Part 1

Physiology of Sports Medicine

1

Measurement and Physiological Relevance of the Maximal Lipid Oxidation Rate During Exercise (LIPOXmax)

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1. Introduction

The intensity of exercise that elicits a maximal oxidation of lipids has been termed LIPOXmax, FATOXmax or FATmax. The three acronyms refer to three original protocols of exercise calorimetry which have been proposed almost simultaneously and it is thus interesting to maintain the three names in this review in order to avoid confusion. The difference among the three protocols is presented in table 1. Since our team has developed the technique called LIPOXmax (Perez-Martin et al., 2001; Brun et al., 2009b;) this acronym will be more employed in this chapter, keeping in mind that LIPOXmax, FATOXmax or FATmax represent obviously the same physiological concept.

As will be reviewed in this paper, the measurement of LIPOXmax by graded exercise calorimetry is a reproducible measurement, although modifiable by several physiological conditions (training, previous exercise or meal). Its measurement closely predicts what will be oxidized over 45-60 min of low to medium intensity training performed at the corresponding intensity. It might be a marker of metabolic fitness, and is tightly correlated to mitochondrial function. LIPOXmax is related to catecholamine status and the growth-hormone IGF-I axis, and occurs in athletes below the lactate and the ventilatory threshold (on the average around 40% VO_{2max}). Its changes are related to alterations in muscular levels of citrate synthase, and to the mitochondrial ability to oxidize fatty acids. A meta-analysis shows that training at this level is efficient in sedentary subjects for reducing fat mass, sparing fat-free mass, increasing the ability to oxidize lipids during exercise, reducing blood glucose and Hba_{1c} in type 2 diabetes, and decreasing circulating cholesterol. In athletes, various profiles are observed, with a high ability to oxidize lipids in endurance-trained athletes and in some samples of athletes trained for sprint or intermittent exercise a profile showing a predominant use of carbohydrates.

acronym	FATOXmax	FATmax	LIPOXmax	SIN model
initial publication	Dériaz et al., 2001	Achten et al., 2002, 2003, 2004; Jeukendrup, 2003; Venables et al., 2005	Perez-Martin et al., 2001; Brun et al., 2009b;	Chenevière et al., 2009b
Duration of steps	5-6 min (until steady state)	3 min	6 min	5 min
Calculation	Visual determination	Visual determination	Power intensity at which the derivative of the curve of lipid oxidation versus power is equal to zero (eg, top of the bell-shaped curve)	This model includes three independent variables (dilatation, symmetry, and translation). This SIN model has been reported to allow a more accurate calculation of Fatmin/LIPOXzero
Expression of results	% of maximal oxygen uptake (%VO_{2max} MFO in kJ.min-1	% of maximal oxygen uptake (%VO_{2max}) MFO in g. min-1	usually % of theoretical maximal power; also % extrapolated maximal oxygen uptake (%VO_{2max} ACSM)] or % maximal oxygen uptake (%VO_{2max}) determined by a previous test	Fatmax, MFO, dilatation, symmetry and translation

Table 1. Definition of LIPOXmax, FATOXmax or FATmax.

2. The physiological basis for measuring lipid oxidation during exercise

2.1 Balance of substrate oxidation during exercise: The "crossover concept"

Pioneering studies (Zuntz et al., 1901; Krogh et al., 1920; Christensen et al., 1939) have demonstrated that a mixture of carbohydrates and fat is used by the muscle as a fuel at rest and during exercise, and that the ratio between VCO_2 and VO_2 was a reflect of the relative proportion of lipids and CHO used for oxidation. It was clear already at this time that exercise intensity, exercise duration and prior diet modified this balance of substrates.

Recent studies have evidenced that quantitatively, the most important substrate oxidized at the level of the exercising muscle is glucose (Bergman et al., 1999; Friedlander et al., 2007). The maximal rate of CHO oxidation during exercise is about two fold higher than that of lipids (Sahlin et al., 2008). However, when substrate metabolism is assessed on the whole body, lipids remain a major source of fuel at rest and during exercise. At rest, lipids provide >50% of the energy requirements, and they remain an important source of energy during low to middle intensity exercise, while CHO become the main substrate at high intensity (>80% VO_2max) (Jeukendrup et al., 1998). As summarized in table 2, exercise may induce a significant amount of lipid oxidation by at least 4 mechanisms (Brun et al., 2011).

During the last quarter of the XXth century the literature became conflictual with several authors emphasizing the importance of carbohydrates and the others the importance of lipids. This controversy was actually clarified by the heuristic proposal of the "crossover concept" by George Brooks (Brooks et al., 1994). The "crossover concept" is an attempt to integrate the seemingly divergent effects of exercise intensity, nutritional status, gender, age and prior endurance training on the balance of carbohydrates and lipids used as a fuel during sustained exercise. It predicts that although an increase in exercise intensity results in a preferential use of CHO, endurance training shifts the balance of substrates during exercise toward a stronger reliance upon lipids (Fig.1).

The idea of developing a simple reliable exercise-test for assessing this balance of substrates thus emerged as a logical consequence of these fundamental studies (Perez-Martin et al.,

2001; Brun et al., 2007, 2011). Accordingly, several teams have developed this measurement and attempted to train patients at a level determined by this exploration, as reviewed below.

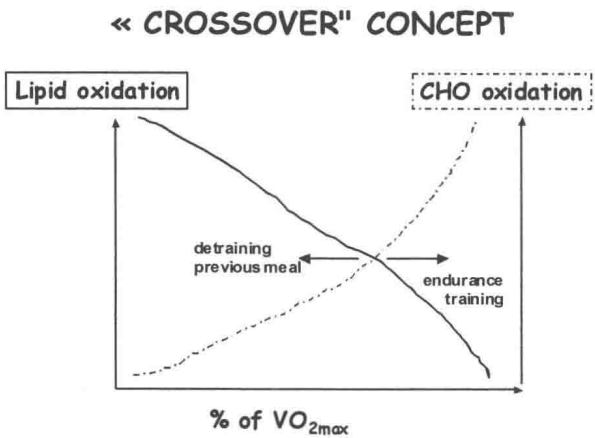

Fig. 1. The crossover concept: the balance of substrates at exercise is a function of exercise intensity, the proportion of lipids used for oxidation continuously decreasing when intensity increases, while CHO become the predominant fuel (>70%) above the "crossover point" (approximately 50% VO_{2max}, see text. This increase in CHO oxidation down-regulates lipid oxidation despite sustained lipolysis. Above the crossover point glycogen utilization scales exponentially. Endurance training, energy supply, overtraining, dietary manipulation and previous exercise modify this pattern. Most trained athletes exhibit a right-shift in this relationship.

a.	Muscular contractile activity by its own may use lipids as a source of energy.	During steady state exercise performed at low intensity, fat is oxidized at an almost constant rate (Bensimhon et al., 2006; Meyer et al., 2007), and there is an intensity of exercise that elicits the maximum oxidation of lipids termed *maximal fat oxidation rate* (MFO).
b.	Progressive rise in lipid oxidation with exercise duration	When exercise is heavy and prolonged enough to result in glycogen depletion, there is a shift toward lipids and their oxidation gradually increases (Ahlborg et al., 1974; Bergman et al., 1999; Watt et al.; 2003). This phenomenon is rather slow in mild to medium intensity exercise when the duration of this exercise does not exceed 1 hr.
c.	Compensatory rise in lipid oxidation after high intensity exercise	High intensity exercise oxidizes almost exclusively CHO but is frequently followed by a compensatory rise in lipid oxidation which compensates more or less for the lipids not oxidized during exercise (Folch et al., 2001; Melanson et al., 2002), but it is inconsistent and frequently quite low (Malatesta et al., 2009; Lazer et al., 2010), even more if exercise is discontinuous (Warren et al., 2009).
d.	Long term regular exercise may increase the ability to oxidize lipids at rest	Long term regular exercise may shift the balance of substrates oxidized over 24 hr toward oxidative use of higher quantities of lipids (Talanian et al., 2007). A training-induced increase in the ability to oxidize lipids over 24-hr is statistically a predictor of exercise-induced weight loss (Barwell et al., 2009).

Table 2. Effects of exercise on lipid oxidation: exercise may increase the oxidative use of lipids by at least 4 mechanisms (after Brun et al., 2011). According to Warren the most important and reliable of these mechanisms is the oxidation during exercise performed around the LIPOXmax or below. (Warren et al., 2009).

2.2 Mechanisms of substrate (fat vs CHO) selection during muscular activity

According to the data presented above, fat is the major energy supply for the muscle below 25% of VO_2max, since in this condition very few glycogen is employed as a source of energy (Romijn et al., 1993). Then, when exercise intensity increases, glycogen will rapidly become the predominant fuel. However, fat oxidation will still increase until the LIPOXmax/FATOXmax is reached. Above this level fat oxidation decreases. Interestingly, this decrease in fat oxidation coincides with lactate increase above baseline, as demonstrated in healthy adolescents during incremental cycling (Tolfrey et al., 2010).

The cellular mechanism of this decrease has been reviewed elsewhere (Sahlin et al., 2008) and is still incompletely understood. Theoretically, lipid supply by lipolysis, lipid entrance in muscle cell, lipid entrance in mitochondria, and mitochondrial fat processing may all be limiting steps. Experiments show that extracellular lipid supply is not limiting, since lipid oxidation decreases even if additional fat is provided to the cell. Limiting steps seem to be the entrance in mitochondria, governed by CPT-1, which can be inhibited by Malonyl-CoA and lactate (Starritt et al., 2000), and possibly downstream CPT-I other mitochondrial enzymes such as Acyl-CoA synthase and electron transport chain. All these steps are sensitive to the rate of CHO oxidation and thus a rise in CHO oxidation seems to depress lipid oxidation despite availability of fat and presence of all the enzymes of fat oxidation.

Experiments using intravenous infusion of labeled long-chain fatty acids in endurance-trained men cycling for 40 min at steady state at 50% of VO_2max clearly demonstrate that carbohydrate availability directly regulates fat oxidation during exercise. An increased glycolytic flux results in a direct inhibition of long-chain fatty acid oxidation (Coyle et al., 1997). Conversely, there is a wide body of evidence that glycogen depletion reverses this inhibition and thus increases fat oxidation, as observed during long duration glycogen-depleting exercise.

These processes are governed by cellular factors, that are under the influence of the central nervous system and circulating hormones (Ahlborg et al., 1974; Kiens & Richter, 1998; Kirvan et al., 1988; Thompson et al., 1998). Intracellular pathways have been reviewed elsewhere and this area of knowledge seems to be rapidly expanding. The activation of the AMPK (AMP-dependent kinase) pathway, together with a subsequent increase in the fatty acid oxidation, appear to constitute the main mechanism of action of these hormones in the regulation of lipid metabolism (Koulmann & Bigard, 2006). To summarize the main hormonal regulators of muscular lipid oxidation, epinephrine increases lipolysis (beta effect) and increases glucose oxidation in muscle (de Glisezinski et al., 2009). Norepinephrine increases lipid oxidation in muscle (Poehlman et al., 1994). Cortisol increases adipogenesis and lipolysis, and decreases non-insulin mediated glucose uptake. β-endorphin induces a lipolysis that can be blunted by naloxone (Richter et al., 1983, 1987). Growth hormone (GH) stimulates lipolysis and ketogenesis (Møller et al., 1990b). In the muscle and the liver, GH stimulates triglyceride uptake, by enhancing lipoprotein lipase expression, and its subsequent storage (Vijayakumar et al., 2010). GH also increases whole body lipid oxidation and nonoxidative glucose utilization and decreases glucose oxidation (Møller et al., 1990a). We have shown that GH-deficient individuals have a lower LIPOXmax and MFO that is restored after GH treatment (Brandou et al., 2006a). Dowstream GH, IGF-I that mediates many of the anabolic actions of growth hormone stimulates muscle protein synthesis, promotes glycogen storage and enhances lipolysis (Guha et al., 2009).

Interleukin-6 (IL-6) coming from the adipose tissue and the muscle acts as an energy sensor and thus activates AMP-activated kinase, resulting in enhanced glucose disposal, lipolysis and fat oxidation (Hoene et al., 2008). Adiponectin increases muscular lipid oxidation via phosphorylation of AMPK (Dick, 2009). Leptin increases muscle fat oxidation and decreases muscle fat uptake, thereby decreasing intramyocellular lipid stores (Dick, 2009).

Although the information on this issue remains limited, it is clear that the level of maximal oxidation of lipids is related to some of these hormonal regulators : norepinephrine, whose training induced changes are positively correlated to an improvement in LIPOXmax (Bordenave et al., 2008) and growth hormone, whose deficit decreases it, a defect that can be corrected by growth hormone replacement (Brandou et al., 2006a). Downstream GH, IGF-I has also been reported to be correlated to LIPOXmax in soccer players as shown on Fig 5 (Brun et al., 1999), reflecting either a parallel effect of training on muscle fuel partitioning or IGF-I release, or an action of IGF-I (or GH via IGF) on muscular lipid oxidation. Other endocrine axes are surely also involved but this issue is poorly known and remains to be studied.

3. Technical aspects of exercise graded calorimetry

3.1 Methodological aspects

As reminded above, the classic picture of Brooks and Mercier's "crossover concept" (Brooks & Mercier, 1994) has led to the development of an exercise-test suitable for routinely assessing this balance of substrates (Perez-Martin & Mercier, 2001; Brun et al., 2007). Based on our previous studies on calorimetry during long duration steady-state workloads (Manetta et al., 2002a, 2002b; Manetta et al., 2005) we developped a test (Perez-Martin et al., 2001) consisting of five 6-min submaximal steps, in which we assumed that a steady-state for gas exchanges was obtained during the 2 last minutes.

We proposed (Perez-Martin et al., 2001) a diagnostic test including four or five 6-minutes workloads, that may be followed by a series of fast increases in power intensity until the tolerable maximum under these conditions is reached. This final incremental part of the test can be avoided in very sedentary patients and the maximal level can be indirectly evaluated by the linear extrapolation according to the ACSM guidelines (VO_2max ACSM) (Aucouturier et al., 2009). The test is performed on an ergometric bicycle connected to an analyzer allowing the analysis of the gaseous exchange cycles by cycle. EKG monitoring and measurements of VO_2, VCO_2, and respiratory exchange ratio (RER) are performed during the test. After a period of 3 minutes at rest, and another period of initial warm-up at 20% of the predicted maximal power (PMP) for 3 minutes, the 6-min workloads set at approximately 30, 40, 50 and 60% of PMP are performed. The phase of recovery comprises two periods during which a monitoring of respiratory and cardiac parameters is maintained: active recovery at 20% of the PMP during 1 minute; passive recovery (*ie*, rest) during the 2 following minutes. At the end of each stage, during the fifth and sixth minutes, values of VO_2 and VCO_2 are recorded. These values are used the calculation of the respective rates of oxidation of carbohydrates and lipids by applying the classical stoichiometric equations of indirect calorimetry:

$$\text{Carbohydrates (mg/min)} = 4.585\ VCO_2 - 3.2255\ VO_2 \quad (1)$$

$$\text{Lipid Oxidation (mg/min)} = -1.7012\ VCO_2 + 1.6946\ VO_2 \quad (2)$$

These calculations are performed on values of the 5-6th minutes of each step, since at this CO_2 production from bicarbonate buffers compensating for the production of lactic acid becomes negligible. The increment in carbohydrate oxidation above basal values appears to be roughly a linear function of the developed power and the slope of this relation is calculated, providing the *glucidic cost of the watt* (Aloulou, 2002). The increase in lipid oxidation adopts the shape of a bell-shaped curve: after a peak, lipid oxidation decreases at the highest power intensities.

The exact mechanism of this reduction in the use of the lipids at the highest power intensities is actually imperfectly known: a reduction in lipolysis is likely to explain a part of it, together with a shift of metabolic pathways within the muscle fiber. The empirical formula of indirect calorimetry that gives the lipid oxidation rate is, as reminded above:

$$\text{Lipid oxidation (mg/min)} = -1.7\ VCO_2 + 1.7\ VO_2 \quad (3)$$

It is easy to deduce from this formula that the relation between power (P) and oxidation of lipids (Lox) displays a bell-shaped curve of the form:

$$Lox = A.P\ (1\text{-}RER) \quad (4)$$

The smoothing of this curve enables us to calculate the power intensity at which lipid oxidation becomes maximal, which is the point where the derivative of this curve becomes equal to zero. Therefore the LIPOXmax calculation is only an application of the classical empirical equation of lipid oxidation used in calorimetry.

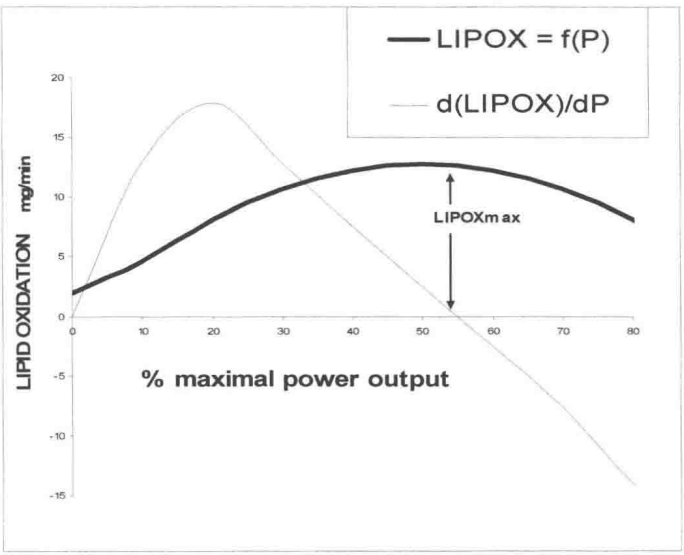

Fig. 2. Calculation of the LIPOXmax: The curve of lipid oxidation (mg/min) is given by the empirical formula of calorimetry Lipox = $-1.7\ VCO_2 + 1.7\ VO_2$. This curve Lipox = A.P (1-RER) (see text) can be derived and the point where its derivative equals zero is the top of the bell-shaped curve and thus represents the LIPOXmax. Actually in some subjects this is a broad zone and in others a narrow range of power intensities.