ASSE 19:540-3, 1987

American College of Sports Medicine

Position Stand on

Blood Doping as an Ergogenic Aid

SUMMARY

Blood doping is an ergogenic* procedure wherein normovolemic erythrocythemia is induced via autologous (i.e., re-infusion of athlete's own blood) or homologous (i.e., transfusion of type matched donor's blood) red blood cell (RBC) infusion (11, 27, 28, 34). The resultant hemoconcentration increases arterial oxygen concentration (CaO_2) (9, 23). During peak exercise, oxygen delivery [cardiac output ($\dot{Q}$)xCaO_2] to skeletal muscle is enhanced, improving maximal oxygen uptake ($\dot{V}O_{2max}$) and endurance capacity (9, 28, 29, 31). Such terms as blood boosting, blood packing, and induced erythrocythemia are also variously used to describe this ergogenic procedure (11, 34).

It is the position of the American College of Sports Medicine that the use of blood doping as an ergogenic aid for athletic competition is unethical and unjustifiable, but that autologous RBC infusion is an acceptable procedure to induce erythrocythemia in clinically controlled conditions for the purpose of legitimate scientific inquiry.

APPLICATIONS: EXPERIMENTAL AND ERGOGENIC

Blood doping was first used as an experimental procedure to study hematological control mechanisms for systemic transport of oxygen during acute hypoxic exposure (23). Subsequent investigations have experimentally manipulated hemoglobin concentration ([Hb]) via RBC infusion to demonstrate the rate-limiting effect of peak Hb flow rate ($\dot{Q}$x[Hb]) and oxygen delivery on $\dot{V}O_{2max}$ and endurance capacity (4, 8, 9, 13, 27–29, 31, 37). These experimental applications have shown that RBC infusion is a valuable laboratory tool when examining the effect of [Hb] on oxygen transport function during dynamic exercise under both normoxic and hypoxic conditions.

While reports of blood doping for scientific purposes appeared as early as 1947 (23), it was not until the 1976 Olympic Games in Montreal that it was suggested the procedure had been used as an ergogenic aid for endurance events (11, 34). Since that time, both athletes and sports officials have publicly admitted having employed homologous RBC infusion as an ergogenic aid during international competition. These actions prompted a call for an unequivocal statement regarding the *ergogenic, physiological, medical,* and *ethical* implications underlying the use of blood doping as an ergogenic aid. This position statement was prepared by the American College of Sports Medicine in response to these concerns.

ERGOGENIC EFFECT

The ergogenic properties of normovolemic erythrocythemia have, in part, been inferred from the increase in oxygen transport capacity that attends prolonged exposure to high altitude. As both $\dot{V}O_{2max}$ and endurance performance are improved under hypoxic conditions following long-term altitude acclimatization, it was hypothesized that artificial production of a normovolemic erythrocythemia via RBC infusion might have a similar ergogenic effect. While documentation of the beneficial effect of blood doping during actual competitive conditions is lacking, a significant amount of experimental evidence supports the ergogenic properties of RBC infusion under both normoxic and hypoxic conditions.

The ergogenic effectiveness of blood doping is dependent on a significant elevation in [Hb] following RBC infusion (11, 34). When autologous blood is used, post-re-infusion hemoconcentration occurs only if normocythemia has been restored prior to artificial expansion of the RBC mass. In investigations where this methodological criterion was met, the pre-phlebotomy to post-infusion increase in [Hb] was associated with a significantly higher $\dot{V}O_{2max}$ (i.e., 3.9 to 12.8%) and/or endurance capacity (i.e., 2.5 to 35%) (4, 23, 27–29, 31, 37). Improvements in maximal aerobic power following blood doping were achieved when subjects received 2,000 ml homologous blood (23) or 900 to 1,800 ml

* An ergogenic aid is a physical, mechanical, nutritional, psychological, or pharmacological substance or treatment that either directly improves physiological variables associated with exercise performance or removes subjective restraints which may limit physiological capacity (35).

eze-preserved autologous blood (4, 27–29, 37). Infusion of smaller volumes of blood was not sufficient elevate [Hb] or to significantly improve $\dot{V}O_{2max}$ and/or endurance capacity (7, 11, 18, 27, 36).

A number of investigations have not found a statistically significant improvement in maximal aerobic power following blood doping (10, 20, 25, 35). Some reasons for this finding include: improper experimental designs, such as the absence of placebo and control conditions; the designation of pre-infusion (anemic) values rather than pre-phlebotomy (normocythemic) values as control levels; 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 an inappropriate storage technique and/or inadequate transfusion volumes and time between phlebotomy and transfusion. Consequently, reviewers of these studies incorrectly concluded that blood doping does not alter $\dot{V}O_{2max}$ or endurance performance (24, 33).

PHYSIOLOGICAL MECHANISM

The physiological mechanism underlying the hemoconcentration that attends blood doping involves a shift of protein-free plasma filtrate from the intra-vascular to interstitial compartment; resolving the immediate post-infusion hypervolemia (16, 35). The resulting decrease in plasma volume produces a comparatively rapid restoration of normal blood volume in the presence of a greater [Hb] and CaO_2. Provided hematocrit does not exceed 50%, $\dot{Q}$ during peak exercise is not attenuated by erythrocythemia (9, 28–30). As such, the higher CaO_2 following blood doping increases oxygen delivery (i.e., $\dot{Q}xCaO_2$). At peak exercise, augmented oxygen delivery increases the difference between arterial and venous oxygen concentration [$C(a\text{-}v)O_2$] (9, 28, 29, 31). The greater tissue respiration increases $\dot{V}O_{2max}$ and endurance capacity. Additionally, both CO_2 transport and acid-base balance are favorably affected by an increase in [Hb]. Such changes in blood-buffering capacity may also contribute to the ergogenic properties of induced erythrocythemia.

Following blood doping, heart rate (4, 9, 23, 27–29), $\dot{Q}$ (28), and lactic acid concentration (4, 9, 13, 29) decrease as $C(a\text{-}v)O_2$ increases for a given sub-maximal oxygen uptake. At exercise intensities ≥40% $\dot{V}O_{2max}$, stroke volume is unaffected by erythrocythemia (28). Although oxygen uptake during sub-maximal exercise is unchanged following blood doping, the relative oxygen (%$\dot{V}O_{2max}$) requirement is reduced as a result of the increased $\dot{V}O_{2max}$.

The blood concentration of 2,3-diphosphoglycerate (4, 9, 11, 28, 37) and the oxygen partial pressure at which 50% of Hb is saturated (P_{50}) (28) are not affected by induced erythrocythemia. These findings indicate there is no change in the affinity of the RBC for oxygen when [Hb] is increased.

The time course of the post-infusion hematologic changes is an important consideration for the application of blood doping. Provided normocythemia has been re-established, both [Hb] and hematocrit are significantly elevated within 24 h following autologus infusion of 900 ml blood (11, 12). The erythrocythemia remains relatively constant for 7 d, whereupon hematologic values return gradually in a linear manner to control levels over a 15-wk period. Thus, increased oxygen-carrying capacity is observed not just for a brief period following the blood re-infusion, but for many weeks thereafter (4, 28). In this context, research involving induced erythrocythemia should be scheduled approximately 120 d (i.e., RBC life span) before an athletic event to insure that normocythemia is restored in experimental subjects prior to their participation in competition.

PROCEDURE FOR BLOOD STORAGE AND RE-INFUSION

Blood is preserved either by refrigeration at 4°C or by a glycerol freezing technique (22). When blood is refrigerated, there is a progressive loss of erythrocytes with a concomitant accumulation of cellular aggregates. As such, regulatory agencies in North America have set 3 wk as the maximum refrigeration storage time for blood. Of concern in an autologous blood doping protocol is that a 3-wk storage period is normally insufficient to restore pre-phlebotomy [Hb] when more than one unit of blood is removed (11, 12). In addition, RBCs are also destroyed in the transfusion process or become so fragile during storage that they hemolyze shortly after they are re-infused. The net result is that only 60% of originally removed cells are viable following re-infusion. The comparatively short storage time and the marked hemolysis associated with storage and transfer make it very difficult to restore normocythemia prior to blood doping when a refrigeration storage procedure is used.

In contrast, when blood is stored as frozen cells, the aging process of the RBC is interrupted, allowing preservation for an indefinite period of time (32). In the context of autologous blood doping, freeze preservation makes it possible to delay re-infusion as long as necessary to insure that normocythemia has been re-established in the donor. Re-establishing normocythemia following phlebotomy is a primary requisite for post-re-infusion erythrocythemia. When used in a blood doping protocol, frozen blood is thawed and reconstituted with physiologic saline to a hematocrit of approximately 50%. The reconstituted blood is usually infused 24 to 48 h prior to laboratory testing or athletic competition.

MEDICAL IMPLICATIONS

While blood doping appears to be an effective ergogenic aid, the safety of its use is suspect. Transfusion of

RBCs to the extent of raising the hematocrit over 60% may subject the individual to a hyperviscosity syndrome which includes intra-vascular clotting, potential heart failure, and death (21). If blood transfusions are performed without adhering to standard medical procedures, severe bacterial infections, air and clot emboli, and major transfusion reactions may occur, in rare instances leading to death (1, 15, 38).

The medical risks of blood doping can be separated into those associated with homologous transfusions and those associated with autologous transfusions. Homologous transfusions, even under standardized medical procedures, carry several risks. Despite appropriate typing and cross-matching of blood, there is a 3 to 4% incidence of minor transfusion reactions consisting of fever, chills, and malaise (2, 19). Delayed reactions can cause destruction of the transfused red cells (26). Both of these reactions can occur without demonstrable incompatibility with the donor cells. Viral infections transmitted by blood also pose a serious risk with homologous transfusions. Malaria (6), hepatitis (14), acquired immune deficiency syndrome (AIDS) (5), and cytomegalovirus (18) are the most common and dangerous of these infections. Although progress has been made in detecting contaminated blood, there is still a slightly less than 1% chance of acquiring one of these diseases from transfused blood despite the use of the best detection methods (17). All of these infections can be fatal. In contrast, autologous transfusions limited to two units of packed RBC and performed under proper medical supervision carry a substantially lower medical risk (3).

ETHICAL CONSIDERATIONS

The International Olympic Committee defines doping as "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 competition" (7). Based on this definition, the International Olympic Committee has banned blood doping as an ergogenic aid. However, techniques to detect an artificially induced erythrocythemia are not available. In addition, if such detection techniques were available, their validity would be confounded by altitude acclimatization, hydration status, and normally occurring individual differences in hematocrit.

CONCLUSIONS

A position statement on the use of blood doping must distinguish between scientific and sport applications of the procedure. *Autologous* RBC infusion is considered a scientifically valid and acceptable laboratory procedure to induce erythrocythemia for legitimate scientific inquiry under clinically controlled conditions. However, because RBC infusion (i.e., autologous and homologous) has attendant medical risks and violates doping control regulations, it is the position of the American College of Sports Medicine that the use of blood doping as an ergogenic aid during athletic competition is unethical and unjustifiable.

REFERENCES

1. BRAUDE, A. I. Transfusion reactions from contaminated blood: their recognition and treatment. *N. Engl. J. Med.* 258:1289–1293, 1958.
2. BRITTINGHAM, T. E. and H. CHAPLIN. Febrile transfusion reactions caused by sensitivity to donor leukocytes and platelets. *J.A.M.A.* 165:819–825, 1957.
3. BRZICA, S. M., A. A. PINEDA, and H. F. TASWELL. Autologous blood transfusion. *Mayo Clin. Proc.* 51:723–737, 1976.
4. BUICK, F. J., N. GLEDHILL, A. B. FROESE, L. SPRIET, and E. C. MEYERS. Effect of induced erythrocythemia on aerobic work capacity. *J. Appl. Physiol.: Respirat. Environ. Exerc. Physiol.* 48:636–642, 1980.
5. CURRAN, J. W., D. N. LAWRENCE, H. JAFFE, et al. Acquired immune-deficiency syndrome (AIDS) associated with transfusion. *N. Engl. J. Med.* 310:69–75, 1984.
6. DOVER, A. S. and W. G. SCHULTZ. Transfusion-induced malaria. *Transfusion* 11:353–357, 1971.
7. DUGAL, R. and M. BERTRAND. Doping. In: *IOC Medical Commission Booklet.* Montreal, Canada: *Comité Orginisateur des Jeux Olympiques* 1976, pp. 1–31.
8. EKBLOM, B., A. N. GOLDBARG, and B. GULLBRING. Response to exercise after blood loss and reinfusion. *J. Appl. Physiol.* 40:379–383, 1972.
9. EKBLOM, B., G. WILSON, and P. O. ÅSTRAND. Central circulation during exercise after venesection and reinfusion of red blood cells. *J. Appl. Physiol.* 40:379–383, 1976.
10. FRYE, A. and R. RUHLING. RBC infusion, exercise, hemoconcentration, and $\dot{V}O_2$ (Abstract). *Med. Sci. Sports* 9:69, 1977.
11. GLEDHILL, N. Blood doping and related issues: a brief review. *Med. Sci. Sports Exerc.* 14:193–189, 1982.
12. GLEDHILL, N., F. J. BUICK, A. B. FROESE, L. SPRIET, and E. C. MEYERS. An optimal method of storing blood for blood boosting. (Abstract) *Med. Sci. Sports* 10:40, 1978.
13. GLEDHILL, N., L. L. SPRIET, A. B. FROESE, D. L. WILKES, and E. C. MEYERS. Acid-base status with induced erythrocythemia and its influence on arterial oxygenation during heavy exercise (Abstract). *Med. Sci. Sports. Exerc.* 12:122, 1980.
14. GRADY, G. F. and T. C. CHALMERS. Risk of post-transfusion viral hepatitis (Abstract). *N. Engl. J. Med.* 271:337, 1964.
15. GREENWALT, T. J. (Ed.). *General Principles of Blood Transfusion.* Chicago, IL: American Medical Association, 1977, pp. 65–74.
16. GREGERSEN, M. and S. CHIEN. Blood volume. In: *Medical Physiology,* V. B. Mountcastle (Ed.). St. Louis, MO: Mosby, 1968, pp. 244–283.
17. HARRISON, T. R. *Harrison's Principles of Internal Medicine.* G. W. Thorn, R. D. Adams, E. Braunwald, K. J. Isselbacher, and R. G. Petersdorf (Eds.). NY: McGraw-Hill, 1977, pp. 1702–1706.
18. HENLE, W., G. HENLE, M. SCRIBA, et al. Antibody responses to the Epstein-Barr virus and cytomegaloviruses after open heart surgery. *N. Engl. J. Med.* 282:1068–1074, 1970.
19. HONIG, C. L. and J. R. BOVE. Transfusion: associated fatalities: review of Biologies reports 1976–1978. *Transfusion* 20:653–661, 1980.
20. KOTS, Y. M., M. M. SHCHERBA, Y. S. KOLNER, V. D. GORODETSKII, and L. D. SIN. Experimental study of the relationship between the blood hemoglobin and physical aerobic working capacity. *Fiziologiya Cheloveka* 4:53–60, 1978.
21. MCGRATH, M. A. and R. PENNY. Paraproteinuria: blood hyperviscosity and clinical manifestations. *J. Clin. Invest.* 58:1155–1162, 1976.
22. MERRYMAN, H. T. and M. HORNBLOWER. A method for freezing and washing red blood cells using a high glycerol concentration. *Transfusion* 12:145–156, 1972.
23. PACE, N., E. L. LOZNER, W. V. CONSOLAZIO, G. C. PITTS, and J. L. PECORA. The increase in hypoxia tolerance of normal men accompanying the polycythemia induced by transfusion of erythrocytes. *Am. J. Physiol.* 148:152–163, 1947.

PATE, R. Does the sport need new blood? *Runner's World Magazine* 1976, pp. 25–27, November.
PATE, R., J. MCFARLAND, J. V. WYCK, and A. OKOCHA. Effect of blood reinfusion on endurance performance in female distance runners (Abstract). *Med. Sci. Sports* 11:97, 1979.
PINEDA, A. A., H. F. TASWELL, and S. M. BRZICA, JR. Delayed hemolytic transfusion reaction: an immunologic hazard of blood transfusion. *Transfusion* 18:1–7, 1978.
ROBERTSON, R. J., R. GILCHER, K. F. METZ, et al. Effect of induced erythrocythemia on hypoxia tolerance during physical exercise. *J. Appl. Physiol.: Respirat. Environ. Exerc. Physiol.* 53:490–495, 1982.
ROBERTSON, R. J., R. GILCHER, K. F. METZ, et al. Hemoglobin concentration and aerobic work capacity in women following induced erythrocythemia. *J. Appl. Physiol.: Respirat. Environ. Exerc. Physiol.* 57:568–575, 1984.
SPRIET, L. L., N. GLEDHILL, A. B. FROESE, and D. L. WILKES. Effect of graded erythrocythemia on cardiovascular and metabolic responses to exercise. *J. Appl. Physiol.* 61:1942–1948, 1986.
STONE, H. O., H. K. THOMPSON, and K. SCHMIDT-NIELSEN. Influence of erythrocytes on blood viscosity. *Am. J. Physiol.* 214:913–918, 1968.
THOMPSON, J. M., J. A. STONE, A. D. GINSBERG, and P. HAMILTON. O_2 transport during exercise following blood reinfusion. *J. Appl. Physiol.: Respirat. Environ. Exerc. Physiol.* 53:1213–1219, 1982.
VALERI, C. R. *Blood Banking and the Use of Frozen Blood Products*. Cleveland, OH: CRC Press, 1976, pp. 9–174.
WILLIAMS, M. H. Blood doping in sports. *J. Drug Issues* 3:331–340, 1980.
WILLIAMS, M. H. (Ed.). Blood doping. In: *Ergogenic Aids in Sport*. Champaign, IL: Human Kinetics Publishers, 1983, pp. 202–217.
WILLIAMS, M. H., A. R. GOODWIN, R. PERKINS, and J. BOCRIE. Effect of blood reinjection upon endurance capacity and heart rate. *Med. Sci. Sports* 5:181–186, 1973.
WILLIAMS, M. H., M. LINDHEJM, and R. SCHUSTER. Effect of blood infusion upon endurance capacity and ratings of perceived exertion. *Med. Sci. Sports* 10:113–118, 1978.
WILLIAMS, M. H., S. WESSELDINE, T. SOMMA, and R. SCHUSTER. The effect of induced erythrocythemia upon 5-mile treadmill run time. *Med. Sci. Sports Exerc.* 13:169–175, 1981.
WILLIAMS, W. J., E. BEUTLER, A. J. ERSLEY, and R. W. RUNDLES. *Hematology*. NY: McGraw-Hill, 1977, pp. 1540–1547.