[Collaborative efforts]

MEDICAL GRAND ROUNDS

MAY 1, 1958

RENAL AND CELLULAR RESPONSES TO ACUTE AND CHRONIC RESPIRATORY ACIDOSIS. NORMAN W. CARTER, DONALD W. SELDIN, AND H. C. TENG.

RENAL AND CELLULAR COMPENSATIONS FOR RESPIRATORY ACIDOSIS WERE STUDIED IN TUBE-FED RATS KEPT IN A METABOLIC CAGE CONSTRUCTED TO MAINTAIN A GIVEN ATMOSPHERIC CO_2 TENSION CONSTANT. BLOOD AND URINE ELECTROLYTES AND ACID-BASE PATTERNS WERE MEASURED; RENAL CARBONIC ANHYDRASE AND GLUTAMINASE ACTIVITIES WERE ASSAYED. RATS WERE SACRIFICED IN GROUPS AT INTERVALS FROM ONE HOUR TO 14 DAYS TO DISTINGUISH ACUTE AND CHRONIC EFFECTS.

AFTER ONE HOUR IN 10 PER CENT CO_2 THERE WAS A RISE IN PLASMA pCO_2 (35.4 ± 2.6 MM. HG TO 91.4 ± 3.1 MM. HG) AND CO_2 CONTENT (24.7 ± 1.8 MEQ. PER L. TO 34.4 ± 1.8 MEQ. PER L.) WHILE THERE WAS A FALL IN PLASMA CHLORIDE (108.8 ± 2.8 MEQ. PER L. TO 96.0 ± 2.5 MEQ. PER L.) AND BLOOD pH (7.43 ± 0.02 TO 7.17 ± 0.04). BY 24 HOURS, AT THE SAME PLASMA pCO_2, CO_2 CONTENT ROSE TO 42.0 ± 3.0 MEQ. PER L. WHILE PLASMA CHLORIDE FELL TO 88.1 ± 4.0 MEQ. PER L. NO FURTHER SIGNIFICANT CHANGES SUPERVENED THEREAFTER.

URINE AMMONIA, TITRATABLE ACID AND CHLORIDE EXCRETION WERE INCREASED DURING THE FIRST DAY ONLY, WHILE POTASSIUM EXCRETION REMAINED ELEVATED THROUGHOUT. SODIUM EXCRETION WAS UNCHANGED. DESPITE PROFOUND ACIDOSIS, ACTIVITIES OF RENAL GLUTAMINASE AND CARBONIC ANHYDRASE DID NOT INCREASE. MUSCLE ANALYSIS DISCLOSED SLIGHT, BUT SIGNIFICANT, DECREASE IN POTASSIUM AND A MORE MARKED DECREASE IN SODIUM. ACETAZOLAMIDE (DIAMOX) ADMINISTRATION, SUFFICIENT TO SUPPRESS MEASURABLE RENAL CARBONIC ANHYDRASE ACTIVITY COMPLETELY, RESULTED IN HIGH PLASMA pCO_2 (180.7 ± 31.8 MM. HG) AND A CO_2 CONTENT OF 51.3 ± 4.40 MEQ. PER L.

FROM THESE STUDIES IT IS CONCLUDED THAT: 1) ELEVATION OF BICARBONATE AND REDUCTION OF CHLORIDE IN PLASMA IS MAXIMAL AT 24 HOURS; THESE CHANGES ARE PRINCIPALLY A CONSEQUENCE OF CELLULAR BUFFERING. 2) RENAL GLUTAMINASE AND CARBONIC ANHYDRASE ARE NOT ACTIVATED BY INTRACELLULAR ACIDOSIS. 3) INCREASED BICARBONATE REABSORPTION CAN OCCUR AS A RESULT OF HYPERCAPNEA IN COMPLETE ABSENCE OF RENAL CARBONIC ANHYDRASE ACTIVITY.

LEFT VENTRICULAR FUNCTION AT REST AND DURING EXERCISE. CARLETON B. CHAPMAN, ORLAND BAKER AND JERE H. MITCHELL.

SIMULTANEOUS LEFT VENTRICULAR VOLUME AND PRESSURE CURVES WERE RECORDED IN FIVE ANESTHETIZED DOGS AT REST AND DURING EXERCISE, USING A BIPLANE CINEFLUOROGRAPHIC TECHNIQUE AT 30 FRAMES PER SECOND. VOLUME WAS CALCULATED FROM THESE TRACINGS FROM EACH PAIR OF FRAMES USING A MODIFICATION OF SIMPSON'S PARABOLIC RULE. THE ERROR OF THE METHOD, AS DETERMINED FROM VENTRICULAR MODEL EXPERIMENTS, IS LESS THAN 10 PER CENT.

RESTING END-DIASTOLIC VOLUME WAS 76.1±7 CC. AND THAT DURING (NOT AFTER) EXERCISE WAS 64.8±7 CC. THE DIFFERENCE WAS CONSISTENT THROUGHOUT THE STUDIES AND IS STATISTICALLY SIGNIFICANT.

EXERCISE PRODUCED SLIGHT INCREASE IN STROKE WORK BUT TOTAL POWER PRODUCTION PER MINUTE ROSE FROM 37±8 TO 55±0.6 THOUSAND GM.-CM. PER KG. KINETIC ENERGY, CALCULATED FROM EJECTION AND VELOCITY CURVES, WAS 2 PER CENT OF TOTAL WORK (RESTING) AND 4 PER CENT DURING EXERCISE. THE UNDERESTIMATE OF POTENTIAL (PV) WORK AS A RESULT OF USING MEAN INSTEAD OF INTEGRATED VALUES WAS NEGLIGIBLE AT REST BUT WAS 13 PER CENT DURING EXERCISE. THE CORRESPONDING FIGURES FOR KINETIC ENERGY WERE 35 AND 51 PER CENT, RESPECTIVELY.

VARIATION IN THE HEART'S APPLICATION OF FORCE FROM STROKE TO STROKE, AND THE DYNAMIC EFFECT OF BIGEMINY AND BRADYCARDIA, ARE EASILY DISCERNIBLE IN THE VOLUME-PRESSURE RECORDS.

THE STUDY DEMONSTRATES THE VALUE OF BIPLANE CINEFLUOROGRAPHIC METHODS FOR OBTAINING "INSTANTANEOUS" VENTRICULAR VOLUME CURVES. IT SHOWS CONCLUSIVELY THAT VENTRICULAR END-DIASTOLIC VOLUME DECREASES DURING EXERCISE, THAT FAILURE TO CALCULATE KINETIC ENERGY AT HIGH FLOWS MAY LEAD TO SIGNIFICANT ERROR, AND THAT USE OF MEAN VALUES FOR CALCULATING VENTRICULAR POWER PRODUCTION IS INADMISSIBLE WHERE HIGH FLOWS ARE INVOLVED.

HEMOLYSIS IN UREMIA: PREVENTION OF INTRACORPUSCULAR DEFECT BY RENAL TISSUE. E. E. MUIRHEAD AND J. A. STIRMAN.

UNDER CERTAIN CONDITIONS, A HEMOLYTIC COMPONENT MAY CONTRIBUTE GREATLY TO THE ANEMIA ASSOCIATED WITH RENAL DISEASE AND UREMIA. HEMOLYSIS HAS BEEN STUDIED IN UREMIA.

ERYTHROCYTES OBTAINED FOUR DAYS FOLLOWING BILATERAL NEPHRECTOMY OF THE DOG WERE TRANSFUSED INTO RECIPIENTS COMPATIBLE BY THE ANTIGLOBULIN TECHNIQUE AND THE LIFE SPAN WAS MEASURED SIMULTANEOUSLY BY THE ASHBY AND RADIOCHROMIUM METHODS. COMPARABLE RESULTS INDICATING A SHORTENED LIFE SPAN WERE OBTAINED BY THE TWO METHODS. THIS APPROACH SUPPORTED THE USE OF THE RADIOCHROMIUM METHOD UNDER THESE CONDITIONS.

ERYTHROCYTES OBTAINED FOUR DAYS FOLLOWING BILATERAL NEPHRECTOMY OF DOGS WERE TRANSFUSED INTO NORMAL RECIPIENTS ON 30 OCCASIONS. A PROMINENTLY SHORTENED LIFE SPAN WAS DETERMINED. THE RESULTS DIFFERED SIGNIFICANTLY FROM THOSE OBTAINED WHEN THE ERYTHROCYTES OF NORMAL DOGS WERE REINTRODUCED INTO THEIR NORMAL ENVIRONMENT OR WHEN THESE CELLS WERE TRANSFUSED INTO NORMAL RECIPIENTS. IN SEVEN EXPERIEMTNS THE SAME SHORTENED LIFE SPAN WAS OBSERVED IN THE NEPHRECTOMIZED DOG AS IN THE NORMAL RECIPIENT. THESE FINDINGS INDICATED AN INTRACORPUSCULAR DEFECT. BY THIS METHOD THIS DEFECT REACHED A MAXIMUM 24 HOURS FOLLOWING NEPHRECTOMY.

In five experiments the ureter was connected to the vena cava and the opposite kidney was removed. Four days later, the erythrocytes from these animals were transfused into normal recipients. The life span approached normal values. There was a significant difference between the life span curves following nephrectomy and those following ureterocaval anastomosis.

The results indicated rapid development of an intracorpuscular defect following nephrectomy. Under the same degree of excretory renal insufficiency (uremia) protection against such a defect by intact renal tissue was demonstrated. Thus the stability of the erythrocyte in the circulation of the dog appears to be due in part to nonexcretory renal function (s).

The Mechanism of the Protein-Sparing Effect of Glucose. Jean D. Wilson and Marvin D. Siperstein.

The mechanisms by which glucose administration during starvation spares protein are unknown. Previous studies in our laboratory demonstrated that glucose oxidation can control lipogenesis by generating rate-limiting cofactors, particularly during the operation of the hexosemonophosphate shunt. The present study was undertaken to investigate the relationship between protein synthesis and the cofactors generated during glycolysis--TPNH, DPNH, and ATP.

The influence of cofactors and substrates on protein synthesis from acetate-C^{14} was studied in cell-free homogenates of rat liver. Addition of TPN plus glucose-6-phosphate (G-6-P) to homogenates increased protein synthesis three- to sevenfold; addition of DPN plus G-6-P stimulated protein synthesis to a lesser extent. Addition of an ATP-generating system (creatine phosphate plus ATP) also accelerated protein synthesis markedly. However, when protein synthesis was maximally stimulated by the ATP-generating system alone, addition of TPN plus G-6-P causes further protein synthesis up to threefold; again, the effect of DPN plus G-6-P was usually less. Furthermore, to establish that pyridine nucleotides generated during glycolysis are, in fact, limiting in protein synthesis, valine-C^{14} incorporation was studied. Again, TPN and DPN were found to stimulate protein synthesis above levels attainable with maximal ATP generation alone.

It is noteworthy that pyridine nucleotides can regulate protein synthesis, since the only reaction in mammals resulting in net amino acid synthesis (a-ketoglutarate to glutamate) requires pyridine nucleotide. Thus, the rate of amino acid is probably rate-limiting in protein synthesis. The conclusion may also be drawn that the generation during glycolysis of the cofactors - TPNH, DPNH, and ATP - may account for the protein-sparing effect of glucose. In addition, the finding that TPNH is more limiting than DPNH suggests that the glucose oxidized via the mexosemonophosphate shunt may be of particular importance in the sparing of protein by glycolysis.