

Cigarette Smoking: Nicotine, Carbon Monoxide, and the Physiological Effects on Exercise Responses

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Worldwide, tobacco use is considered the leading preventable cause of morbidity and mortality. The most common form of tobacco use is cigarette smoking. Smoking increases a person's risk for diseases such as heart disease, cancer, and chronic obstructive pulmonary disease. Associated with these increased risks for disease is a shortened lifespan in smokers. Research has also shown that cigarette smoking alters the body's response to exercise. Nicotine and carbon monoxide are two compounds in cigarette smoke that may affect cardiorespiratory function, thereby modifying the body's exercise response. Additionally, research has shown that compared to nonsmokers, smokers demonstrate a greater reliance on glucose as a fuel source during exercise. A focus of this review is on the cigarette smoke compounds nicotine and carbon monoxide and the mechanisms by which these compounds affect the human body. Also addressed are the physiological effects of cigarette smoking on exercise tolerance, aerobic capacity, and substrate utilization.

Keywords: tobacco, aerobic capacity, cardiovascular physiology

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Introduction

Tobacco use is identified as the number one preventable cause of death in the United States (United States Department of Health and Human Services [USDHHS], 2004) and worldwide (World Health Organization, 2011). In the U.S., cigarette smoking is the most popular method of using tobacco (National Institute on Drug Abuse [NIDA], 2009), with a current estimate of approximately 24.2 percent of the population (NIDA, 2009). Adult smoking rates in other countries around the world vary with the United Kingdom, Germany, and Romania reporting rates of 26.5, 35.0, and 43.5 percent respectively (World Health Organization, 2002). Regardless of rates, compared to nonsmokers, those who smoke face more health problems and a greater loss of productivity during their lifetime, a lifetime that is approximately 14 years shorter than that of a nonsmoker (USDHHS, 2004).

In addition to being a major public health concern, cigarette smoking has been shown to adversely affect exercise performance. While most studies analyzing smoking and exercise performance have focused on cardiorespiratory function, there is evidence indicating that compared to nonsmokers, smokers have a greater dependence on glucose as a fuel source during submaximal exercise (Colberg, Casazza, Horning, & Brooks, 1994; Huie, Casazza, Horning, & Brooks, 1996).

Compounds of Cigarette Smoke

There are over 4000 chemicals in tobacco smoke (NIDA, 2009), but most research involving the effects of cigarette smoking on exercise has focused on the compounds nicotine and carbon monoxide. Each compound has independent effects on the human body.

Nicotine

Nicotine is recognized as one of the most commonly used addictive drugs and cigarette smoking is the most prevalent form of nicotine addiction in the United States (NIDA, 1998). The typical cigarette on the United States market contains approximately 10 milligrams or more of nicotine (NIDA, 1998). Through inhaling of cigarette smoke, smokers absorb into the body an average of one to two milligrams of nicotine per cigarette (NIDA, 2009).

Nicotine and catecholamine release. Nicotine exposure through cigarette smoking causes a stimulation of the sympathetic nervous system (Cryer, Haymond, Santiago, & Shah, 1976) leading to an increased release of

the catecholamines epinephrine and norepinephrine from the adrenal medulla (Burn, 1960b). The increased release of epinephrine and norepinephrine from the adrenal medulla causes a rise in the circulating levels of these catecholamines, and this rise has been associated with the nicotine-induced increases in heart rate and blood pressure (Grassi, et al., 1994). Additionally, these cardiovascular changes are attenuated during alpha- and beta-adrenergic blockade (Cryer, et al., 1976), indicating that they are mediated by adrenergic mechanisms. However, the nicotine-induced cardiovascular changes have been shown to occur prior to measurable increases in plasma catecholamines (Cryer, et al., 1976). This observation indicates that the initial hemodynamic changes may be due to local release of norepinephrine from within the cardiovascular system (Cryer, et al., 1976). In 1951, Goodall showed that norepinephrine was present in the heart muscle of sheep, and in 1958, Burn and Rand demonstrated that the action of nicotine on the hearts of rabbits was due to the release of norepinephrine from stores within the heart.

Similar mechanisms may be responsible for the peripheral vessel constriction associated with nicotine exposure. Kottegoda (1953) studied the constrictor actions of nicotine in the vessels of rabbit ears. His data suggested that nicotine-induced constriction was due to the release of epinephrine or norepinephrine from sites in or near the walls of the vessels. In 1958, Burn and Rand presented data that indicated that the constriction in rabbit ear vessels after nicotine exposure was due to the local release of norepinephrine.

The local release of norepinephrine from the heart and peripheral vessels raises the question of storage sites. Wiesel and Busacchi described the presence of chromaffin tissue in human hearts, and Trinci showed that chromaffin tissue was present in the hearts of guinea pigs and cats (as cited in Burn, 1960a). Additionally, chromaffin cells have been identified in the skin of rabbit ears. Thus, Burn suggested that nicotine may stimulate the release of norepinephrine from chromaffin tissue in the heart (1960a) and in the skin (1960b) and that this local catecholamine release may produce the increased heart rate and blood vessel constriction. Grassi and others (1994) have more recently discussed the catecholamine release from chromaffin tissue at peripheral sympathetic sites. Thus, the nicotine-induced cardiovascular effects can be attributed to stimulation of catecholamine release from peripheral sympathetic nerve endings and the adrenal medulla (Haas & Kübler, 1996).

Nicotine and hemodynamic effects. Through the secretion of norepinephrine from chromaffin tissue in the heart and in or near blood vessels and the release of epinephrine from the adrenal medulla, nicotine causes several hemodynamic effects. The two effects most discussed in literature are increases

in heart rate and blood pressure. However, other cardiovascular effects such as increases in heart muscle contractility, cardiac output, and stroke volume occur from nicotine exposure.

Increases in plasma nicotine levels occur immediately after smoking (Koch, et al., 1980), and the effects of smoking on heart rate and blood pressure have been demonstrated to be caused by the nicotine contained within the cigarettes (Brunel, Girerd, Laurent, Pannier, & Safar, 1992; Cryer, et al., 1976; Haymond, Santiago, & Shah, 1976; Koch, et al., 1980; Tachmes, Fernandez, & Sackner, 1978). Brunel and colleagues (1992) compared the hemodynamic effects of cigarette smoking in six healthy, nonsmoking males aged 19 to 36 years. Subjects rested for 30 minutes in the supine position before beginning either a sham smoking or a cigarette smoking trial. The sham smoking trial was performed using an epoxy tube, whereas the cigarette smoking trial was accomplished by smoking two cigarettes containing 1.34mg of nicotine within a 10-minute period. No inhalation of the cigarette smoke occurred. Each subject performed both trials. During the sham smoking trial, no changes in mean blood pressure or heart rate occurred. In contrast, subjects demonstrated a significant increase in mean blood pressure during the cigarette smoking trial and this increase was maintained for approximately one hour.

In a study by Benowitz, Kuyt, and Jacob (1984), habitual smokers with an average cigarette consumption of 30 cigarettes per day were subjects. Six healthy men and four healthy women with an age range of 21 to 63 years were studied in four three-day treatment blocks. The four treatments consisted of smoking their own brand of cigarette, smoking a high nicotine (2.5mg) cigarette, smoking a low nicotine (0.4mg) cigarette, and abstaining. Daily cigarette consumption was standardized (30/day) at one cigarette every 30 minutes for 15 hours (8:30am to 11:00pm). Subjects were instructed to smoke each cigarette to a marked 30-millimeter butt length. Twenty-four hour cardiovascular measurements were made on the second day of each treatment. Heart rate and blood pressure were higher after smoking any cigarette compared to abstinence. Nicotine concentrations were highest during the high nicotine cigarette treatment followed by the usual brand treatment and then the low nicotine treatment. However, increases in heart rate did not significantly differ between the three smoking treatments. The authors concluded that the heart rate effect did not differ as a function of nicotine exposure. However, findings from other studies have contradicted these results.

Tachmes and colleagues (1978) conducted one such study that demonstrated a heart rate effect determined by the amount of nicotine exposure. They studied the hemodynamic effects of smoking high and low nicotine cigarettes in a group

of young smokers. Five men and three women with ages of 18 to 30 years performed three trials for the study. In random order, on three separate days, each subject smoked (in his or her usual fashion) a cigarette of high nicotine content (2.4mg), a cigarette of low nicotine content (0.1mg), and cigarette in sham fashion. Hemodynamic measurements were repeated in duplicate and averaged at 5, 15, 60, 90, and 120 minutes after the conclusion of smoking. Heart rate increased significantly after smoking, but the increase was more dramatic with the high nicotine cigarette. The smaller, but significant increase in heart rate for the low nicotine cigarette was evident at five minutes, but was not significantly different from baseline at 15 minutes. In contrast, the significant increase in heart rate caused by the high nicotine cigarette was still evident at 15 minutes. At 60 minutes, no differences in heart rate were seen for any treatment. Changes in systolic and diastolic blood pressure measurements for the low and high nicotine cigarettes followed very similar patterns to the changes in heart rate measurements. Sham smoking of a cigarette resulted in no changes in heart rate or blood pressure.

Researchers have reported various time durations for the different cardiovascular effects of cigarette smoking. In a review article including results from several cigarette-smoking studies, Omvik (1996) reported that smoking causes increases of 10 to twenty-five mmHg and six to 12 mmHg for systolic and diastolic blood pressures respectively. In a study not included in Omvik's review, Benowitz, Porchet, Sheiner, and Jacob (1988) demonstrated that smoking a cigarette causes a rise in heart rate of 10 to 20 beats per minute and an increase in blood pressure of five to 10 mmHg. Benowitz et al. (1988) reported that the rise in blood pressure lasts for approximately 30 minutes while the increased heart rate persists for up to one hour. Grassi and colleagues (1994) saw hemodynamic changes due to smoking that were still observable after 30 minutes. These researchers suggested that their results provide evidence that the cardiovascular effects of smoking are long lasting and that in a person who smokes two to three cigarettes per hour the cardiovascular system is likely to be under the permanent hemodynamic responses of smoking. Thus, increased myocardial oxygen demands as reflected by an increased double product become the norm for a smoker with such a habit.

Studies have demonstrated that cardiac output also increases in response to nicotine exposure (Irving & Yamamoto, 1963; Tachmes, et al., 1978). The increase in cardiac output is due mostly to an increase in heart rate (Omvik, 1996; Tachmes, et al., 1978) although some studies indicate that nicotine also causes an increase in stroke volume (Irving & Yamamoto, 1963). Thus, stroke volume may play a role in the elevation of cardiac output following exposure to nicotine.

The increased cardiac output observed with smoking begins to return to baseline levels in 10 to 15 minutes after smoking is stopped (Irving & Yamamoto, 1963).

Nicotine exposure through injection has been shown to increase the myocardial contractility in animals (Hebekk & Lekven, 1974), and increases in myocardial contractility following smoking have been observed in human subjects by using echocardiography and systolic time intervals (Rabinowitz, Thorp, Huber, & Abelmann, 1979) and other methods (Behr, Leong, & Jones, 1981). Under conditions of increased myocardial contractility, slight increases in stroke volume have been observed (Omvik, 1996). Thus, an increased myocardial contractility may assist in elevating the cardiac output.

Carbon Monoxide

Carbon monoxide is produced by the incomplete combustion of tobacco, and its concentration in cigarette smoke is 1.5 to 4.5 percent (Hirsch, Sue, Wasserman, Robinson, & Hansen, 1985). Carbon monoxide exposure from smoking causes several changes in the body's ability to absorb and utilize oxygen.

Formation of carboxyhemoglobin. When inhaled, cigarette smoke enters the lungs and travels to the air sacs called alveoli. In the alveoli, the carbon monoxide that is present in the smoke binds with hemoglobin forming the compound carboxyhemoglobin. A globular protein found on red blood cells, hemoglobin contains four heme groups and under normal circumstances binds four oxygen molecules, one to each heme group. However, in the presence of carbon monoxide, a hemoglobin molecule may become fully saturated with carbon monoxide. The formation of carboxyhemoglobin easily occurs, considering that carbon monoxide has an affinity for hemoglobin that is 210 times that of oxygen (Rietbrock, Kunkel, Wörner, & Eyer, 1992). Thus, carbon monoxide combines with hemoglobin at a much lower pressure than is required for the binding of oxygen. Its affinity for hemoglobin is so great that carbon monoxide can displace oxygen from hemoglobin (Hirsch, Sue, Wasserman, Robinson, & Hansen, 1985). This is illustrated by the following reaction:



This reaction is very difficult to reverse (Rietbrock, Kunkel, Wörner, & Eyer, 1992) and leads to a decline in oxygen availability for the tissues of the body.

Oxygen saturation and transport. As a smoker inhales, carbon monoxide enters the lungs, reaching the alveoli where gas exchange takes place. With its

strong affinity, the carbon monoxide readily binds with the hemoglobin in the blood forming carboxyhemoglobin. This impedes the saturation of the blood with oxygen. In a smoker, carbon monoxide may substitute anywhere from three to over 15 percent of the blood's oxygen carrying capacity (Klausen, Andersen, & Nandrup, 1983). Others have cited similar percentages for carboxyhemoglobin concentrations in smokers (Hirsch, Sue, Wasserman, Robinson, & Hansen, 1985). In comparison, a nonsmoker will have a carboxyhemoglobin range of 0.3 to 1.6 percent (Rodrigo, 2000). A smoker's concentration of carboxyhemoglobin in the blood will depend on the type or brand of cigarette smoked, the number of cigarettes smoked, the number of puffs from each cigarette, and the inhalation characteristics of each puff (Rodrigo, 2000). Regardless of the smoking characteristics, the presence of carbon monoxide decreases the oxygen carrying capacity of the blood resulting in less oxygen being available for release to tissues (Hirsch, Sue, Wasserman, Robinson, & Hansen, 1985). The decline in oxygen availability could have serious implications for smokers, especially during times of physical stress.

Oxygen-hemoglobin dissociation curve. The oxygen-hemoglobin dissociation curve is a graphical representation of the relationship between the partial pressure of oxygen and the oxygen saturation of hemoglobin. At a normal body temperature (37° Celsius) and normal pH (7.40), hemoglobin is 50 percent saturated at a PO₂ of 27 mmHg. This is known as the p50 of hemoglobin (Bell, 1999). The s-shape of the curve illustrates the sigmoidal relationship between oxygen saturation and the partial pressure, which facilitates the release of oxygen in the tissues.

Exposure to carbon monoxide causes a leftward shift of the oxygen-hemoglobin dissociation curve, resulting in a less efficient release of oxygen in the tissues. This is due to the increased formation of carboxyhemoglobin in the capillaries of the lung and the increased affinity of hemoglobin for oxygen in the tissue capillary beds. Additionally, carbon monoxide reduces the amount of 2,3 diphosphoglycerate (a by-product of red blood cell glycolysis) which contributes to the leftward shift of the curve (Rodrigo, 2000). Also relevant is research by Rietbrock and colleagues (1992) demonstrating that smokers exhibit a slower oxygen dissociation rate from hemoglobin.

Bunn and Forget reported that a shift of the curve to the left can occur at carboxyhemoglobin levels as low as four percent (as cited in Rietbrock, 1992), which is a level commonly seen in smokers. However, no subjective symptoms appear at rest as long as carbon monoxide concentration in the blood is less than 10 percent (Åstrand & Rodahl, 1977). Adverse effects at this level become noticeable only during physical stress (Åstrand & Rodahl, 1977).

Oxygen transport to mitochondria. The increased carboxyhemoglobin level in the blood may attenuate the delivery of oxygen to muscle mitochondria (King, Dodd, & Cain, 1987). Myoglobin, a globular protein present in skeletal muscle, acts as a shuttle for oxygen by transporting it from the cellular membrane into the muscle mitochondria. Myoglobin has an affinity for carbon monoxide that is 200 times greater than that for oxygen (Rodwell, 1990), and unlike hemoglobin, a myoglobin molecule contains only one heme group and thus, binds with only one molecule of oxygen. Therefore, the binding of carbon monoxide to myoglobin can cause a significant reduction in oxygen transport to muscle mitochondria. A significant reduction in intracellular transport of oxygen may limit mitochondria adenosine triphosphate (ATP) production leading to non-oxidative energy production.

Effects of Smoking on Exercise

Many of the effects of cigarette smoking due to nicotine and carbon monoxide cause cardiorespiratory changes in the body that may not hinder functioning at rest. However, these effects from smoking can become more apparent during times of physical stress or activity.

The effects of smoking on the responses to exercise are well researched. While some studies have looked at the effects of smoking on exercise tolerance and performance (Conway & Cronan, 1992; Cooper, Gey, & Bottenberg, 1968; Gordon, et al., 1987; Louie, 2001), others have focused on the acute effects of smoking on cardiorespiratory function during exercise (Hirsh, et al., 1985; Klausen, et al., 1983; Rotstein & Sagiv, 1986). Also, numerous studies have researched the independent effects of carbon monoxide on exercise responses (Aronow & Cassidy, 1975; Horvath, Raven, Dahms, & Gray, 1975; Klausen, et al., 1983; Pirnay, et al., 1971), and some of these have compared carbon monoxide responses to those following cigarette smoking (Aronow & Cassidy, 1975; Klausen, et al., 1983). Because the studies in this area are so numerous and use various and non-standard experimental protocols, it is difficult to compare results.

Exercise Tolerance and Performance

Research has demonstrated differences between smokers and nonsmokers in regards to their exercise tolerance and performance. In 1968, Cooper and associates compared endurance performance in 419 airmen of the United States Air Force (mean age of 19.1 years) before and after six weeks of basic training. Using a 12-minute maximum distance walk/run field test, the researchers showed that nonsmokers covered significantly more distance than the current smokers both before and after basic training. Also, the improvement in performance

from pre to post training was greater in nonsmokers, but significantly greater only when compared to smokers with a habit of 10 to 30 cigarettes per day. In fact, pre and post training performance decreased as the number of cigarettes smoked and duration of smoking habit increased.

Smokers have demonstrated slower running times than nonsmokers during physical endurance tests. Conway and Cronan (1992) conducted a study involving 3,045 Navy personnel (2,712 men, 333 women) with an age range of 17 to 59 years and mean of 28.7 years. The cardiorespiratory endurance component of the study was a 1.5-mile run/walk. Smokers ran the distance significantly slower than did the nonsmokers. After controlling for the exercise history of the participants, results indicated that smoking had an independent significant association with the increased 1.5-mile run times. More recently, Louie (2001) found that compared to teenage nonsmokers, teenage smokers recorded significantly slower one-mile run times.

Decreased performance has been noted in smokers during graded exercise laboratory tests. In a study of 7,515 hypercholesterolemic men aged 34 to 60 performing a symptom-limited graded exercise test, smokers discontinued exercise due to exhaustion, fatigue, dyspnea, or leg pain at nearly twice the rate of nonsmokers. This finding was significant ($p < .001$) even after accounting for other risk factors (Gordon, et al., 1987). The authors also noted a clear dose-response relationship within the smokers when grouped according to the number of cigarettes smoke.

The acute effects of cigarette smoking have been shown to affect the performance times of smokers during maximal exercise testing. Utilizing a lower limb cycle ergometer protocol, Klausen, et al. (1983) studied the responses of 16 healthy, male smokers (average age of 24.5 years). On separate days, subjects performed the test either after smoking three cigarettes immediately prior to testing or after at least an eight-hour abstinence from smoking. During the smoking trial, test duration times significantly ($p < .05$) decreased from 8.77 minutes to 7.01 minutes, a 20 percent decline.

Aerobic Capacity

Studies comparing the aerobic capacities of smokers versus nonsmokers have differed in their results. Morton and Holmik (1985) measured maximum oxygen uptake in 14 male, well-trained sportsmen using a graded treadmill exercise test. The subjects were equally divided with regards to smoking status. The smoking subjects averaged 15 cigarettes per day for at least a six-month period. The nonsmoking subjects recorded slightly higher, but non-significant

relative maximum oxygen uptake values (58.62 ± 4.64 vs. 57.90 ± 6.51 ml/kg/min) when compared to smoking subjects.

A study by Knapik, Zoltick, Rottner, et al. (1993) revealed different results from those reported by Morton and Holmik (1985). Relative maximum oxygen uptakes in 202 male United States Army officers (ages 36 to 51) were measured using a treadmill protocol and results for smokers and nonsmokers were compared. Smokers had significantly ($p < .01$) lower values than nonsmokers after correcting for age.

It has been suggested that the inconsistent results from studies comparing maximum oxygen uptake between smokers and nonsmokers may reflect the theory that maximum aerobic capacity is genetically determined and that the mixed results may be due to random population sampling (Huie, 1996). Other possibilities for the mixed results may be the number and fitness level of the subjects used in the studies. Klausen et al. (1983) demonstrated that subjects with a high level of aerobic capacity are less sensitive to the effects of smoking on physical performance.

Several studies looking at the acute effects of smoking on aerobic capacity have been performed. Hirsch et al., (1985) analyzed the exercise responses in nine male smokers (ages 19 to 35 years) on a smoking day and a nonsmoking day. On the smoking day, subjects smoked three cigarettes per hour for five hours, while on the nonsmoking day subjects did not smoke after 7 a.m. Exercise was performed at approximately the same time of the day for each trial. The exercise test consisted of three minutes at rest, three minutes of unloaded cycling, and incremental increases in work rate of 25 watts per minute until exhaustion. During exercise, maximum oxygen uptake and anaerobic threshold were significantly ($p < .05$) lower after smoking. The authors suggested that the reduced maximum oxygen uptake and anaerobic threshold result from reduced oxygen availability for the exercising muscles through the effect of elevated carboxyhemoglobin and/or impaired peripheral redistribution of blood flow.

Results from studies looking at the independent effects of carbon monoxide indicate that reduced oxygen availability for skeletal muscle during maximal exercise is due to the elevated carboxyhemoglobin levels. Pirnay, et al. (1971) conducted exercise tests on five male subjects (1 smoker, 4 nonsmokers) under a control situation and following carbon monoxide intoxication yielding a carboxyhemoglobin level of approximately 15 percent. Subjects had decreased measurements for maximal oxygen consumption ($p < .001$) and oxygen pulse ($p < .001$). There was also a small, but significant ($p < .01$) increase in maximal heart rate under the carbon monoxide treatment.

Vogel and Gleser (1972) demonstrated the detrimental effects of carbon monoxide on light (50%), heavy (75%), and maximal (100%) exercise in eight male subjects ranging in ages of 20 to 23 years. Carbon monoxide intoxication resulted in carboxyhemoglobin levels of approximately 20 percent. The subjects, three of whom were smokers, displayed significantly lower ($p < .001$) maximal oxygen uptakes during the carbon monoxide treatment. Submaximal oxygen uptake values were also lower during the carbon monoxide treatment, however the decreases did not reach significance. Lower submaximal oxygen uptakes have also been reported following smoking (Rotstein & Sagiv, 1986). Additionally, Vogel and Gleser reported higher ($p < .05$) cardiac output and heart rate measurements at submaximal workloads, but similar readings at maximal exercise for these variables during the carbon monoxide treatment. At submaximal levels, an increase in cardiac output helps meet the oxygen demands of tissues when levels of oxyhemoglobin are decreased due to carbon monoxide exposure (Vogel & Gleser, 1972). Stroke volume was not different between the two treatments at any exercise level. Vogel and Gleser along with Pirnay, et al. (1971) agree that formation of carboxyhemoglobin due to elevated levels of carbon monoxide cause changes in oxygen availability that decrease maximal oxygen consumption.

The results of the studies by Pirnay et al. (1971), and Vogel and Gleser (1972) demonstrate significant effects from carbon monoxide exposure, but the carboxyhemoglobin levels in these two studies of approximately 15 and 20 percent respectively are higher than levels experienced by a typical smoker. Horvath et al. (1975) looked at the effects on maximal aerobic capacity of different levels of carboxyhemoglobin with the purpose of determining the precise level at which aerobic capacity is impaired. Four adult males aged 24 to 33 performed graded exercise to exhaustion during three treatments: breathing filtered air (COHb of .33%), breathing 75ppm carbon monoxide (COHb of 3.35%), and breathing 100ppm carbon monoxide (COHb of 4.3%). Horvath et al. reported that no significant declines in maximum oxygen uptake occurred until levels of carboxyhemoglobin reached 4.3 percent, a level that is common in smokers.

Klausen et al. (1983) have provided further evidence of carbon monoxide's influence on oxygen uptake from studies by comparing the effects of smoking with the effects of carbon monoxide exposure on maximal exercise. Utilizing a lower limb cycle ergometer protocol, Klausen et al. studied the responses of 16 healthy, male smokers (average age of 24.5 years). The subjects performed the test under three different conditions: after at least an eight-hour abstinence from smoking, after smoking three cigarettes immediately prior to testing, and after inhalation of an amount of carbon monoxide that gave subjects the same degree of carbon monoxide poisoning as smoking the three cigarettes (approximately

5%). Maximal oxygen uptake was significantly reduced (7%) in the smoking and carbon monoxide treatments compared to the control. Smoking and carbon monoxide exposure also caused significant reductions in exercise time, an effect that has been noted in other studies (Aronow & Cassidy, 1975). Furthermore, compared to the carbon monoxide treatment, exercise duration for the smoking treatment was significantly ($p < .05$) lower. The authors suggested that compounds in cigarette smoke other than carbon monoxide might influence work capacity.

Fuel Utilization

One final area to discuss concerning the effects of smoking on the body's response to exercise is fuel utilization. Studies have indicated that compared to nonsmokers, smokers have a greater dependency on glucose as a fuel source (Colberg et al., 1994; Huie, et al., 1996). Colberg et al. studied glucose kinetics in 14 male subjects (7 smokers, 7 nonsmokers). Nonsmokers were tested one time, whereas smokers were tested twice, once after an eight-hour smoking abstinence and again after acute smoking. Results demonstrated that smokers, with and without acute smoking, had higher rates of glucose appearance during rest and submaximal, steady state exercise at approximately 50% of peak oxygen consumption. Glucose rates of disappearance were equivalent to the rates of appearance. This tightly regulated blood glucose homeostasis during rest and exercise limited the changes in plasma glucose concentration. Additionally, smokers demonstrated a greater dependence on blood glucose as an oxidizable substrate and as a percentage of total carbohydrate oxidation than nonsmokers during exercise. Colberg et al. suggested that the increased use of glucose in smokers possibly results from a downregulation of their β -adrenergic response to circulating catecholamines (Laustiola, Lassila, Kaprio, & Koskenvuo, 1988) and an attenuated use of glycerol and free fatty acids. Colberg et al. based this suggestion on work conducted by Laustiola, et al. (1988), which showed that long term smokers exhibit a lower density of beta-adrenergic receptors in lymphocytes and an attenuated lipolytic response to catecholamines released during an acute session of exercise. Increased blood glucose utilization has been reported to occur during submaximal exercise in hypoxic conditions (Brooks, Butterfield, Wolfe, Groves, Mazzeo, Sutton, et al., 1991), and it is possible that smoking-induced hypoxia may have similar effects.

Research by Huie, et al. (1996) builds upon the work by Colberg et al. (1994). Using the same protocol as in the study by Colberg et al. (1994), Huie et al. studied the lactate kinetics in smokers and nonsmokers. After acute smoking, smokers had increases in lactate appearance and disappearance during exercise that were significantly higher than measurements for nonsmokers. Absent of

acute smoking, smokers had lactate appearance and disappearance values that were similar to nonsmokers. The authors suggested that acute smoking may enhance lactate mobilization. Resting lactate concentrations were similar between groups and each had increases during exercise. However, the increases in the smokers after abstinence were significantly lower than those for the nonsmokers and the smokers after acute smoking. The researchers suggested that lactate production may be blunted by smoking abstinence. These findings for lactate concentrations during exercise contrast those reported by Colberg, Casazza, Horning, and Brooks (1995). After observing similar resting lactate levels in nonsmokers, acute smokers, and abstaining smokers, Colberg and colleagues (1995) reported that acute smokers demonstrated increases in exercise lactate concentrations that were significantly ($p < .01$) higher than the increases seen for the other two groups.

An additional finding by Huie, et al. (1996) was a higher rate of lactate conversion to glucose among smokers during exercise. Colberg et al. (1994) noted a higher amount of glucose recycling in smokers during exercise. Lactate can be used as a gluconeogenic substrate, and Huie et al. suggested that the higher lactate turnover rate and increased lactate mobilization in smokers following smoking may provide additional substrate that is necessary to sustain the increased gluconeogenic rate in smokers during exercise, thereby maintaining glucose homeostasis.

Conclusion

Research involving the effects of cigarette smoking on exercise has primarily focused on the compounds nicotine and carbon monoxide. It has been demonstrated that each of these compounds has independent effects on the body that can influence the responses of the body to exercise.

Nicotine exposure through cigarette smoking has been shown to stimulate the sympathetic nervous system causing an increased release of the catecholamines epinephrine and norepinephrine. This sympathetic stimulation and increased catecholamine release causes several hemodynamic effects. The two most discussed in research are increases in heart rate and blood pressure, however other nicotine-induced cardiovascular effects include increases in heart muscle contractility, stroke volume, and cardiac output.

Carbon monoxide from cigarette smoke causes several changes in the body's ability to absorb and utilize oxygen. Carbon monoxide binds with hemoglobin forming the compound carboxyhemoglobin. The formation of carboxyhemoglobin decreases the oxygen carrying capacity of the blood. Exposure to

carbon monoxide also causes a leftward shift of the oxygen-hemoglobin dissociation curve, illustrating a less efficient release of oxygen into the tissues (muscles). Additionally, carbon monoxide can bind with myoglobin, causing a significant reduction in oxygen transport to skeletal muscle mitochondria.

The many physiological effects of cigarette smoking due to nicotine and carbon monoxide may not impair functioning at rest, but can influence the responses of the body during times of physical stress. The acute and chronic effects of smoking on exercise are well researched. Also numerous studies have examined the independent effects of carbon monoxide on exercise responses. Smokers tend to demonstrate a decreased exercise tolerance, exercise performance, and aerobic capacity. Furthermore, there is evidence that compared to nonsmokers, smokers exhibit a greater dependency on the use of glucose as a fuel source during submaximal, steady state exercise. Because carbohydrate stores in the body are limited, this increased reliance on glucose may contribute to premature fatigue in smokers during physical exertion. Also, due to the limited number of studies addressing the effects of cigarette smoking on fuel utilization in smokers, this may be a viable area for future research.

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