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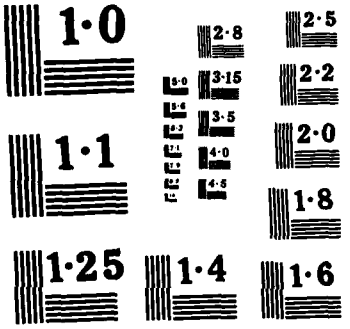

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REPORT #1

"A Program for Clinical Care in Physical Trauma"

ANNUAL SUMMARY REPORT

Francis D. Moore, M.D.

MARCH 1976

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U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
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Department of Surgery
of
Harvard Medical School
Peter Bent Brigham Hospital

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20. ABSTRACT *(Continue on reverse side if necessary and identify by block number)*

Studies were performed to determine substrate interactions as they relate to body nitrogen balance in fasting man. Carbohydrate at all levels of infusion markedly improves the utilization of amino acids. Thus, ketosis does not seem to favor nitrogen economy.

Studies with indwelling cardiac catheters demonstrate vegetations on heart valves within 24 hours in dogs. These aseptic endocardial lesions easily become septic with intentional contamination of the blood stream in these animals.

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"A PROGRAM FOR CLINICAL CARE IN PHYSICAL TRAUMA"

ANNUAL REPORT, JANUARY 31, 1976

During this 12 months period we have exploited extensively our standardized model for body fuel interactions in man. This consists in the employment of normal human volunteer subjects who are given fluids only by mouth for a period of 5-10 days. During this time they are given intravenously either pure substrates to examine substrate interaction, or a combination of hormones to reproduce the body fuel utilization patterns seen after injury.

The following categories have been essentially completed: amino acids alone, amino acids with low dose glucose, amino acids with high dose glucose, glyercerol alone, glycerol with amino acids, and intravenous fat emulsions. In addition we have examined the effect of continuous or intermittent oral glucose, and the effects of catecholamines, cortisol and glucagon.

In this brief annual report no effort will be made to detail all the findings. They are being written up extensively at this time and all the manuscripts will be submitted to the Army Medical Research and Development Command, Surgical Office. Instead, we will undertake here a brief description of the data on amino acids alone.

Nitrogen intake daily was 13.5 grams, entirely by intravenous in the model mentioned above. Excretion daily after stabilization ranged from 17.5-21.1 grams per day. There was thus a wastage of nitrogen equal to the entire infusion plus some additional small contribution (4-7 grams) from endogenous sources. Assuming that totalurea synthesis is a measure of gluconeogenesis it is possible to calculate the energetics of this fuel interaction: exogenous amino

acids substituting for glucose, and sparing body nitrogen. Positive nitrogen balance is not achieved with this program; the degree of nitrogen economy achieved with 90 grams of amino acids each day is approximately equivalent to that achieved with 500 grams of glucose alone. And yet the inter-conversion calculus suggests that this is achieved with a gluconeogenetic rate equivalent to only about 220 grams of glucose. The endocrine response is being analyzed in detail. Glucagon rises; blood glucose remains constant. The cost of this infusion of amino acids is approximately 5 times that of the equivalent amount of glucose. As mentioned in the foregoing, there is only a minor improvement in nitrogen economy.

Data on the plasma amino acids, and the changes induced in them by this infusion, are of the greatest interest. They show that the resting values for these normal male human subject volunteers who have been in good nutrition prior to the experiment, show levels somewhat higher than those reported in the literature. Citrulline, ornithine, and serine, three amino acids not present in the infusion material ("Freeamine II") or present at low concentrations, all fall. The other amino acids undergo appropriate changes with some startling exceptions.

It is evident from other studies that we have completed in the past year that carbohydrate markedly improves the utilization of amino acids at all levels and under all infusion circumstances. The infusion of this carbohydrate reduces the level of ketones to a mere zero; free fatty acids are markedly reduced. Serum triglycerides do not rise unless the glucose is given in excess. These data provide con-

vincing proof of the fact that in man neither ketone bodies specifically, nor ketosis as a whole, in any way favors nitrogen economy. The impression gained from the literature that ketosis is a favorable setting for protein synthesis or protein sparing is traceable to the fact that many of the experiments have been performed in rats which have a different economy for the utilization of ketone bodies. Or, alternatively, they have been performed in man by the infusion of ketone bodies in sufficiently large amounts so that the kidney oxidation has provided a source of carbohydrate energy.

Studies of this type will be continued and further explored in severely injured patients.

During the past six months the dog model employed to study the effect of cardiac catheterization and long indwelling monitor catheters in the cardiac chambers of pulmonary artery have been essentially brought to completion. These demonstrate that within 24-36 hours the animal shows sterile platelet vegetations on the heart valves. The intentional contamination of the blood stream of the animals even transiently (as in clinical burns) results in infection of these platelet thrombi on the heart valves and reproduces the septic endocarditis occasionally observed with long indwelling cardiac catheters in man. The clinical message is clear: in severely injured septic or burn patients it is very hazardous to employ indwelling cardiac catheters that traverse the heart valves. Even the central venous line must constantly be checked by withdrawal cultures to be sure it is not the source of blood stream infection.

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