

Memorandum 1

DATE : 19 January 1971

FROM : Code 712
 VIA : Code 71 *4 fm (see memo)*
 TO : Code 7
 Code 2 *QT*

*3rd to SG M imp
 to base letter
 UR WJ*

SUBJECT : Further information from Dr. Weinstein concerning proposed study
 "Splanchnic Metabolism During Chronic Stress in Active Duty Personnel"

1. Clinical Investigation Center, Oakland, California has been active in the study of liver metabolism in stress situations. They have demonstrated that starvation leads to lipolysis then to ketosis and decreased carbohydrate tolerance. Amelioration of ketosis using nicotinic acid (inhibits lipolysis, appeared to lessen the carbohydrate intolerance but did not substantially correct it.

During exercise (mile run), the parameters of carbohydrate utilization are increased with enhanced carbohydrate tolerance. Yet during exercise, a ketotic state occurs similar to that seen during caloric deprivation.

The Randle hypothesis states that increased levels of fatty acids and/or ketone bodies inhibit carbohydrate utilization by muscle tissue.

This hypothesis seems contradictory when laboratory studies from C-I-C indicate that both increased and decreased carbohydrate tolerance exist during ketotic states. Thus preliminary studies suggest that the primary defect may lie in liver metabolism and its ability to utilize carbohydrate. This question can be answered by observing arterio-venous differences across the liver.

The clinical methodology to measure such changes, the mechanical expertise to place the catheter and the valuable assistance of Dr. Richard Havel (Professor of Medicine, University of California) as co-investigator are present. Dr. Havel is an authority on carbohydrate and lipid interaction during fasted states. He has performed the procedure of hepatic vein catheterization in 35 individuals without complications due to the procedure. He will be present at Oakland when the initial procedure is performed and will be readily available for consultation throughout the study.

Finally, it should be noted that animal models with the exception of the rat do not exist for the study of ketosis. The rat is unsatisfactory for this study since their metabolic pathway for carbohydrate is different from the human.

Very respectfully,

R. L. Bernstine
 R. L. BERNSTINE

This study may shed some light on how or if the liver is involved in the high glucose levels and tolerance absent in Viet Nam casualties (trauma).



INVESTIGATION

DATE : 11 January 1971

FROM : CODE 712

TO : CODE 7

SUBJECT : Reference Memo from Code 2 to Code 7

1. Dr. Weinstein will be in Washington on 13-14 January 1971.
2. He will be prepared to discuss his background in hepatic vein catheterization and their previous work in liver function during stress.
3. Could he present a briefing in person or submit a written report?

Very respectfully,

R. L. Bernstein
 R. L. BERNSTINE

please as it must be given to SG for his consideration.
 R

Code 7

What has Oakland
been doing along these
lines in the past
Connection of this
function in stress studies

gone
2

52-2-26

DEPUTY SURGEON GENERAL

712 -

any info
on what CIC
has been doing
in the past

See Code 2

Winn
H

DATE: 1 December 1970

MEMORANDUM

FROM : Code 712

TO : Code 71

SUBJECT : NH Oakland request for use of human volunteers on effect of stress as measured by certain hepatic functions monitored via hepatic vein catheterization

1. The expertise of the co-investigators stems from "a thorough familiarization with the procedure by the primary investigator". In addition, "support has been elicited from co-investigators (Departments of Surgery and Radiology, Naval Hospital, Oakland) to perform the catheterizations and assume responsibility for care of the subject during and after the study". (Statements quoted are from ADM Makin's letter.)
2. Their experience with this particular technique of liver catheterization stems from their contact and instruction in Dr. Havel's laboratory.
3. In order to compare peripheral and splanchnic samples (i.e. liver metabolism), a catheter must be placed in the hepatic vein.
4. I talked with other surgeons at NMRI and none expresses any serious concern with the procedure as such. Whether it should be performed in healthy volunteers depends upon weighing the "minimal" risk and discomfort against possible benefits (i.e. biochemical mechanisms which are altered in chronic stress of fasting).
5. Dr. Weinstein will be in town sometime within the next two weeks.

Very respectfully,

R. L. Bernstein

R. L. BERNSTINE



This form must be paid all correspondence submitted for approval to the duty Chief of the Bureau.

	APPROVED	DATE	INFORMATION OR COMMENTS	DATE SIGNED
ASSISTANT CHIEF	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<i>RSW</i>	3 Nov 70
DEPUTY CHIEF	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<i>JMC</i>	
CHIEF OF BUREAU	<input checked="" type="checkbox"/>			

PREPARED BY: CAPT L. Bernstine, MC, USN, CODE: 712

PREPARED IN REPLY TO: DIRECTOR OF, OR IN REPLY TO: NSIR 3900.39 of 28 Apr 1970 and CO NH Oakland ltr 78-cw of 1 Sep 1970

BRIEF

Permission is requested to use human volunteers in a research proposal submitted by Naval Hospital, Oakland.

Human volunteers are essential to the project since metabolic responses in animals are not sufficiently similar to those of man to produce reliable guidelines.

Volunteers will be healthy young males who are patients recovering from mild conditions such as simple fractures.

SIGNIFICANT ASPECTS OF MATERIAL FOR SIGNATURE

Use of human volunteers.

CLEARANCES (Explain nonconcurrences or clearances indicated but not obtained)

SIGNATURE: CAPT MC USN, Director, Research Division DATE: 5 Oct 1970

presented by J. H. H. H.
1 December 1970

Cole 712

Cole 71

Re Oakland request for use of human volunteers on effect of stress as measured by certain hepatic functions monitored via hepatic vein catheterization

1. The expertise of the co-investigators stems from "a thorough familiarization with the procedure by the primary investigator". In addition, "support has been elicited from co-investigators (Department of Surgery and Radiology, Mc Kean Hospital, Oakland) to perform the catheterizations and assume responsibility for care of the subject during and after the study". (Statements quoted are from AMM's letter.)
2. Their experience with this particular technique of liver catheterization stems from their classes and instruction in Dr. Havel's laboratory.
3. In order to compare peripheral and splanchnic samples (i.e. liver metabolism), a catheter must be placed in the hepatic vein.
4. I talked with other surgeons at MCH and none expressed any serious concern with the procedure as such. Whether it should be performed in healthy volunteers depends upon weighing the "minimal" risk and discomfort against possible benefits (i.e. biochemical mechanisms which are altered in chronic stress of fasting).
5. Dr. Weinstein will be in town sometime within the next two weeks.

Very respectfully,

R. L. BRINCHER