Introduction. Given the vulnerability of the central nervous system to relatively brief periods of hypoxia-anoxia and oligemia-ischemia, it appeared useful to develop means to monitor the sufficiency of oxygen delivery at the cellular level during general anesthesia. To be effective the method should fulfill the following criteria.

1) Signals should be derived from CNS structures or components highly sensitive to oxygen insufficiency.
2) The signals should reflect direct relevance to the oxidative metabolic state of the neurons.
3) The signals should indicate incipient oxygen insufficiency well before neuronal injury occurs.
4) The readout should be on-line, rapid and quantitative.
5) The method should be non-invasive,atraumatic and conveniently performed in the OR setting.

For this purpose we have developed an optical method to monitor the redox state of cytochrome c oxidase in the cerebral cortex by means of differential laser spectrometry making use of the semitransparent qualities of skin and bone tissue in the near infra-red region.

Cytochrome c oxidase, also known as "cytochrome a₃a₃", is the terminal member of the mitochondrial respiratory chain and catalyzes approximately 95% of all O₂ utilization. In the parallel process of oxidative phosphorylation free energy is conserved in the form of adenosine triphosphate (ATP) which is in turn utilized to meet the needs of cell maintenance and physiological function. In the oxidized state the enzyme exhibits an absorption band in the 820-870 nm region of the near infra-red spectrum which disappears upon reduction. Previous animal experimentation as well as observations on healthy volunteers had shown that moderate depression of the F₀/F₂ is reflected significantly in the traces well before injurious levels of hypoxia were reached.

Hemoglobin (Hb) and oxyhemoglobin (Hbo₂) also absorb light in the near IR region. Thus the optical signals are affected by the amounts of venous- and arterially-colored blood in the field of observation. Multiple monochromatic light signals are required to eliminate the interference of Hb and Hbo₂ with the cytochrome signals. Conversely, however, it proved advantageous to display the Hb and Hbo₂ signals simultaneously with the cytochrome signals. This provides some diagnostic capability concerning the possible cause of an observed occurrence of oxygen insufficiency.

In this report we will describe our observations on the first clinical applications of this technique, with emphasis on the events during induction.

Methods. Three Ga-Al-As laser diodes were used as near IR light sources. They were sequentially pulsed for 200 nanoseconds at 1 kHz each, their outputs collected, mixed and guided to the subject's forehead by means of glass fiber-optics. Using a reflectance mode, photons were collected 4 to 6 cm lateral from the point of entry. Using appropriate detection, demodulation and amplification techniques three separate signals were obtained for the three wavelengths at 200 msec update intervals. From these the trends of the three biochemicals (a₃a₃, Hb and Hbo₂) were derived by calculation using algorithms obtained from animal experimentation. Readout was by means of three traces on a chart recorder using a 2 second time constant. Informed consent and institutional approval for the study were obtained.

Results. The technique was used in addition to conventional monitoring in patients undergoing general anesthesia for a variety of surgical procedures. Anesthesia was induced with sodium thiopental (3-4 mg/kg) using a test dose of 50 mg followed by a sleep dose. Oxygen (100%) was administered by mask, endotracheal intubation was performed following the administration of succinylcholine and anesthesia was maintained with either halothane, enflurane or N₂O demi-C₂₂. Administration of the test dose of thiopental (50 mg) resulted in a small, sometimes transient oxidation of cyt a₃a₃ and a shift towards more arterially colored blood in the tissue (Hbo₂⁺, Hb⁺). The sleep dose usually produced a further oxidation or a gradually increasing and long lasting cyt a₃a₃ oxidation and shifts toward increased tissue Hbo₂. Ventilation with P₂O₂ 1.0 produced increased cyt a₃a₃ oxidation and Hbo₂ in all cases. Administration of the volatile anesthetics mostly produced yet further oxidations of cyt a₃a₃ and increases in tissue Hbo₂. In a minority of the cases no further response was noted or even a small change in the opposite direction might be observed. In no instance, however, did the traces return to or fall below the pre-induction baseline.

Discussion. These admittedly preliminary observations show that during induction oxygenation of cerebro-cortical tissue is improved (Hbo₂⁺, Hb⁺) and the oxygen delivery to cytochrome c oxidase is increased (cyt a₃a₃ oxidation). This is perhaps indicative of a decreased CBF, as suggested by other workers, and an increase of microvascular autoregulation. Oxygen inhalation always increased this trend toward improved oxygen availability. The occasional, partial reversal during administration of volatile anesthetics may reflect the accompanying decrease in P₂O₂.

We tentatively conclude that the 5 prerequisite criteria have been met.

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