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Blood doping and related issues: a brief review

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ABSTRACT

GLEDHILL, NORMAN. Blood doping and related issues: a brief review. *Med. Sci. Sports Exercise*, Vol. 14, No. 3, pp. 183-189, 1982. The intent of blood doping is to increase maximal aerobic power by increasing the capacity of blood to carry oxygen. This manipulation gained notoriety in the sports world because of rumors of blood doping by competitors in endurance events. Researchers also have become interested in induced erythrocythemia because its study provides insight into the limiting factor(s) of maximal aerobic power ($\dot{V}O_{2max}$). It is concluded in this review that to increase $\dot{V}O_{2max}$, it is necessary to elevate significantly the hemoglobin concentration by infusing at least 900 ml of blood. The use of inadequate reinfusion volumes, premature reinfusion of the blood following withdrawal, and storage of the blood by refrigeration rather than by freezing are major reasons for the contradictory findings from earlier studies of blood doping. Changes in blood volume and 2,3-Diphosphoglycerate following blood doping are transient and, other than during the first 24 h post infusion, appear to be inconsequential. In addition, this review also examines related issues such as attendant hemodynamic and lactate changes, the need of controls, and ethical considerations in blood doping.

INDUCED ERYTHROCYTHEMIA, BLOOD BOOSTING, $\dot{V}O_{2max}$, BLOOD STORAGE, BLOOD VOLUME, CARDIAC OUTPUT, LACTIC ACID, 2,3-DPG, DOPING CONTROLS, ETHICS

During the past decade there has been persistent interest in the topic of induced erythrocythemia, commonly termed blood doping or blood boosting. An experimental subject or athlete who has a normal level of red blood cells (RBCs) is given additional blood with the intention of increasing maximal aerobic power ($\dot{V}O_{2max}$). Blood doping has received considerable attention in both scientific and lay publications. Researchers have examined induced erythrocythemia both because of its purported effect on performance and because of its potential relevance in understanding the limiting factor(s) of $\dot{V}O_{2max}$. The interest of the general public stems from published accusations that the use of this technique played a major role in some outstanding track performances in recent Olympiads. The purpose of this review is to survey published reports concerning blood doping and to examine the related literature and issues.

The physiological basis for the effectiveness of blood doping is the contention that an elevated hemoglobin concentration [Hb] increases arterial O_2 content (CaO_2) and, hence, systemic O_2 transport (cardiac output x CaO_2). With additional O_2 available to the working muscles, the expected result is an increase in both $\dot{V}O_{2max}$ and performance. This assumes that a) maximal cardiac output ($\dot{Q}max$) is unaffected by the corresponding increase in blood viscosity, b) the distribution of blood to the working muscles is unaltered, and c) the muscle possesses adequate oxidative capacity to utilize the additional O_2. Many researchers remain unconvinced about the last of these assumptions, and this concern has motivated them to examine the topic of induced erythrocythemia. It is argued by some investigators that the oxidative capacity of muscle is far greater than the amount of O_2 delivered during maximal aerobic exercise, and therefore, systemic O_2 transport must be the limiting factor (5,17). Others contend that under normal conditions more than enough O_2 is provided to the working muscles, but the oxidative machinery is taxed to its limit and cannot utilize any additional O_2 (23,32). A variety of experimental approaches have been undertaken to examine these theories, which have been reviewed previously (39), but there is still some question as to what is the limiting factor of $\dot{V}O_{2max}$. However, if an acute increase in O_2 transport can be documented to produce an increase in O_2 utilization, this would constitute strong evidence that the O_2 transport system is the limiting factor.

Due to the reported ergogenic benefit of blood doping, the interest of athletes and coaches in erythrocythemia is much more pragmatic than that of researchers. Because of the political prestige and financial profit that can result from athletic success, the advantages of using ergogenic aids to improve performance can overcome any misgivings coaches and competitors may have. Training programs are designed to increase maximal aerobic power, and, if the overnight increase in $\dot{V}O_{2max}$ attributed to blood doping is correct, the implications for endurance athletes are enormous, particularly at the international level where the margin of difference between competitors is so small.

TRANSFUSIONS AND BLOOD STORAGE

It is possible to produce erythrocythemia by means of transfusions of fresh blood from a matched donor (homologous transfusions). The earliest reported study of blood doping utilized this procedure (30). However, when using

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homologous transfusions, even with the most stringent safeguards, there exists a possibility of hepatitis or bacterial communication and blood type incompatibility (29). Homologous transfusions have even been described as liquid organ transplants with the same possible complications and effects. Therefore, research involving human subjects should not be conducted using blood from matched donors. For this reason studies of blood doping have generally involved the removal, storage, and subsequent reinfusion of the subject's own blood (autologous transfusions).

Blood can be stored either by refrigeration at 4°C or as frozen cells. The majority of blood storage is done by refrigeration; all of the early studies of blood doping employed this technique. The average life-span of a red blood cell (RBC) is 120 d (28). Therefore, each day approximately 1% of any RBC population is lost. The process of erythropoiesis continuously provides replacement erythrocytes in vivo, but in blood removed from the body the number of RBCs declines constantly. Thus, with the refrigeration technique of storing blood, there is a progressive loss of erythrocytes so that approximately 15-20% of the RBCs are lost prior to reinfusion (44). Also, some erythrocytes adhere to the storage containers or are otherwise lost in handling, and additional RBCs become so fragile during storage that they break up shortly after they are reinfused (44). Because of the constant build-up of cellular aggregrates in stored blood, health regulations in North America dictate that the maximum refrigeration storage time be 3 wk. (In some countries this time is extended to 4 or 5 wk.) Thus, following blood removal, if the maximum 3 wk is allowed for the restoration of a normal level of erythrocytes in the donor, approximately 60% of the RBCs removed would actually be viable post reinfusion.

The high glycerol freezing technique of blood storage is employed by transfusion services to maintain a constant supply of rare blood types available on short notice (27). Unlike the refrigeration technique, by which blood is stored as frozen cells, the aging process of the RBCs is interrupted and cell fragility post reinfusion is not affected (44). Thus, blood can be stored for an indefinite period of time. Loss due to handling amounts to approximately 15% whether the storage time is 2 d or 2 yr. Therefore, this technique not only maximizes the recovery of RBCs ($\sim$ 85%), but also enables investigators to wait as long as necessary to insure that the normal erythrocyte level has been reestablished in the donor prior to reinfusion.

CHANGES IN BLOOD VOLUME AND 2,3-DIPHOSPHOGLYCERATE

In the freeze-preservation technique, blood is centrifuged and stored with glycerol at a hematocrit (Hct) of approximately 90%. In the thawing and washing process at the conclusion of storage, the RBCs are separated from the other cellular components of blood and are reconstituted with physiological saline to a Hct of approximately 50%. Since the reinfused "blood" has essentially the same Hct as normal blood, there is no immediate increase in Hct. Hemoconcentration takes place over the next 24 h as the excess fluid is lost to reduce the acute hypervolemia.

It might be suspected that inducing erythrocythemia would cause a sustained hypervolemia. Since increases in blood volume can reportedly increase O_2 transport via a Frank-Starling effect on stroke volume and cardiac output, this could result in a spurious interpretation of the effects of erythrocythemia (37). Gregerson and Dawson (18) reviewed the literature pertaining to blood loss and concluded that acute reductions in blood volume are compensated for by an expansion of the plasma volume in a matter of hours. Similarly, when subjects receive transfusions of whole blood, the effect on blood volume is buffered by a reduction in the plasma volume so that the immediate post-infusion hypervolemia is only transient (18).

Mollison (28) observed a 10% increase in [Hb] and Hct from 5 min post transfusion to 24 h post transfusion when subjects received 1000 ml of whole blood. The accuracy of such changes in [Hb] as an index of alterations in blood volume has been substantiated in a number of investigations (7,20). Blood volume has not generally been measured in studies of blood doping, but Ekblom et al. (12) and Von Rost et al. (46) reported that blood volume was unchanged from the control 24 h post reinfusion of 800-900 ml of whole blood. Also, in a recent study in which subjects received 900 ml of freeze-preserved blood, Buick et al. (5) estimated control blood volumes from a standard prediction formula and then applied the principle of mass balance to calculate post-infusion blood volumes from the known amount of transfused Hb and the resultant increase in [Hb]. They reported a small non-significant increase in blood volume equal to the volume of the added RBCs at both 24 h and 7 d post infusion.

It has been argued that because of the decrease in RBC 2,3-Diphosphoglycerate (2,3-DPG) during storage with both refrigeration and freeze-preservation, the reinfusion of stored blood cannot bring about an increase in O_2 delivery and $\dot{V}O_{2max}$ (41). Since Hb has a preferential affinity for 2,3-DPG over oxygen, a reduced level of 2,3-DPG results in an increased O_2 affinity. This causes a leftward shift of the oxyhemoglobin dissociation curve and a decreased O_2 unloading at the tissues. However, when RBCs with decreased 2,3-DPG are transfused, it takes less than 24 h for the 2,3-DPG level in the mixed RBC population of the recipient to be restored to normal (4). In studies of blood doping in which 2,3-DPG levels were measured, no significant differences were reported between control and 24 h post-reinfusion values both at rest and during exercise (5,12,50). Furthermore, if the first 24 h following an infusion are critical for a particular application, it is possible to incubate the cells prior to reinfusion with a rejuvenation mixture of pyruvate, inosine, glucose, phosphate, and adenine, which increases the 2,3-DPG of the stored cells to

200% of the normal in vivo level (44). This causes a temporary rightward shift of the dissociation curve and an increased O_2 unloading.

TIME COURSE OF HEMATOLOGICAL CHANGES FOLLOWING THE REMOVAL AND INFUSION OF BLOOD

Since the Bureau of Biologics has restricted the storage period of refrigerated blood to 3 wk, the time course of hematological changes following blood removal (phlebotomy) is a major concern. Similarly, for the timing of experiments or competitions following induction of the erythrocythemic condition, a knowledge of the time course of post-infusion hematological changes is essential.

Wadsworth (47) reported that after 400-ml phlebotomies in healthy subjects, the [Hb] remained low for 1-2 wk and increased rapidly thereafter, reaching control levels 3-4 wk after the phlebotomy. Gledhill et al. (15) removed 900 ml of blood from normal healthy males and stored the cells by the high-glycerol freezing technique. Following blood removal, the [Hb] and Hct of the donors decreased by 11%. They remained low for 1-2 wk, then began increasing rapidly, and required a total of 5-6 wk to return to control values. In a subsequent study from that laboratory involving trained runners, it took up to 10 wk for the hematology values to return to control levels (5).

Following reinfusion of the 900 ml of blood into the normocythemic donors, Gledhill et al. (15) reported that [Hb] and Hct were elevated by 8% after 24 h and 11% after 1 wk. The progressive increase was attributed to a continuing hemoconcentration. Over the next 15 wk, hematology values returned gradually, in a linear fashion, from erythrocythemia to control levels. These data are illustrated schematically in Figure 1.

Some important implications for blood doping are apparent in Figure 1. Most importantly, 3 wk after a 900-ml phlebotomy, hematological values in normal subjects returned only half-way to control values. Therefore, given

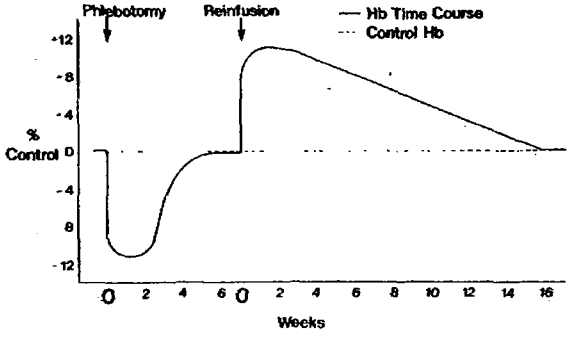

Figure 1—Time course of hematology changes following the removal and reinfusion of ~900 ml of autologous freeze-preserved blood.

that in North America, the maximum allowable storage duration for refrigerated blood is 3 wk and that only about 60% of the originally removed RBCs are viable following reinfusion, it is virtually impossible to induce erythrocythemia by using refrigeration-stored autologous blood. It should also be noted, however, that in a study conducted outside North America, the reinfusion of 800-1200 ml equivalent whole blood following 4 wk of refrigeration storage did not produce a significant increase in [Hb] (11). A second important implication for blood doping illustrated in Figure 1 is that the erythrocythemic condition was maintained for an extended period of time. Thus, the increased O_2 carrying capacity is of value not just for a brief period following the infusion, but for several weeks thereafter.

STUDIES OF BLOOD DOPING (INDUCED ERYTHROCYTHEMIA)

It is frequently reported (21,25,40) that a positive relationship exists between total-body Hb and $\dot{V}O_{2max}$ or endurance exercise capacity. However, studies relating [Hb] and $\dot{V}O_{2max}$ have been contradictory. In some investigations, hemoglobin concentrations as low as 8.2 g/100 ml were associated with a normal exercise capacity (8,34,38), while other reports indicated that anemia was accompanied by a reduced exercise capacity (1,24,43). A number of investigators have addressed this topic by examining the relationship between erythrocythemia and $\dot{V}O_{2max}$ and have reported similarly conflicting results. Some reasons for their lack of agreement include the following: improper experimental designs, such as the absence of placebos and controls; the designation of pre-reinfusion (anemic) values rather than pre-phlebotomy (normocythemic) values as control values; protocols that could have produced a training effect in the experimental subjects; and most importantly, failure to achieve a significant increase in [Hb] due to inadequate transfusion volumes or inappropriate storage technique. However, these confounding weaknesses were avoided in two recent investigations, and following blood doping, significant increases in both $\dot{V}O_{2max}$ and endurance exercise capacity were observed in one study (5), and faster endurance racing times were observed in the other (50).

Studies of the relationships between blood doping and exercise reported to date are summarized in Table 1. Changes in hematology, $\dot{V}O_{2max}$, and endurance exercise capacity were calculated from measurements made in the pre-phlebotomy and post-reinfusion conditions. This designation is important, as it differentiates these changes from improvements reported in some investigations that were calculated from the post-phlebotomy anemic condition. In all of the summarized studies, an increase in $\dot{V}O_{2max}$ and/or endurance capacity was observed post reinfusion, but only five of these increases were statistically significant. An additional four investigators also reported no significant improvement in $\dot{V}O_{2max}$ or endurance fol-

TABLE 1. Summary of studies of blood doping and exercise.

Authors	Date	Storage Technique	[1]Volume Infused	Time of Reinfusion Post Phlebotomy	Hb or Hct vs [2]Control	$\dot{V}O_{2max}$ vs [2]Control	[3]End. Capacity vs [2]Control
Pace et al. (30)	1947	[7]fresh	2000 ml	—	+26%[4]	N.R.	+34.7%[4]
Gullbring et al. (19)	1960	refrig.	610 ml	7 d	+0.7%	N.R.	+3%
Robinson et al. (37)	1966	refrig.	1000 ml	2 wk	+4.8%	+1.4%	N.R.
Ekblom et al. (11)	1972	refrig.	800 ml	4 wk	+2.1%	+5.5%[5]	+15.6%[5]
		refrig.	1200 ml	4 wk	+1.3%	+1.6%[5]	+25.1%[5]
Von Rost et al. (46)	1975	refrig.	900 ml	3 wk	+2.7%	+9.0%[5]	+37.0%[5]
Bell et al. (3)	1976	refrig.	500 ml	3 wk	+1%	+5.6%[6]	+7.5%
Ekblom et al. (12)	1976	refrig.	800 ml	~5 wk	+4.5%[5]	+8.0%[4]	N.R.
Videman and Rytömaa (45)	1977	refrig.	4-600 ml	2-3 wk	+2.6%	N.R.	+3.8%
Robertson et al. (35)	1978 Abst.	N.R.	1800 ml	N.R.	N.R.	+12.8%[4]	+15.6%[4]
Williams et al. (49)	1978	frozen	460 ml	3 wk	+3.3%	N.R.	+4.1%
Cottrell (9)	1979 Abst.	frozen	405 ml	9 wk	N.R.	~+2%[6]	N.R.
Robertson et al. (36)	1979 Abst.	N.R.	800 ml	N.R.	+15.8%[4]	+30.5%[4]	+13.1%[4]
Buick et al. (5)	1980	frozen	900 ml	7 wk	+11%[4]	+5%[4]	+35%[4]
Spriet et al. (42)	1980 Abst.	frozen	800 ml	11 wk	+7.9%[4]	+3.9%	N.R.
			1200 ml	12 wk	+10.7%[4]	+6.6%[4]	N.R.
Williams et al. (50)	1981	frozen	920 ml	7 wk	+7%[4]	N.R.	+2.5%[4]

[1]Whole blood or equivalent whole blood
[2]Control = pre-phlebotomy measurement
[3]Endurance exercise capacity, physical work capacity or performance time
[4]Statistically significant ($P \leq 0.05$).
[5]No statistical analysis reported.
[6]Predicted from submaximal exercise heart rate.
[7]Fresh homologous blood; all other studies used autologous blood.
N.R. = data not reported

lowing blood doping (14,26,31,48). However, since neither hematological data nor pre-phlebotomy exercise capacity measurements were reported in these studies, they cannot be properly compared with the studies in Table 1 and, therefore, are not included.

It is apparent from Table 1 that a significant increase in $\dot{V}O_{2max}$ and/or endurance exercise capacity was observed consequent to a significant increase in [Hb] (5,30,36,42,50). These increases in [Hb] were accomplished when subjects received 2000 ml of fresh homologous blood (30) or 900-1350 ml of freeze-preserved autologous blood (5,36,42,50). The infusion of smaller volumes of freeze-preserved blood did not bring about a sufficient increase in [Hb] to affect $\dot{V}O_{2max}$ significantly. A significant increase in $\dot{V}O_{2max}$ was reported in two additional studies included in Table 1. However, in one of these, no hematological data were reported (35), and in the other, no statistical analysis of the increase in [Hb] was reported (12). It is concluded from this overview that to bring about a significant improvement in $\dot{V}O_{2max}$ and/or endurance capacity, at least two units of blood must be infused, and the preservation of autologous blood must be conducted by freezing techniques. In addition, since an acute increase in systemic O_2 transport produced an overnight increase in O_2 utilization in studies in which a significant erythrocythemia was successfully induced, this finding supports the conclusion that the transport of O_2 to the muscle is a limiting factor of $\dot{V}O_{2max}$.

An examination of changes in $\dot{V}O_{2max}$ following the reinfusion of blood into relatively anemic donors provides information concerning the relationship between total-body Hb and $\dot{V}O_{2max}$, but it does not address the issue of erythrocythemia. For example, Ekblom et al. in their initial study reported overnight increases in physical performance and $\dot{V}O_{2max}$ of 23% and 9%, respectively, following a 13% increase in [Hb] from the pre-infusion (anemic) condition (11). However, the actual increase in [Hb] above the pre-phlebotomy control was only 2.1% (Table 1), and the corresponding increases in $\dot{V}O_{2max}$ and performance likewise were considerably lower.

It is apparent in Table 1 that although a number of investigators have undertaken to study blood doping, owing to inappropriate methodologies many were unsuccessful in inducing erythrocythemia. Therefore, a consideration of the hemodynamic and related effects of blood doping will be limited to those studies in which a significant increase in [Hb] and/or $\dot{V}O_{2max}$ was reported. During submaximal exercise in the erythrocythemic condition, both heart rate (5,12,36) and cardiac output (12) decreased while stroke volume remained unchanged (12). Maximal heart rate was unchanged or decreased slightly (5,12,42), and both $\dot{Q}$max and maximal stroke volume were reported to be either unchanged (12,36) or substantially increased (42). In the last investigation, the dramatic increase in Q max was attributed to an improved myocardial oxygenation that perhaps is specific to highly trained endurance runners. Consequent to the increase in oxygen-carrying capacity with blood doping, the arterial-to-venous O_2 difference ($a\text{-}\bar{v}DO_2$) increased during both submaximal and maximal exercise (12,36,42). However, the increase in $a\text{-}\bar{v}DO_2$ reported in two studies (12,36) was substantially greater than the observed increase in arterial O_2 content,

suggesting that following blood doping there is more complete O_2 extraction in the tissues leading to a greater desaturation of mixed venous blood.

In the erythrocythemic condition, the lactic acid concentration [La] following submaximal exercise was either unchanged (36) or decreased (5,12,16). Maximal [La] was also reported to be either unchanged (5,12,36,50) or decreased (16). However, in the study in which a decreased maximal [La] was reported, the subjects did not exercise to exhaustion following erythrocythemia (as they did in the studies in which maximal [La] was reported to be unchanged). Instead, the subjects repeated the identical workload that elicited a $\dot{V}O_{2max}$ in the control condition (16). Gledhill et al. (16) attributed the decreased [La] to 1) the increase in $\dot{V}O_{2max}$ that accompanied erythrocythemia, such that the constant exercise work load required a smaller percentage of the new $\dot{V}O_{2max}$ thereby reducing anaerobiosis, and 2) an increased buffering capacity from the additional hemoglobin.

SUBJECT SAFETY, DOPING CONTROLS AND ETHICAL CONSIDERATIONS

Concern has been expressed that the cardiovascular system and therefore subject safety may be compromised while exercising in the erythrocythemic condition. It was established in the previous section that cardiac output appears to be unaffected or improved following blood doping (12,36,42). Spriet et al. (42) also reported that post erythrocythemia, exercise electrocardiograms indicated no evidence of abnormalities or ischemia and that, as reported previously by Ekblom et al. (12), directly measured blood pressures were unaltered from the control condition. Spriet et al. concluded that there was no apparent evidence to contraindicate the reinfusion of up to three units of freeze-preserved autologous blood in normal healthy subjects.

Although the use of drugs in athletic competitions was documented more than a century ago, doping control tests were not conducted at the Olympic Games until 1968. The definition of doping that is the basis for doping control programs at the Olympics prohibits "the use of physiological substances in abnormal amounts and with abnormal methods with the exclusive aim of attaining an artificial and unfair increase of performance in competitions" (10). This excerpt appears to apply to blood doping. However, the International Olympic Committee (I.O.C.) recognizes that it can ban only those doping agents for which suitable analytical methods can be devised for unequivocal detection.

A consideration of the similarity between blood doping and altitude acclimatization complicates the issue of controls in doping studies. Athletes who reside at sea level are at a disadvantage when competing in endurance events at altitude (13). However, due to an increased [Hb], altitude residents are not at an equal disadvantage. For this reason, many athletes were taken to altitude in the weeks prior to the Mexico Olympics to gain the benefits of altitude acclimatization. Some even resided at altitudes higher than Mexico City to increase their [Hb] even further and gain an added advantage. This practice was not banned by the I.O.C.

A problem with altitude training, however, is that during an athlete's acclimatizing to altitude, his/her maximum exercise capacity is somewhat reduced, and therefore, since the intensity at which the athlete can train is slightly below normal, some detraining occurs (2). The effect of the detraining partially negates the benefits of acclimatization and the net result is that only a small advantage is gained over the non-acclimatized athlete. However, it has been shown that it is possible to avoid this problem by transporting the athletes to a lower altitude for their daily training sessions or by training them in an oxygen-enriched environment while residing at altitude (2).

Consequently, it was then reasoned that if no concurrent detraining took place during altitude acclimatization, the adaptations should be even more beneficial to maximal performance upon returning to sea level. Using an experimental design that ruled out the potential interference from detraining, Horstman et al. (22) reported that a 10% increase in [Hb] due to altitude acclimatization resulted in an increase of 6% in $\dot{V}O_{2max}$ and 25% in endurance exercise capacity upon returning to sea level. The magnitude of the reported changes in [Hb], $\dot{V}O_{2max}$, and endurance capacity are virtually identical to the findings in subjects who engaged in blood doping (5). Thus, it is possible to gain all of the benefits of blood doping through the manipulation of altitude acclimatization, a procedure which the sports governing bodies have permitted. The financial cost involved in this protocol is considerably greater than simply removing, storing, and reinfusing blood, and hence, only a few countries can afford it.

An additional problem is that of establishing what constitutes an abnormally high RBC level. In studies in which erythrocythemia has been successfully induced, the [Hb] has been well within the range of [Hb] values found in the general population. That is, the normal [Hb] of some individuals is already at or above the levels reported in individuals who have engaged in blood doping. Hemoglobin concentrations of this magnitude were observed in a survey of athletes who competed in the 1976 Olympiad and were not suspected of blood doping (6). On the other hand, some athletes have an [Hb] below the average normal level, as was the case with Canadian Olympic athletes in 1976 (6). It is possible that these athletes were at a disadvantage in endurance performance and could have achieved a normal [Hb] by blood doping. In such a situation, the use of blood doping could be rationalized by some as therapeutic.

A major problem confronting the I.O.C. is that it is presently not possible to determine whether or not an individual has engaged in blood doping. Although the determination of [Hb] is a simple procedure, as yet there is no test that can establish whether the measured [Hb]

is the athlete's normal level or whether it resulted from either altitude acclimatization or blood doping. Presumably, it is for this reason that the I.O.C. to date has not acted to control blood doping at Olympic competitions. Moreover, the chairman of the Olympic Medical Commission, Dr. A.H. Beckett, was quoted prior to the 1980 Olympiad as stating, "nothing will be done to stop blood dopers" (9). Nevertheless, strict application of the definition of doping must include induced erythrocythemia. Therefore, in light of recent findings, it is recommended that the I.O.C. take a firm position on the practice of blood doping. Until usage can be controlled by testing, the I.O.C. will have to rely upon the integrity of the athletes, coaches, and their medical support personnel to comply with its ruling.

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