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NOTE

BLOOD  $PO_2$  AND pH IN MONKEYS  
AFTER INCAPACITATING DOSES  
OF IONIZING RADIATION

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ARMED FORCES RADIOBIOLOGY RESEARCH INSTITUTE  
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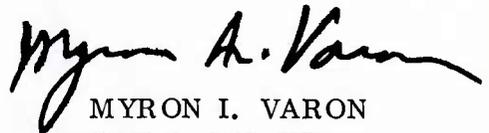
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BLOOD PO<sub>2</sub> AND pH IN MONKEYS  
AFTER INCAPACITATING DOSES  
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FOREWORD  
(Nontechnical summary)

Trained monkeys usually fail to perform satisfactorily for a brief period very soon after receiving 2000 to 4000 rads of pulsed mixed gamma-neutron radiation. The primary objective of this study was to evaluate the possibility that poor oxygenation of the brain might cause this period of early transient incapacitation (ETI).

Female monkeys were surgically prepared so that blood oxygen content ( $PO_2$ ) and hydrogen ion concentration (pH) could be measured continuously.  $PO_2$  and pH of arterial blood which supplied the brain and  $PO_2$  of venous blood from the brain were monitored before and after each monkey received a 3000-rad midline tissue dose pulse of mixed gamma-neutron radiation.

After irradiation the  $PO_2$  did not decrease in arterial or venous blood. Therefore, it was concluded that, if ETI is caused by lack of oxygen in any part of the brain, it must result from poor blood supply rather than lack of oxygen in the blood.

## ABSTRACT

Aortic blood  $PO_2$  and pH and internal jugular blood  $PO_2$  were measured continuously in monkeys (Macaca mulatta) that received a 3000-rad midline tissue dose pulse of mixed gamma-neutron radiation. Immediately after irradiation the aortic blood  $PO_2$  and pH increased slightly (5 to 10 torr and 0.05 pH unit, respectively); these changes were consistent with earlier reports that monkeys hyperventilated after similar irradiation. Venous blood  $PO_2$  did not change after irradiation. It was concluded that lack of oxygen in the blood does not contribute to radiation-induced early transient incapacitation (ETI). If brain hypoxia does cause ETI, it must result from inadequate blood supply to all or part of the brain.

## I. INTRODUCTION

Trained monkeys usually fail to perform satisfactorily for a brief period after receiving 2000 to 4000 rads of pulsed mixed gamma-neutron radiation.<sup>3,7</sup> This early transient incapacitation (ETI) generally starts about 3 minutes after irradiation and has a duration of between 3 and 20 minutes. In addition to performance changes, hypotension,<sup>7</sup> tachycardia,<sup>7</sup> hyperventilation,<sup>7</sup> and electroencephalogram changes\* have been observed during ETI. Norepinephrine has been used experimentally to maintain aortic blood pressure during the first 30 minutes postirradiation; however, the norepinephrine did not prevent ETI.<sup>8</sup>

The primary objective of this study was to measure oxygen levels in aortic and internal jugular blood of irradiated monkeys to evaluate the possibility that brain hypoxia is associated with ETI.

## II. PROCEDURE

Six female monkeys (Macaca mulatta) that weighed between 4 and 6 kg were used. Silicone rubber catheters<sup>†</sup> were implanted surgically as follows: in the aorta via the femoral artery; in the inferior vena cava via the femoral vein; and in the internal jugular vein (Figure 1). A T-shaped catheter was used in the internal jugular vein to maintain flow without blood withdrawal, and, thereby, avoid clotting at the catheter tip due to stasis. After surgery the monkeys were allowed to recover in primate chairs for about 3 days before experimentation.

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\* Unpublished: McFarland, W. L., Armed Forces Radiobiology Research Institute, Bethesda, Maryland

† Meditube silicone tubing, Extracorporeal Medical Specialties, Inc., Mount Laurel Township, New Jersey

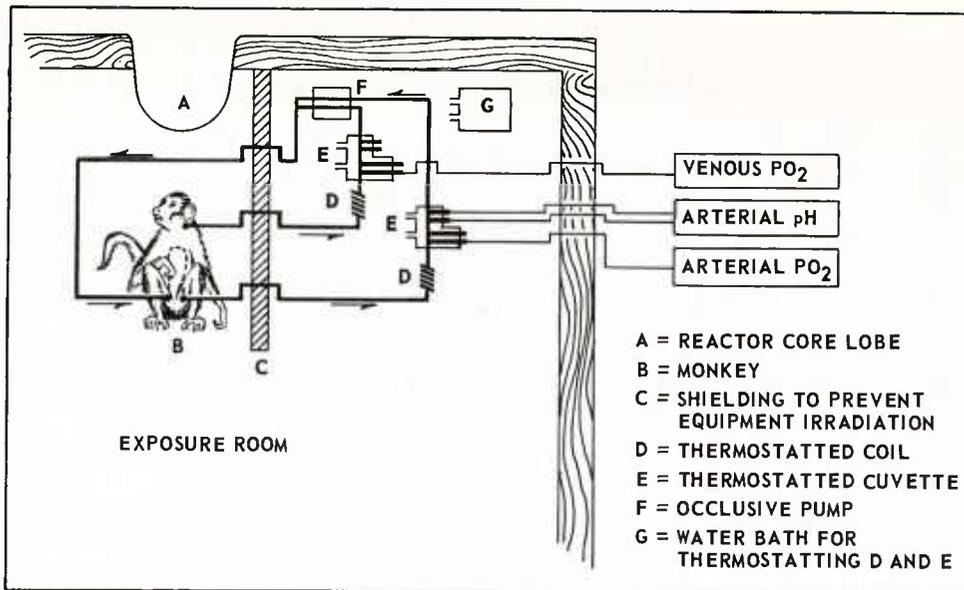


Figure 1. Block diagram of exposure conditions for measuring PO<sub>2</sub> and pH in blood of irradiated monkeys

Henningsen's methods<sup>2</sup> were adapted for continuous monitoring of oxygen (PO<sub>2</sub>) and hydrogen ion concentration (pH) in blood. The implanted catheters were used to establish extracorporeal loops of arterial (aortic) and venous blood. Blood from each source flowed through a thermostatted\* coil into a thermostatted\* cuvette† equipped with electrodes for measuring PO<sub>2</sub>, pH, or both. Blood from each cuvette was carried through an occlusive pump‡ into a common catheter for return to the animal via the inferior vena cava.

\* Thermostatted to 37.5°C by means of Heto Water Bath, model T6K, The London Company, Cleveland, Ohio

† Flow-through Cuvette, model DS66014 equipped with electrodes E5036 (PCO<sub>2</sub>), E5046 (PO<sub>2</sub>), G265C (Glass), and KS67053 (calomel), The London Company, Cleveland, Ohio

‡ Roller Pump, Elmeco Engineering, Rockville, Maryland

As described by Henningsen,<sup>2</sup> the pH electrodes were calibrated with buffer solutions and the PO<sub>2</sub> electrodes were calibrated with humidified, thermostatted gases. However, the equipment was moved from the site of calibration to the radiation exposure room where recalibration was accomplished with buffer solutions and with water bath water that had equilibrated with room air.

Henningsen has demonstrated the accuracy and precision of this equipment for continuously measuring blood PO<sub>2</sub> and pH. However, for this study it was necessary to expose the cuvette and electrodes to some ionizing radiation. Therefore, to determine the effect of radiation upon the equipment, PO<sub>2</sub> and pH of buffer solutions were measured before and after the equipment was irradiated under conditions identical to those of the monkey exposures.

The monkeys were irradiated with the AFRRI-TRIGA reactor operated in the pulse mode (approximately 20 msec pulse width at half maximum height). Each monkey received a midline tissue dose of 3000 rads. Sulfur tablets and miniature, tissue-equivalent ion chambers were used to monitor each exposure. Doses were calculated by comparing the readings with those obtained in other exposures wherein midline tissue doses in a cadaver were measured with miniature tissue-equivalent ion chambers and correlated with similar monitors. The monkey was seated in a primate chair facing away from the reactor core with its center line 100 cm from the core vertical center line. The catheters were connected to establish the extracorporeal loops, and the equipment was shielded from irradiation by wood impregnated with boron and lead. Electrodes for measuring arterial PO<sub>2</sub> and pH and venous PO<sub>2</sub> were

connected to meters\* located outside the exposure room (Figure 1). The meters were read and the  $PO_2$  and pH values were manually recorded throughout the first 30 minutes after irradiation.

### III. RESULTS

Response of the equipment itself to irradiation is presented in Figure 2. After each pulse the  $PO_2$  reading immediately increased from 140 to 144 torr; the reading returned to 140 torr within about 1 minute. The pH values decreased less than 0.1 pH unit after each pulse. Within 2 minutes the pH values were about the same as before irradiation.

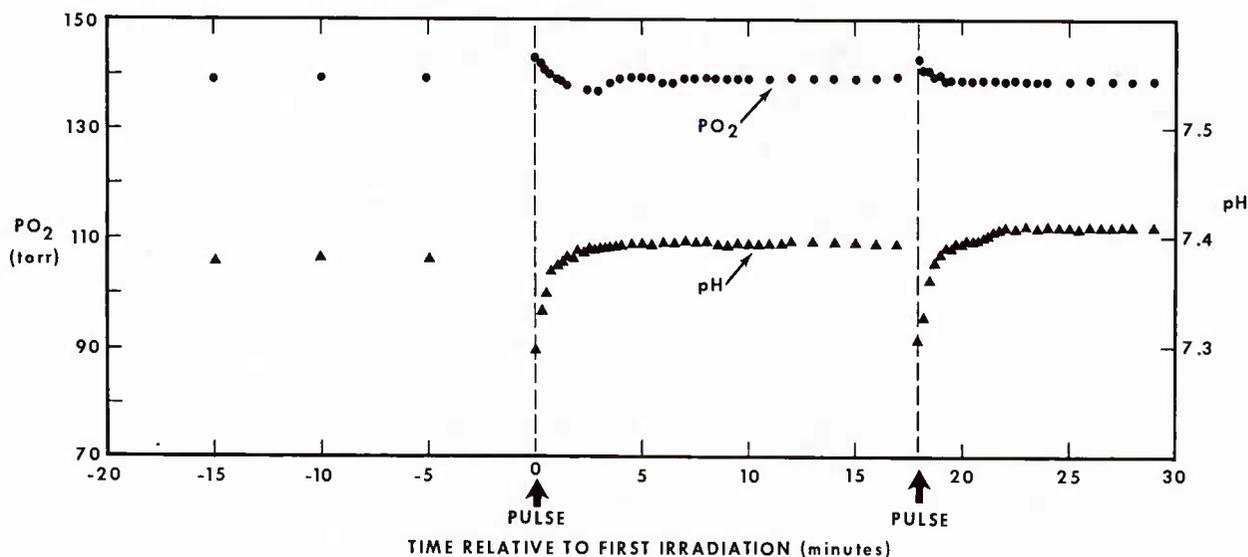


Figure 2.  $PO_2$  and pH measurements in buffer solutions before and after equipment irradiation

Arterial  $PO_2$  and pH and venous  $PO_2$  were measured simultaneously after irradiation of three monkeys (Figures 3-5). In addition, arterial  $PO_2$  and pH (Figure 6), arterial  $PO_2$  (Figure 7), or venous  $PO_2$  (Figure 8) was measured in three

\* Radiometer Acid-Base Analyzer type PHM-71 equipped with modules PHA 930 and PHA 931, or Radiometer Digital Acid-Base Analyzer type PHM-72 equipped with modules PHA 932 and PHA 933, The London Company, Cleveland, Ohio

other monkeys. Venous  $PO_2$  was between 20 and 40 torr before irradiation and did not change after irradiation. Arterial  $PO_2$  generally was between 60 and 80 torr before irradiation. After irradiation the arterial  $PO_2$  usually increased slightly (5 to 10 torr) within 2 or 3 minutes. Within 6 to 10 minutes postirradiation the arterial  $PO_2$  had declined to about its preirradiation level, and no other sudden changes were recorded. Before irradiation, the arterial pH was about 7.5. With all monkeys, pH decreased immediately after irradiation, similar to the results obtained when only the equipment was irradiated. In one monkey (Figure 6) the pH soon increased to its preirradiation level and no other change was observed. In three monkeys (Figures 3-5) the pH increased to slightly higher than the preirradiation level (about 0.05 pH unit); later the pH returned to its preirradiation level. The arterial  $PO_2$  and pH increases occurred simultaneously.

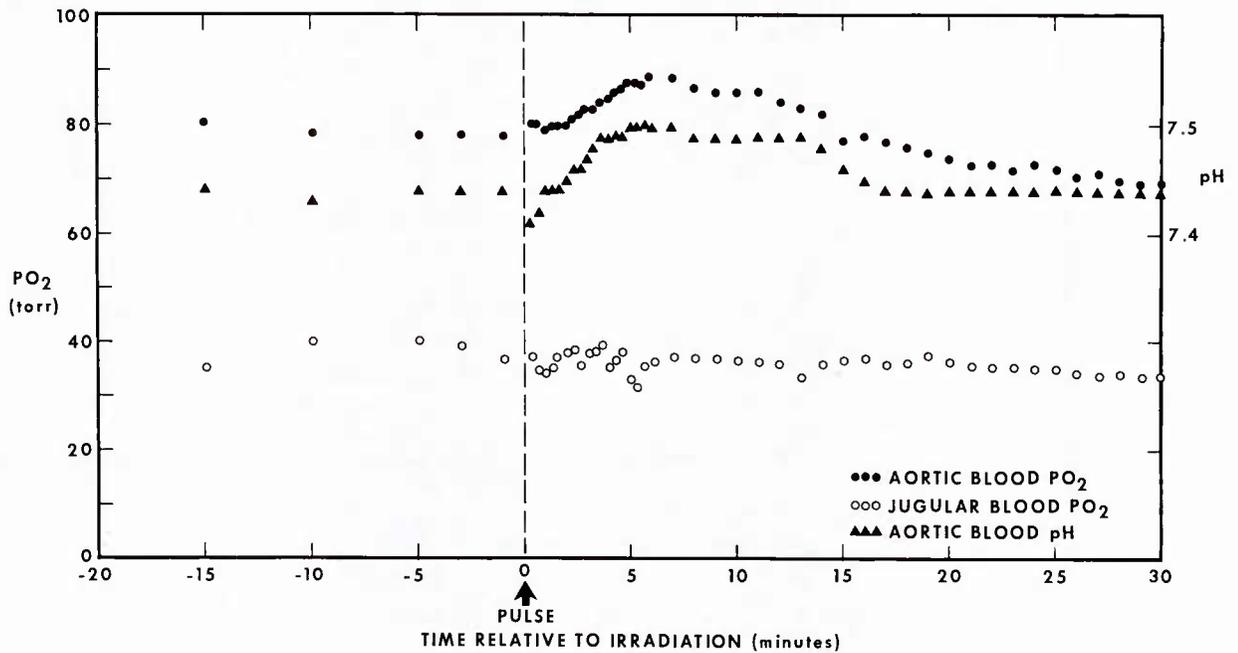


Figure 3. Postirradiation blood  $PO_2$  and pH (monkey B-78)

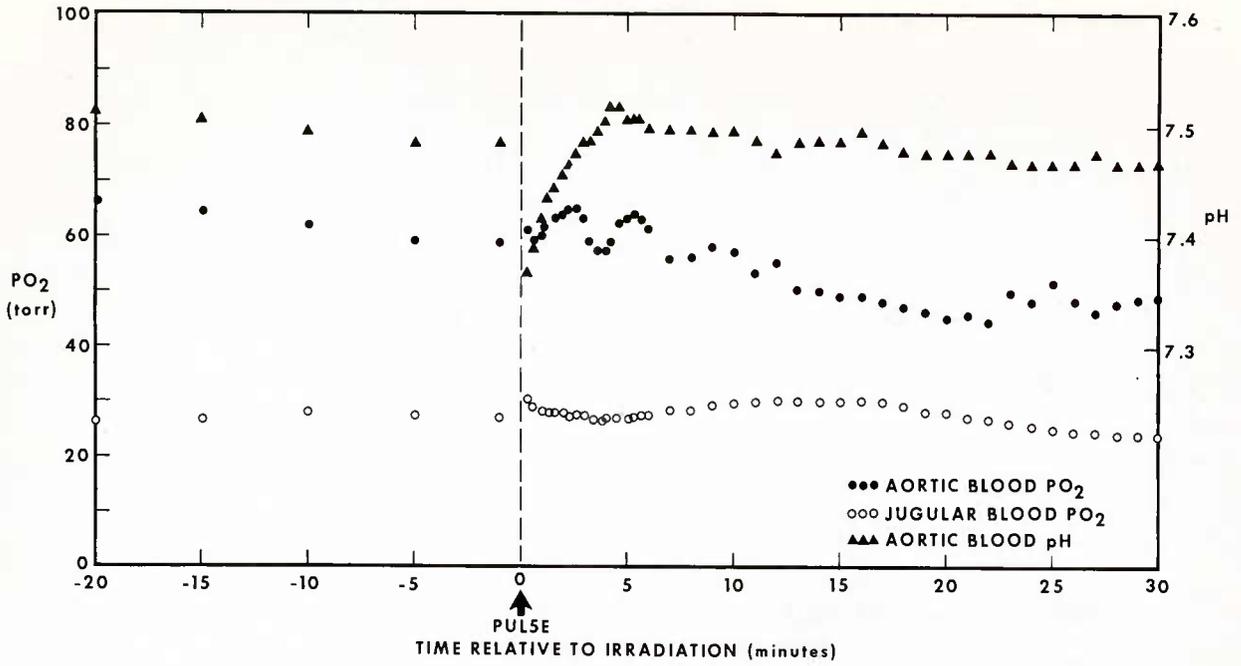


Figure 4. Postirradiation blood PO<sub>2</sub> and pH (monkey B-64)

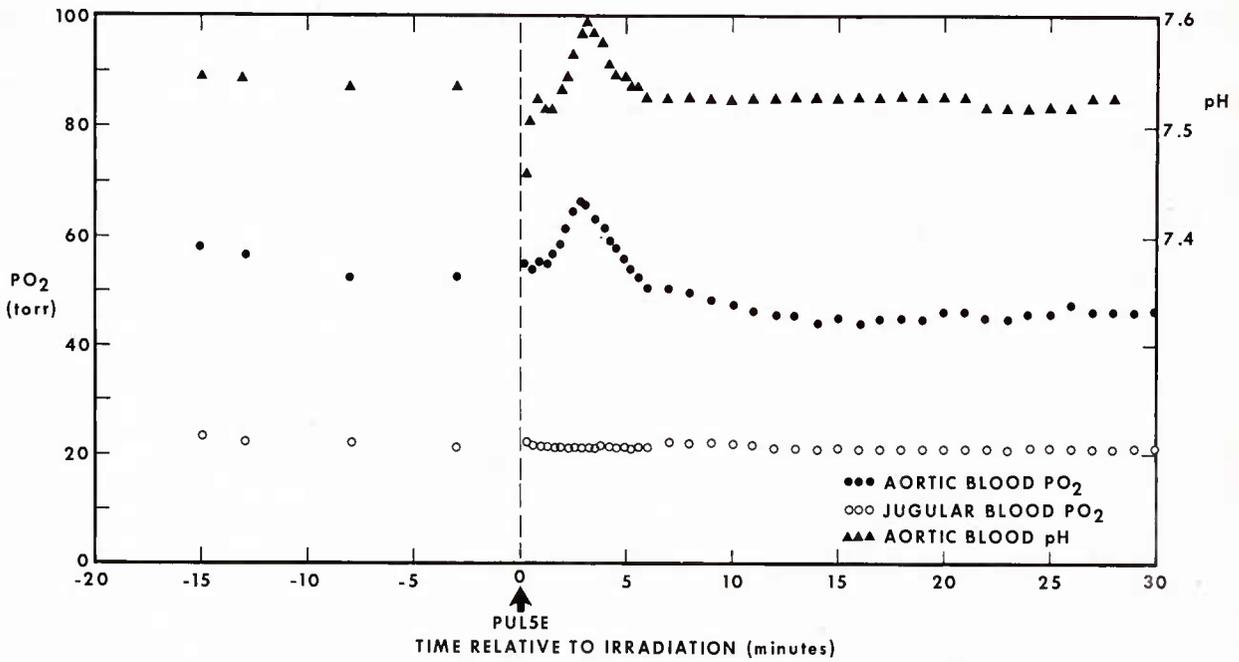


Figure 5. Postirradiation blood PO<sub>2</sub> and pH (monkey A-71)

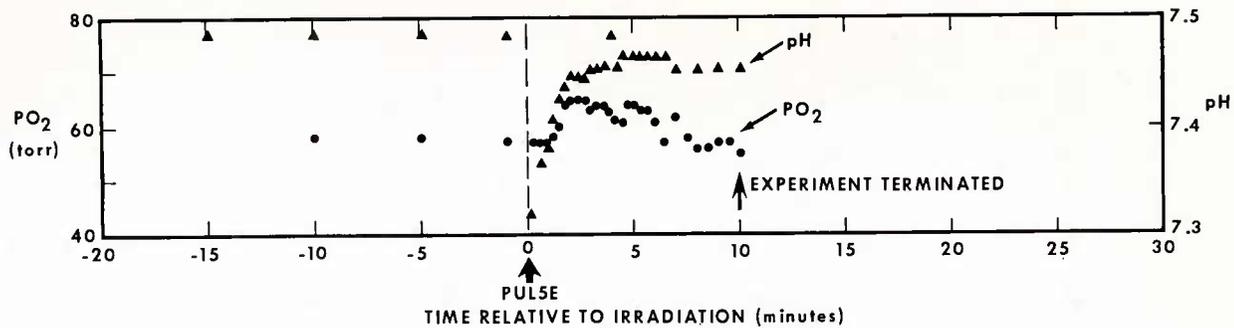


Figure 6. Postirradiation blood  $PO_2$  and pH (monkey 153)

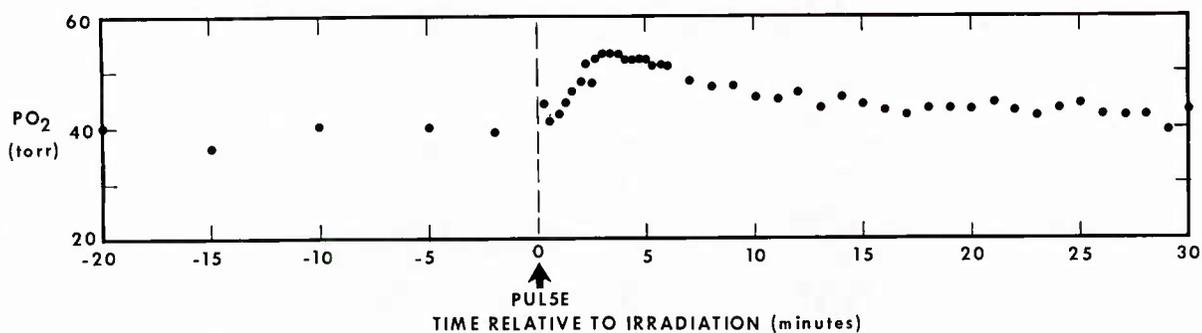


Figure 7. Preirradiation and postirradiation aortic blood  $PO_2$  (monkey D-20)

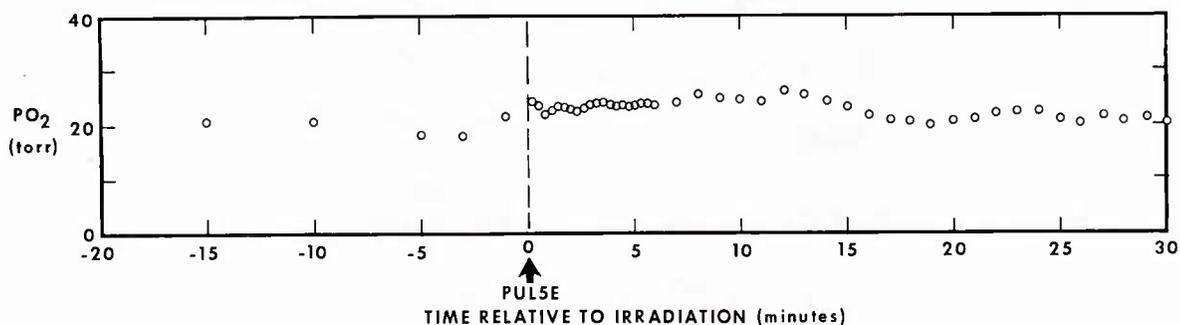


Figure 8. Preirradiation and postirradiation jugular blood  $PO_2$  (monkey B-48)

#### IV. DISCUSSION

Based upon results obtained when only the equipment was irradiated (Figure 2), it was concluded that irradiation had a minimal effect upon  $PO_2$  readings, and that effect would be evident during only the 1st minute postirradiation. It also was concluded that pH readings could decrease immediately after irradiation and remain slightly below preirradiation levels for about 2 to 5 minutes without indicating a physiological change in the monkey. After 5 minutes postirradiation, low pH readings were considered to reflect physiological changes, and pH readings substantially above preirradiation levels were considered to indicate physiological change at any time after irradiation.

Other reports indicate that arterial  $PO_2$  should be about 100 torr in monkeys.<sup>1,4,6</sup> However, in this study the preirradiation values for arterial  $PO_2$  consistently were between 60 and 80 torr, even when measured in the laboratory where electrode calibration could be monitored and controlled more precisely than in the exposure room. Perhaps the arterial blood of these monkeys was relatively poorly oxygenated as a result of the monkeys' response to surgery and restraint. Low  $PO_2$  values have been recorded in arterial blood after surgery in humans.<sup>5</sup> Preirradiation values for arterial pH were consistent with those published earlier.<sup>1,4,6</sup> Values for jugular blood  $PO_2$  were not found in other reports.

The slight increase observed in arterial  $PO_2$  after irradiation would be expected as a result of the hyperventilation that has been reported after similar irradiation of monkeys.<sup>7</sup> Furthermore, hyperventilation would increase  $CO_2$  elimination which might have caused the concomitant increase in arterial pH. Hyperventilation can

result from hypoxia or acidosis, among other factors. It is unlikely that hypoxia caused the hyperventilation under the conditions of this study, because the  $PO_2$  did not decrease in aortic or internal jugular blood. It is possible that irradiation causes a prompt increase in hydrogen ion concentration which elicits hyperventilation through the brain respiratory centers.

There was no substantial decrease in the blood  $PO_2$  during the period when ETI normally occurs. Therefore, if ETI does result from hypoxia, it must be caused by poor blood supply to all or part of the brain rather than lack of oxygen in the blood. If all parts of the brain receive adequate blood supply during ETI, then hypoxia does not cause or contribute to ETI.

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