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INVESTIGATION ON THE SATURATION AND CLEARANCE OF HYDROGEN GAS IN THE BRAIN AND EXTREMITIES OF MAN,

AND

INVESTIGATIONS ON BIOMEDICAL MONITORING OF DIVERS IN WET-SUITS.

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FINAL REPORT.

15 Mar 72 - 14 Nov 76

C.W. Sem-Jacobsen, M.D.

10 14 Nov 76

The EEG Research Institute

Gaustad, Oslo 3, Norway

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ACKNOWLEDGEMENT.

For their support of these studies I wish to express my gratitude to the U.S. and Norwegian Government for funds provided from the Royal Norwegian Council for Scientific and Industrial Research, from U.S. Army and the Atomic Energy Commission.

I wish to acknowledge the support and stimulating interest extended to me by dr. K. Aukland, and O.B. Styri.

I also wish to give my recognition to the staff at the EEG Research Institute for their extremely valuable assistance, contributions and steady interest.

To Mr. E. Hohn and Mr. O. Tjugen I would like to express a special thank for their steady interest and hard work in developing the mathematical models and the computer program.

ABSTRACT

A unique clinical situation at the EEG Research Institute has made it possible to collect gas clearance data in men. Hydrogen gas clearance and saturation in the brain have been monitored in 22 subjects - twice in 4 of them with 6 - 12 months interval. Each subject has been studied with from 18 to 36 chronically implanted electrodes. The T_{1/2} for H₂ gas clearance/saturation has been measured from 1 to 76 times around each of the 460 electrodes.

→ The half time for hydrogen gas clearance/saturation in the human brain may fluctuate between 1/2 minute and 30 minutes in grey matter and between 6 and 14 minutes in white matter. In the ear-lobes it may vary from 1 to 5 minutes, and from 2 to 20 minutes in the skeletal muscles. 8% CO₂ added to the breathing air caused a drastic reduction of the half time only in some areas in the brain. → There must be a focal mechanism regulating the blood flow to various areas of the brain.

The information obtained in these studies should be taken into account in the development of diving tables for diving on oxygen/hydrogen. The data may help to improve the understanding and treatment of decompression sickness and increase the safety of deep sea diving important to the U.S. Navy.

→ The Vesla on Person Biomedical Monitoring Equipment has been refined. Four channels of data are modulated, mixed and recorded on one track of a battery powered cassette tape-recorder modified for remote operation. The unit is fitted in a water tight clam shell, to be carried on the diver's back.

The Vesla on Person Biomedical Monitoring has been demonstrated to the Navy, to LCDR Call and his group at El Centro Calif. and LCDR Reid and his group at Point Mugu Calif.

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With the Marine Biomedical Institute, University of Texas, Galveston, we have started monitoring of divers in the Gulf of Mexico. The data from the Gulf and the North Sea will be comparable.

The accomplishment under this contract has made us ready for biomedical monitoring of operational working and inspection-dives in the North Sea for the study of work-load, euphoria, mental impairment and the diving reflex to improve diving efficiency and diving safety.

With support from the directorate of Labour Safety and the Norwegian Research Council this studies are now in progress in the North Sea.

INTRODUCTION

The main purpose of this contract has been to study saturation and clearance time for hydrogen gas in man to establish the half time for hydrogen gas, clearance and saturation in the brain and the skeleton muscles.

Investigations of biomedical monitoring of divers in wet-suits has been the second purpose of this contract.

Since 1952 the main investigator has carried out research in the human brain using intracerebral electrodes to examine and treat patients suffering from selected diseases in the brain.

In our laboratory at Gaustad these studies are carried out as part of depth-electrographic/neurosurgical treatment of patients suffering from Parkinson's disease and other neurological diseases. These examinations give us unique opportunities not only to improve the safety of the treatment, but are used to aid where the therapeutic coagulation most successfully may be applied.

In this way the intra-cerebral studies with the hydrogen gas clearance technique are unique for this laboratory. The chronic implantation in the human brain of sensors as well as the development of a technique by which blood flow changes of only two to four minutes' duration may be obtained, are new and unique for this laboratory. Preliminary data indicate that there is a steady fluctuation and change in the blood flow to the various nuclei and various systems within the brain.

The investigators feel very strongly that the research described in this report will open up a new area in the study of the functioning of the human brain and to which extent malfunctioning in the brain may be attributed to breakdown of blood flow.

The multiple focal intra-cerebral blood flow studies may open up a new area in the same way as the intra-cerebral depth-electrographic studies opened up a similar area 25 years ago.

In obtaining important, needed, basic information about changes in cerebral blood flow following neurosurgery and brain oedema. These data are unique information about absolute blood flow in different areas in the brain during the clinically critical post operative period. Hitherto it has only been possible to compute these data indirectly.

Our studies are of practical value for deep sea diving on the Continental shelf. For divers compression and decompression time are of great importance. No compression or decompression table for the treatment or management of divers can be complete without data about the focal gas clearance from the brain and the effect of recirculation.

Our preliminary results indicate that half time for gas clearance in the brain may vary from less than a minute up to half an hour or more, pending the activity of the diver and location in the brain.

The main investigator with a team from the EEG Research Institute participated under contract with the Navy and carried out EEG and EKG monitoring of the divers topside, during diving, inside the Sealab II habitate, and during decompression. This early experience prompted the main investigator to embark on a long range study mapping out EKG and EEG changes in divers during shallow and deep dives in simulator as well as in open sea dives even in hot water heated wet-suits.

A number of new technical developments had to be undertaken and operational problems had to be solved to make the data available on magnetic tape for further advanced electronic analysis and comparison.

To stimulate these two studies of interest to the U.S. Navy, the Office of Naval Research in Washington, in part supported the EEG Research Institute's investigation on gas clearance and saturation as well as biomedical monitoring of divers.

After preliminary negotiation this contract N00014-72-C-0345 was started on March 15, 1972. The contract was after several renewals completed on Nov. 14, 1976. The main purpose of the contract has been unchanged the whole time.

The investigation on the saturation and clearance of hydrogen gas in man was completed with a special report to Office of Naval Research in 1976.

The investigation on biomedical monitoring of divers advanced the state of the art of biomedical monitoring in chamber and open sea diving. We can today even monitor divers in hot water, heated wet-suits down to 400 meter continuously for up to 24 hours.

With substantial support from the Norwegian Research Council and the Norwegian Directorate of Labour Safety the study of divers has now been made the main task for the Research Institute with all needed support. The initiation of the current program was the result of the work carried out with ONR's support.

Investigations on the saturation and clearance of hydrogen gas in man.

The results of these studies are summarized below. The complete report enclosed.

Hydrogen gas clearance and saturation in the brain have been monitored in 22 subjects - twice in 4 of them with 6 - 12 months interval. Each subject has been studied with from 18 to 36 chronic implanted electrodes. A total of 460 electrodes have been used. Measurements have been made in 1 to 18 sessions each with from 1 to 7 H₂ gas saturation and 1 to 7 gas clearance measurements. Thus T/2 for H₂ gas clearance saturation has been determined from 1 to 76 times around each of the 460 electrodes.

On the basis of the monitored data T/2 for hydrogen gas clearance and saturation has been calculated.

Changes - fluctuations in the half time for hydrogen gas clearance and saturation has been studied in relation to prolonged and transient changes in the physiological conditions of the subject.

The studies have been carried out while the subject is unrestrained lying on a bed or sitting in a chair.

Under this program we have found:

- 1) The half time for hydrogen gas clearance/saturation in the human brain may fluctuate between 5 minutes and 30 minutes in grey matter.
- 2) The half time for hydrogen gas clearance/saturation in the human brain may fluctuate between 6 - 14 minutes in white matter.
- 3) Fluctuation in the focal blood flow produces a steady focal fluctuation in the half time for gas clearance and saturation? Independently in various areas of the brain.
- 4) The changes in half time is related to whether the area of the brain in question is active or inactive. Just as in skeletal muscles.
- 5) Because it is hard to control the activity in the brain, an extremely rigid protocol must be adhered to obtain identical data.
- 6) There must be a focal mechanism regulating the blood flow to various areas of the brain.

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- 7) Changes in respiration produces great fluctuation in the half time for gas clearance and saturation.
- 8) Changes in blood flow to some parts of the body due to the subjects position produces drastic changes in the half time for gas clearance and saturation.
- 9) The half time for hydrogen gas clearance and saturation in the ear-lobes may vary from 1 to 5 min. and from 2-20min. in the skeletal muscles.
- 10) 8% CO₂ added to the breathing air caused a drastic reduction of the half time for saturation/clearance found in certain areas in the brain. It was found to be as short as half a minute in certain regions.
- 11) Different effect of 8% CO₂ on different areas of the brain. No reduction or change was found in certain central areas of the brain.
- 12) Changes in half time during physical and mental activity has been found.

These studies of longitudinal changes over prolonged periods, have added a new dimension to the study of hydrogen gas clearance and saturation.

In the course of this program we have further successfully achieved.

- 13) The modification of the H₂ gas clearance technique developed earlier for use with intracerebral platinum electrodes in man.
- 14) Development of technique for measurements of half time of H₂ gas clearance and saturation short episodes of 3-4 minutes duration.
- 15) Found that H₂ electrodes are monitoring gas clearance from a larger area around the sensor than 1 x 4 mm radio isotope Krypton sensors.
- 16) The development of the DY2010B data collecting system for the monitoring of H₂ gas clearance and saturation.
- 17) Development of a computer program for handling of gas saturation/clearance data.

- 18) Demonstration of the need for proper clearance and saturation baselines to obtain reliable data.
- 19) New emphasis of the dangers of the mixing of H₂ gas with air.
- 20) New emphasis of the time factor involved in the mixing of H₂ gas and O₂. Two weeks of mixing is needed to obtain a 1:1000 uniformity of the gas mixture within a bottle.
- 21) New technique for the administration of H₂ gas to the patient from manufactured bottles.

Other investigators have found the half time for hydrogen gas clearance in man to be $\frac{1}{2}$ - 3 min. for Uterus, $\frac{1}{2}$ - 3 min. for Cor, and 8 - 60 min. for Os Femoris. Studies in animal have shown half times to be always below 5 min. except for skeletal muscles where it is found to be up to 35 minutes.

In future studies, continuous gas analyze of respiratory air to make valid baseline for recirculation and other pulmonary factors influencing the uptake and clearance of H₂ in the brain must be added.

A unique clinical situation at the EEG Research Institute has made it possible to collect this badly needed data about half time for hydrogen gas clearance and saturation in the brain, ear-lobes and muscles.

The data illustrate the complex focal changes in the blood flow in the brain.

The study has given us unique valuable bits of information regarding half time for hydrogen gas clearance in man.

The information should be taken into account in the development of diving tables for diving on oxygen/hydrogen.

The data may help to improve the understanding and treatment of decompression sickness and increase the safety of deep sea diving important to the U.S. Navy.

Investigations on biomedical monitoring of divers in wet-suits.

The history of diving goes back several thousand years. The dangers of diving and diving sickness has been known for a long time.

Already hundred years ago during the building of the bridge across the Mississippi river a physician made a good description of how 300 people tolerated to work under that pressure with rather rapid compression and decompression without any clinical symptoms or discomfort. The same physician described in detail how the remaining 50 of the workers on the project experienced from discomfort, to serious decompression-sickness, a number of them died.

With the recent development on the continental shelf there is an increasing need for man to be able to carry out work not only in shallow water but at greater depths.

The U.S. Navy's Sealab project was a major step trying to learn more about man's ability to work and live under water for a prolonged time. In this project the main investigator and the EEG Research Institute was responsible for the biomedical monitoring of the divers. The EEG, the EKG and the respiration was monitored using the original Vesla biomedical recording unit.

Just like in earlier studies of jet fighter pilots where significant changes in the EEG and EKG in response to the environment and the workload was encountered, marked changes were also seen in the data from the divers. Biomedical monitoring can reveal the subjects' physiological and mental response to the task required, the workload/overload can also be assest. Studies in simulators can give valuable information but the only way to learn the final answers is to monitor the divers in the environment in which he is going to function.

The technical problems in the biomedical monitoring of EEG was emphersized by dr. Carl Schaefer. "There are obviously great difficulties in obtaining good EEG records during extended simulated dives in chambers".

The problems of monitoring, EEG and EKG from divers in salt water heated wet-suits are even greater, but can be done using specially developed glue and water resistant seal.

Since the initiation of the contract in 1972 the Vesla On Person Biomedical Monitoring Equipment has been refined and has undergone severe testing.

In the Vesla system four channels of analog data are amplified, modulated, mixed and recorded on single track battery powered cassette tape-recorders, modified for remote operation. The units are fitted in a water tight clam shell, which is carried on the diver's back together with the air bottles. The unit performs satisfactory. See enclosed report. Ref. 1, 2, 4, 10.

For recording of the EKG only from divers in chambers and chamber-operators, the Vesla Seatpad has been modified. With the Seatpad EKG can be monitored from sitting subjects through the seat of their pants. Ref. 2, 6, 10.

In this investigation we started out with Vesla I biomedical monitoring system. It was basically subminiature four channel EEG machine. It was battery powered with four ink pens, writing on eight micron thick paper. It was capable of 45 minutes of recording time and tolerated 8G in any direction.

During the ONR contract period the Vesla biomedical recording system has been redesigned and tested out with the following new improvements.

1. The analog signals are amplified and modulated on 4 frequencies.
2. The modulated signals from four channels are mixed into one channel.
3. The four data channels can thus be recorded on any inexpensive battery powered single track tape recorder.
4. The speed fluctuation, the wow in the tape-recorder is corrected by a built in 7K HERTZ signal, used for flutter compensation.
5. The output of the Vesla unit can be transmitted by any standard airline radio .

6. For special purpose the signal is by a light emitting diode, converted into a light signal for transmission through fiber optic cables. The light emitting diode is placed inside the Vesla II unit.
7. The recording of the data on standard cassette tapes has greatly facilitated rapid exchange of data, between centers in Western Europe and America.
8. The new Vesla system including tape-recorder is placed in the same water tight clam shell as used during Sealab II.
9. With special developed glue and seal from Askim Gummi-varefabrikk and improved electro technique, it is possible to attach the electrodes to the divers 48 hours before the dive.
10. With the Norwegian Veritas we have a computer program for electronic analysis of the data.
11. For monitoring of EKG, from divers in chambers and from chamber operators the Vesla Seatpad developed earlier for pilots has been successfully modified.
12. The Vesla Seatpad makes it possible to record the EKG from sitting subjects inside and outside pressure chamber without attachments of leads through the seat of their pants.

The improved Vesla II system has been tested out in dives in the Oslofjord and on the west-coast of Norway.

In co-operation with the Aker Group for operation in the North Sea . Bounce dives down to 600 feet have successfully been monitored.

The On Person Biomedical Monitoring was successfully demonstrated to the Navy, LCDR Call and his groups at the Test Range, El Centro, Calif. and to LCDR Reid and his group at the US Navy Missile Test Range, Point Mugu, Calif. Reports enclosed. Ref. 8, 12.

With the Marine Biomedical Institute, University of Texas, Galveston, we have started monitoring of divers in the Gulf of Mexico. The data from the Gulf and the North Sea will then be comparable.

With support from the Norwegian Government, the department of Labour Safety and the Norwegian Research Council, studies of inspection and working divers during operations in the North Sea are now in progress to improve the effectiveness and the safety of divers.

Oslo, November 14. 1976.

C.W. Sem-Jacobsen

LIST OF PUBLICATIONS

1. Sem-Jacobsen, C. W., Kaiser, E.
"EEG AND EKG RECORDING ON STANDARD SINGLE TRACK CASSETTE TAPES"
The Vesla System for Data Collection and World-Wide Data Exchange.
Paper presented at the 1972 International Meeting of the Pavlovian Society, Oslo, Sept. 1972. (In press).
2. Sem-Jacobsen, C. W., Hasbrook, A.H.
"MONITORING OF EEG WITH THE VESLA II EQUIPMENT AND SEAT PAD IN SIMULATORS AND AIRCRAFTS"
The 44th Annual Scientific Meeting of the Aerospace Medical Association, Las Vegas, May 7 - 10 1973,
3. Sem-Jacobsen, C.W., Styri, O.B.
"MANIPULATION OF EMOTION"
Electro-Physiological and Surgical Methods.
Symposium PARAMETERS OF EMOTION, Karolinska Institute, Stockholm, June 4 - 6, 1973.
4. Sem-Jacobsen, C.W., Kaiser, E.
"REMOTE EEG MONITORING AND RECORDING"
The Vesla System for Data Collection and World-wide Data Exchange.
Round Table Conference. POSSIBILITIES AND LIMITATIONS OF NEW METHODS OF DATA COLLECTION AND ANALYSIS, Marseille, September 1 - 7, 1973.
Journal of EEG and Clinical Neurophysiology, Vol 36, No. 6, p. 566 - June 1974.

5. Sem-Jacobsen, C.W.

"MENTAL AND PHYSIOLOGICAL ENVIRONMENTAL
REQUIREMENTS IN MANNED FLIGHTS"

Paper presented at the NATO Agard Conference,
Soesterburg, Holland, September 3 - 7, 1973.

6. Sem-Jacobsen, C.W.

"MONITORING OF HEART FAILURE VIA SEAT PAD EKG"

A Safety Device for Commercial Airliners.
A "Dead Man's Button".

Paper presented at the Flight Safety Foundation's
26th International Air Safety Seminar, Lisbon,
Portugal, November 4 - 7, 1973.

7. Sem-Jacobsen, C.W.

"WORKSHOP ON ETHICAL CONSIDERATIONS IN HYPER-
BARIC RESEARCH"

Introduction to the Discussion.

Proceedings of the First Annual Scientific Meeting
of the European Undersea Biomedical Society,
Stockholm, June 13 - 15, 1974. Försvarsmedicin,
Vol. 9, No. 3, 1973. p.p. 382-383.

8. Sem-Jacobsen, C.W.

"SITE VISIT AS A CONSULTANT AND A LIVE DEMON-
STRATION OF BIOMEDICAL MONITORING OF PARACHUTING"

The Naval Aerospace Recovery Facility, El Centro,
California, May 1975. Report to Office of Naval Research.

9. Sem-Jacobsen, C.W., Hauglie-Hanssen, E.

"DORSAL COLUMN & TRANSCUTANEOUS ELECTRICAL
STIMULATION FOR INTRACTABLE PAIN"

Paper presented at the Seventh Annual Conference
of the Neuroelectric Society, New Orleans,
November 20 - 23, 1974.

10. Sem-Jacobsen, C.W.

"EKG MONITORING OF HEART FAILURE AND PILOT
LOAD/OVERLOAD BY THE VESLA SEAT PAD"

A Safety Device, a Dead Man's Button and Overload
Warning System for Commercial Air Traffic.

Aviation, Space and Environmental Medicine. (In press.)

11. Sem-Jacobsen, C.W.

"ELECTRICAL STIMULATION AND SELF-STIMULATION IN
MAN WITH CHRONIC IMPLANTED ELECTRODES"

Interpretation and Pitfalls of Results.

Paper presented at the First International Conference
on Brain Stimulation Reward, Janssen Pharmaceutica,
Beerse, Belgium, April 21 - 24, 1975.

12. Sem-Jacobsen, C.W.

"SITE VISIT AS A CONSULTANT AND A LIVE DEMON-
STRATION OF BIOMEDICAL MONITORING WITH VESLA
SEAT PAD IN ALTITUDE CHAMBER"

The Pacific Missile Test Range, Point Mugu, California,
May 1975. Report to Office of Naval Research.

13. Sem-Jacobsen, C.W.

"ANXIETY AND STRESS, STIMULATION TO ACHIEVEMENT".

A Nato Agard International Conference on Anxiety and
Stress. Voksenåsen, Oslo, Norway, June 30. 1975.

14. Sem-Jacobsen, C.W.

"MENNESKETS ARBEIDSMULIGHETER PÅ HAVBUNNEN":
(Man's ability and capability for work on the
ocean floor).

Symposium on Marine Technology. Norwegian Society
of Chartered Engineers. Geilo, December 1-5. 1975.
Norway. (in Norwegian)

15. Sem-Jacobsen, C.W.

"STRESS RESPONSE AND STRESS TOLERANCE IN FIGHTER
PILOTS DURING 6 G MANOEVRES".

Agard, Specialists Aerospace Medical Panel Meetings,
Copenhagen, Denmark, 5-9. April 1976.

16. Sem-Jacobsen, C.W.

"CLEARANCE AND SATURATION OF HYDROGEN GAS IN MAN".
(with Special Emphasize on the Brain)

Report to Office of Naval Research, 1976. Contract
No. N00014-72-C-0345.

17. Sem-Jacobsen, C.W.

"ANXIETY AND STRESS' STIMULATION TO ACHIEVEMENT'
SATISFACTION, AND WELL-BEING AS WELL AS BREAK
DOWN".

XXIVth International Congress of Aviation and Space
Medicine. Johannesburg Republic of South Africa.
October 24. - 29. 1976.

The main investigator has during the contract period, participated and presented material at the following meetings:

1. EEG and EKG recording on standard single track cassette tapes.
The Vesla System for Data Collection and World-Wide Data Exchange.

International Meeting of the Pavlovian Society, Oslo Sept. 1972.
2. Monitoring of EKG with the Vesla II equipment and seat pad in simulators and aircrafts.

The 44 th Annual Scientific Meeting of the Aerospace Medical Association, Las Vegas, May 7 - 10 1973.
3. Remote EEG monitoring and recording.

Round table conference. Possibilities and liminations of new methods of data collection and analysis, Marseille, Sept. 1 - 7. 1973.
4. A dead man's button in commercial airliner.

The XXI International Congress of Aviation and Space Medicine Munich, Sept. 17 -21 1973.
5. Mental and physiological environmental requirements in manned flights.

NATO Agard Conference, Soesterburg, Holland, Sept. 3 - 7 1973.
6. Monitoring of heart failure via seat pad EKG.
A safety device for commercial airliners.
A dead man's button.

Flight Safety Foundation's 26th International Air Safety Seminar, Lisbon, Protugal, Nov. 4 -7 1973.
7. Workship on ethical considerations in hyperbaric research.
Introduction to the discussion.

First Annual Scientific Meeting of the European Undersea Biomedical Society, Stockholm, June 13 - 15, 1974.

8. Dorsal column & transcutaneous electrical stimulation for intractable pain.

Seventh Annual Conference of the Neuroelectric Society, New Orleans
Nov. 20 - 23. 1974.

9. Anxiety and stress stimulation to achievement, satisfaction, well-being and pathological behavior.

Nato Agard International Conference. Dimensions of anxiety and stress
Voksenåsen, Oslo Norway June 30. 1975.

10. Menneskets arbeidsmuligheter på havbunnen.
(Man's ability and capability for work on the ocean floor.)

Symposium on Marine Technology. Norwegian Society of Chartered
Engineers, Geilo, December, 1. - 5. 1975. Norway.

11. Stress response and stress tolerance in fighter pilots during 6 G maneuvers.

Agard, Specialists Aerospace Medical Panel Meetings, Copenhagen,
Denmark, April 5 - 9 1976.

12. Navy-wide workshop on high pressure biomedical research,

Naval Coastal Systems Laboratory, Panama City, Florida,
March 9 - 11 1976.