"Anoxaemia not only stops the machine
but wrecks the machinery."

J. S. Haldane

The expectation that oxygen might improve the ailing patient is nearly as old as the discovery of oxygen itself. The belief that his newly found "dephlogisticated air" would be of medical benefit was recorded by Joseph Priestly after the meager trial of being sampled by two mice and himself [35]. John Hunter proposed its use for resuscitation in 1776 [21]. Since then, the desire to get more oxygen into patients has been pursued with great vigor, even though its pulmonary toxicity had been noted in the literature (albeit in mice) by 1796 [4]. Since then, the methodology, understanding, and limitations of getting more oxygen to the tissues have been, in large part, worked out. Now the problems of oxygen delivery have become so seemingly trivial that they are prematurely being treated with indifference by those who fund research programs. This will continue unless something dramatic is offered, such as extracorporeal oxygenation.

The purpose of this chapter is to outline the limits of oxygen transport and to show how present knowledge and practice may be extending the
adaptations of circulatory physiology to meet the needs of the tissues in hypoxic and low-flow states.

HYPOXIA

The term "hypoxia" lacks a good definition. The common description "lower arterial oxygen tension that should be expected from the inspired oxygen concentration" is more a commentary on the performance of a patient's lungs than on an insufficient oxygen supply. Joseph Barcroft tried to face this problem when giving his famous address on anoxemia to the British Association for the Advancement of Science in 1920 [3]. In this he proposed the well-known classification of oxygen deficiencies: (a) anoxic—when blood was not filled with oxygen in the lungs due to pulmonary insufficiency or reduced inspired oxygen tension, (b) anemic—when the oxygen carrying capacity of the blood was reduced by anemia or conversion of hemoglobin to methemoglobin, and (c) stagnant—when various or all tissues become short of oxygen due to diminished blood flow.

In this paper, Barcroft pointed out that in anoxemia it was not possible to produce a predictable permanent deficit of function unless the subjects were pushed to "within a measurable distance of death" or were "elderly or unsound persons."

Later, the hypoxic quartet was completed by Peters and Van Slyke with histotoxic anoxemia [33]. This condition was considered to be of secondary importance. The oxygen delivered to the cell was in sufficient quantity to meet metabolic needs, but the cell could not use the oxygen—the sort of condition that might be due to cyanide poisoning. In the field of shock, this had now become the most grave of the hypoxic states, and when severe, has the very worst prognosis.

The study of oxygen transport to the tissues is fraught with the problem of estimating whether delivery is adequate. Oxygen transport (the product of arterial-blood oxygen content and cardiac output) was used by Nunn [31] to restate Barcroft's classification in therapeutic terms. Venous oxygen tensions and saturations can be measured as a reflection of tissue oxygenation. It is still questionable whether it is better to measure central venous or mixed venous blood. The former has the advantage that it is more easily obtained, and most of the blood comes from a region of fairly constant oxygen uptake. Mixed venous oxygen may reflect the contributions of various organ systems (e.g., splanchnic and renal) that have very differing venous oxygen tensions.

The value of oxygen tension over saturation has been demonstrated by such observations as the state of consciousness being related to tension [14] and not saturation [22] during inadequate cerebral oxygen delivery. The absolute oxygen utilization (uptake) can be used as a measure of oxygen delivery, and the efficiency of the system measured in the utilization co-