Mechanism of Baroreceptor-Induced Changes in Heart Rate*

MARC D. THAMES (M-69)

The mechanism of mediation of baroreceptor-induced changes in heart rate is uncertain. According to the classical view reciprocal changes in parasympathetic and sympathetic efferent activity are involved; newer studies, however, suggest that increases in heart rate in response to systemic hypotension are mediated exclusively by increased sympathetic activity while decreases in heart rate in response to systemic hypertension are due solely to increases in parasympathetic activity. To resolve these differences, we studied dogs unanesthetized, anesthetized with chloralose and urethane, or with chloralose and morphine. Beta-adrenergic receptor blockade with propranolol reduced significantly but did not abolish the tachycardia in response to the hypotension induced by intravenous nitroglycerin. It also reduced significantly the bradycardia in response to hypertension produced by intravenous phenylephrine. Parasympathetic efferent blockade with atropine essentially abolished the tachycardia in response to nitroglycerin and the bradycardia in response to phenylephrine. In a second group of experiments, propranolol reduced but did not abolish the tachycardia in response to bilateral carotid arterial occlusion. In a third group of experiments, parasympathetic blockade with atropine reduced but did not abolish the bradycardia in response to bilateral electrical stimulation of the carotid sinus nerves. These results clearly show that baroreceptor-induced changes in heart rate are mediated by reciprocal alterations in cardiac parasympathetic and sympathetic efferent activity.

Preceptor: HERMES A. KONTOS, Division of Cardiovascular Disease, Medical College of Virginia.

Inhibition of Fibroplasia with Lung Implants in the Peritoneal Cavity of the Swiss White Mouse*

KENNETH D. YOUNER (M-71)

Well documented observation has shown that pneumococcal lobar pneumonia undergoes resolution without the fibroplasia that often follows inflammatory processes. As noticed by Dumont, neutrophiles invade the lung alveoli, however, the usual lymphocyte infiltration does not follow. Using pulmonary homografts in dogs, Barnes et al, have shown that intralveolar edema, inflammation and neutrophilic infiltration occur. However, lymphocytes either do not appear, or do so only in the peripheral vessels. An attempt was made to compare the ability of lung tissue to inhibit fibroplasia using tissue implants into the peritoneal cavity of a Swiss white mouse. The lung of a donor mouse and the kidney of the same mouse were used as the experimental-comparison tissues. Three variables were considered. First the tissue types were chosen due to close anatomical and histological similarity. Each organ has a parenchyma with a basement membrane type structure with a connective tissue capsule surrounding the entire organ. The presence of the capsule, and the possible role it may play in stopping a lymphocyte infiltration was the second factor. Each mouse received the entire left kidney and the entire left lung, each with an intact capsule. Half of the other lung and half of the other kidney was also implanted into the same mouse. The remaining half of each tissue was used as a normal histological comparison. The third factor is time. Barnes noted a maximum tissue response at 5-6 days. Therefore, I used two series. Series of 6 and 12 days were used. The second series was used to see if any effect the lung may have on fibroplasia is time dependent. The whole lung implant gained more weight (used to

* Supported in part by an A. D. Williams Fellowship
reflect the amount of fibrosis) than the whole kidney. However, once the capsule is opened the half kidney gains more weight than the whole lung. With the 12 day series whatever effect the lung parenchyma had on fibrosis is now gone, for the whole lung and the half lung both gained more weight than the whole or half kidney. These weight findings were corroborated by histological sections comparing the amount of fibrosis in the implanted tissues.

Preceptor: WILLIAM REGELSON, Department of Medical Oncology, Medical College of Virginia.

Roentgen Evaluation of the Hepatic Arterial Bed

PARHAM R. FOX (M-71)

Angiographic alterations sustained by the hepatic arterial bed in diffuse parenchymal disorders such as cirrhosis, and congestion, have heretofore not been critically evaluated. Tortuosity of intrahepatic arteries, a readily detectable and often striking angiographic feature, has generally been considered as indicative, or even specific for cirrhosis. The influence of aging, liver size, and other factors, have not been objectively considered. We have attempted to correlate the gross and histologic appearance of thirty livers at post mortem with the roentgen appearance of their barium injected hepatic arteries; this report constitutes our preliminary results. Diagnostic criteria of in vivo hepatic arteriography will be subject to correlative evaluation with the data provided by these post mortem studies. Liver weight, gross description, color photographs, and microscopic sections were obtained for pathologic correlation. Pertinent clinical details were culled from the patients' chart. High resolution radiographs were randomized and shown to a panel of three radiologists who assessed and categorized each into the following groups:

1. Normal ............... 14 cases
2. Tortuosity ............... 10 cases
   a. Mild
   b. Moderate
   c. Severe
3. Hypo-and hypervascularity; curvilinear stretching .... 6 cases

Of the 10 cases radiographically demonstrating hepatic arterial tortuosity, none showed gross or histologic evidence of cirrhosis. Of the cases with histologically proven cirrhosis the radiographic arterial pattern was assessed “Normal” in all. It is clear from our data that the specificity of arterial tortuosity as a reflection of cirrhosis, a concept generally accepted, does not withstand objective appraisal. In view of this significant (although negative) observation we are encouraged to continue efforts in seeking a statistically significant correlation with this angiographic finding.

Preceptors: MELVIN VINIK, Department of Radiology; I. NAKONECZNA, Department of Pathology, Medical College of Virginia.

Effect of Gravity on the Distribution of Blood in the Dog Lung

DAVID H. BRISTOW (M-71)
FRANK MARTORANO (M-71)
BATTINA GROOME

The distribution of blood was measured in nineteen anesthetized dogs. Ten were placed vertical, head up, and nine were placed head down. The dogs were in the vertical position for at least an hour and a half, then blood samples were drawn, the heart was fibrillated, the thorax entered, the major vessels of the heart and lung were clamped, the heart and lung removed together and frozen in liquid nitrogen. Cubes were cut from the lungs at various levels from apex to base and were measured on each edge, weighed, and ground in a colloid mill. Blood pigments were extracted from the ground cubes and measured to find blood volumes in each cube. The total volume of each cube was known and tissue and gas volumes were calculated with algebraic equations. In the head up dogs, per cent of blood was three times as great in the base as in the apex and tissue increase 1.5 times from the apex to the base. In the head down dogs, there was no gradient from apex to base of blood or tissue. One implication of these results is anatomic difference between the apex and base of the lung.

Preceptor: JOHN L. PATTERSON, JR., Division of Cardiopulmonary Laboratories and Research, Medical College of Virginia.
A Study in CPK Iso-Enzymes

JOHN ELWOOD OWENS (M-71)

Heart muscle has three CPK iso-enzymes; CPK₁ in smallest amount and nearest the anode on electrophoresis; CPK₂ in medium amount and in the middle of electrophoretic pattern; and CPK₃ in greatest amount at the cathode end. The four chambers of the heart and the septum of the heart are apparently possessive of slightly different levels of concentration of CPK enzyme, a fact which, upon CPK iso-enzyme differential analyses of the four chambers and septum of heart, may be resolved by proving that the fluctuating total level of CPK in a particular area is a function of a certain specific iso-enzyme of CPK. CPK₂ and CPK₃ appear to be the enzymes that fluctuate not only among the extracts of cardiac muscle from these five areas of the heart but also among the extracts of cardiac muscle of different pathological states. With respect to tissue from the same heart, there appears to be a decreasing level of CPK₃ in going from RA to RV to LA to LV to septum. This is particularly true in cases where death had heart involvement. This pattern does not hold true at present in cases where death had no heart involvement. Results are apparently well-reproducible not only in different electrophoretic chambers but also with long intervals of time intervening (i.e., if tissue and/or extracts are frozen). The prospects of this study include the possibility of diagnosing area of heart muscle involvement by serum analysis of altered CPK iso-enzyme levels.

Preceptor: FRANKLIN LIM, Division of Clinical Pathology, Medical College of Virginia.

Drug Usage in a Medical Ward

JAMES B. BLITCH (M-70)
JEFFREY BIENER (M-71)

Drugs are an essential part of medical therapy and their use has increased rapidly in recent years. Their benefits are obvious. Nevertheless, the physician must be ever aware of their hazards. A six week drug study under the direction of A. J. Wasserman, M. D. was conducted in order to assess the use of drugs in a general medical ward. Drug sheets containing information about dosage, route, instructions, indications, discontinuation and side effects were kept for every drug order for each patient during the entire six weeks. Data was collected by two medical students who accompanied the house staff on daily rounds and questioned each doctor about his patients' medications. This study included 85 patients with a total of 884 drug sheets. There was a mean of 10.5 ± 8.2 S.D. drug sheets per patient with a range of 1 to 47, and a mean of 6.3 ± 3.7 S.D. drugs per patient with a range of 1 to 22. 13% (11 out of 85) of the patients had side effects (this result is similar to that obtained in other drug studies on side effects). There was no statistically significant correlation between side effects and age, sex, number of drugs per patient or number of days in the hospital. However, a correlation between side effects and number of days in the hospital may have existed although it was not statistically significant in this study. In addition, only 5% of the drugs were discontinued because they were effective and no longer necessary. 15% of the drugs were continued at time of discharge, and 8% were discontinued at time of discharge. These figures cast doubt on the efficacy of drugs being employed. Concerning route of administration, 52% were p.o., 17% I.M., 5% S.C. and 20% I.V. 20% I.V. is a surprising high figure. Tabulation of instructions for drug usage revealed 48% standard orders, 10% p.r.n. and 40% stat. That 40% of the orders were stat is again a surprising figure.

Preceptor: ALBERT J. WASSERMAN, Division of Clinical Pharmacology, Medical College of Virginia.

Acquired Absence of Alpha Lipoproteins and Acanthocytosis in Severely Burned Patients*

MARVIN ZELKOWITZ (M-70)

Severely burned patients develop decreased to absent alpha lipoprotein (LP) and concomitant “burr shaped” RBC. In serial observations of all hospitalized burn patients, only one of 13 having more than 30% body burn did not develop decreased alpha LP during the first to the tenth week after the burn, the onset depending on the severity of the burn. The beta LP and other lipid measurements tended to be low, although two patients had increased beta LP. Acanthocytic RBC (30–90%) were found in each patient with absent alpha LP, and the findings were temporally related. Patients with less than 30% total body burn did not develop either abnormality. Neither septicemia, hepatic failure, or renal failure could be incriminated. Preliminary studies of the lipid content of RBC membranes from acanthocytic cells suggest that the phospholipid content is less than that of normal RBC, but the cholesterol content is unchanged, as is the distribution of RBC phosphatides. We suggest the following sequence: alpha LP weep through the damaged skin in amounts exceeding synthetic capacity; the RBC phosphatides which are in equilibrium with the plasma phosphatides are leached from the cells.
altering membrane lipids and membrane structure with a resultant change in shape. Thus, an alaphalipoproteinemia developing after a severe burn can be associated with burr-cell formation, perhaps because of membrane lipid changes. These findings contrast with the absence of morphologic RBC changes in hereditary an-alaphalipoproteinemia (Tangier Disease) and provide another facet to the association between LP and acanthocytosis.

Preceptor: William R. Harlan, Jr., Clinical Research Center, Medical College of Virginia.


Proteinuria and Glomerular Lesions in Rats Induced by Sera from Human Renal Transplant Recipients

R. C. Smallridge (M-70)  
D. B. Waldman (M-72)

Glomerulonephritis appears to be due to a variety of factors, one of which may be circulating antibodies to glomerular basement membrane. Since some kidney transplant recipients develop massive proteinuria, a model was established to see if kidney lesions could be produced in experimental animals by inoculations of serum from patients with recurrent proteinuria. Sera (5-8 cc.) taken after transplant rejection from 5/7 transplants produced no proteinuria or histologic changes in the kidneys of unilaterally nephrectomized rats. One patient's serum produced massive proteinuria of 36.6 mg./24 hrs. and 127 mg./24 hrs. in two rats. (control rats averaged 8 mg./24 hrs.) No significant changes were observed on microscopic examination. The serum and acid eluate from the kidney of another patient produced glomerular lesions with obliteration of Bowman's space, thickening of the glomerular vasculature, increased cellularity, and the deposition of PAS positive material in the region of the glomerular basement membrane. We conclude that transferrable serum factors present in some patients with glomerulonephritis are even pathogenic in rats. Thus far, we have seen two different effects: (1) massive proteinuria, and (2) obliteration of glomeruli without significant proteinuria. It is possible that this type of bioassay will help in determining which patients have a high risk of recurrent glomerulonephritis following transplantation, and, more important, that it will distinguish types of glomerulonephritis.

Preceptor: G. Melville Williams, Department of Surgery, Medical College of Virginia.