the superficial injury the absence of glycogen could be attributed to heightened epithelial activity which precluded an accumulation of glycogen in the prickle cell layer. An alternate reason for the absence could be that not enough glycogen was available for storage due to the discontinuity of the epithelium and connective tissue as shown by the absence of the basement membrane.

In the healing of the deep wounds, the accumulated glycogen was not used for there was no activity of the epithelium as shown by the complete lack of granules.

Summary. Morphological healing in the oral mucosa as indicated by hematoxylin and eosin preparations precedes histochemical healing. Epithelial proliferation in wound healing appears to be associated with the disappearance of glycogen. Lack of epithelial growth appears to be manifested by an accumulation of glycogen. The metabolism of the epithelial basal cells as indicated by the presence of succinic dehydrogenase appears to be related to epithelial and connective tissue continuity. Its presence in the basal cells of the epithelium confirms that metabolic activity is highest where there is no visible glycogen. Injury to the epithelium of the mucous membrane causes glycogen accumulation similar to that in skin. Succinic dehydrogenase is distributed in the mucous membrane of the anterior palate of the rat much as it is in the skin.

We gratefully acknowledge the technical assistance of Miss Audrey Feldman.

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Received June 28, 1962. P.S.E.B.M., 1962, v111.

Effect of Acute Pulmonary Artery Constriction on the Form of the Indicator-Dilution Curve.* (27923)

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Indicator-dilution curves are of value in detecting valvular insufficiency; however, these curves have not proven as useful in the diagnosis of valvular stenosis because such lesions do not always produce predictable changes(1,2). An opportunity recently presented itself(3) to evaluate the effects of experimental pulmonary artery constriction on the form of the indicator-dilution curve. These observations, in addition to delineating the effect of acute pulmonary artery constriction, may suggest an explanation for the inconsistent effects of stenotic lesions on the form of the indicator-dilution curve.

Method. The experimental preparation utilized has been described(3). Briefly, a ligature was placed around the base of the pulmonary artery of the anesthetized dog. This ligature was attached to a calibrated screw device so that tightening the instrument reduced the size of the loop. The size of this loop for each setting was known. In addition, these measurements were checked at the conclusion of the experiment by *in situ* measurement. Indicator-dilution curves were recorded and the ligature was loosened to permit return to control conditions. The procedure was then repeated with increasing degrees of constriction until right ventricular failure occurred as indicated by a marked

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drop in systemic blood pressure and rise in right ventricular diastolic pressure. Tricarbocyanine dye (Cardio-Green®)§ was used as the indicator. This was injected into the right atrium using a standard technic(4). Blood was withdrawn from the femoral artery through a Colson densitometer and the dilution curves were recorded with an Electronics-for-Medicine recorder. Respiration was interrupted during each recording. Heparin was used as the anticoagulant.

Results and discussion. 58 Indicator-dilution curves were obtained from 6 animals during various degrees of pulmonary artery stenosis. Each animal served as its own control. A typical curve, labeled to show the parameters measured in this study, is shown in Fig. 1. The descending limb of the curve was extended to the base line by extrapolating the slope using a semilog plot. The alterations in the form of the curve produced by increasing degrees of pulmonary artery constriction are shown in Fig. 2. These curves, which are typical of those obtained in all experiments, were recorded from the same animal and have been redrawn to a common origin. The appearance time, build-up time and decay time for each curve decreased with mild pulmonary artery constriction, then increased with more severe degrees of stenosis. The degree of constriction necessary to cause the reversal in these values varied with each experiment. The peak concentration of indicator, however, always decreased with increasing degrees of constriction of the pulmonary artery.

An explanation for this pattern of indicator-dilution curves can be formulated from the dynamics of pulmonary artery constriction. The form of an indicator-dilution curve recorded from a multi-chamber system is theoretically controlled by the residual volume of the system and the flow volume into which the indicator mixes(5,6). It has been shown that mild degrees of pulmonary artery stenosis produce a slight increase in cardiac output(3,7) without change in right ventricular diastolic pressure(8). The increased output in these experiments is apparently due to reflex stimulation of the right ventricle

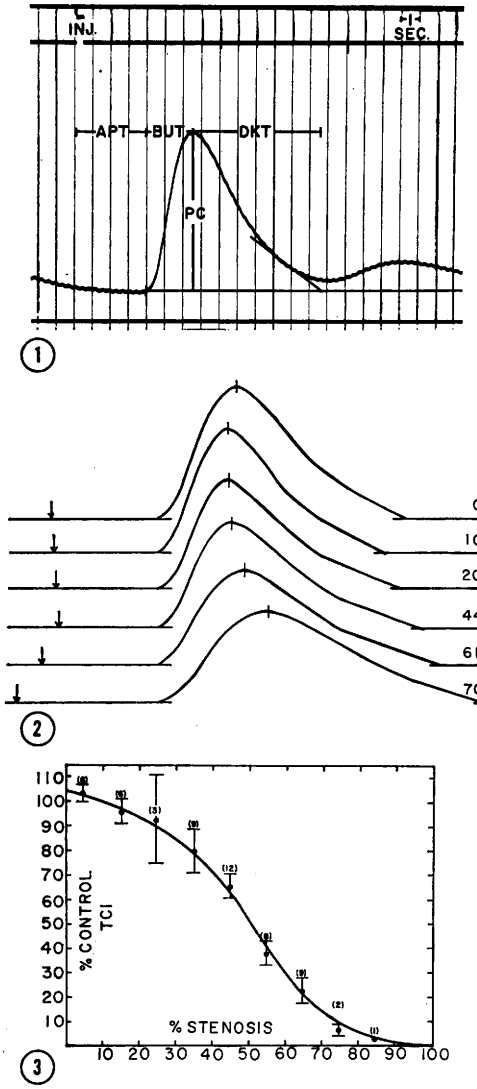

FIG. 1. Indicator-dilution curve recorded from femoral artery. APT is appearance time; BUT, build-up time; DKT, decay time. PC is peak concentration. Indicator injected into right atrium at signal mark.

FIG. 2. Series of indicator-dilution curves from the same animal with varying amounts of pulmonary artery stenosis redrawn to a common origin. Arrows indicate time of injection of indicator and small vertical line the point of peak concentration for each curve. Reduction in lumen of the pulmonary artery indicated in %. See text for discussion.

FIG. 3. Average time concentration index (TCI) as % of control plotted against % stenosis of pulmonary artery. Vertical lines indicate standard error of mean. Figures are number of observations for each point.

§ Supplied by Hynson, Westcott & Dunning, Baltimore, Md.

with greater cardiac emptying(7,9). This suggests that the residual volume of the right ventricle is decreased and the flow volume is increased. More severe constriction causes the right ventricular diastolic pressure to rise(7) and cardiac output to fall(3,8). This is consistent with a drop in flow and increase in residual volume.

Using this method of analysis, the amount of indicator ejected per beat through the constricted area of the pulmonary artery in our experiments would be directly related to (A) amount of indicator in the right heart and (B) ratio of the total right ventricular volume to the right ventricular residual volume (5,6). Under the dynamic conditions described for mild pulmonary artery constriction, the indicator should be "washed out" of the heart at a more rapid rate than normal. The finding of an earlier appearance time and shorter build-up and decay time in our records is consistent with this concept. With more severe occlusion of the pulmonary artery, the total amount of indicator ejected per beat by the right ventricle will be expected to be less than normal. Again this is in keeping with the finding of a prolonged appearance, build-up and decay time.

This analysis suggests that the form of the indicator-dilution curve recorded in the presence of pulmonary artery stenosis is dependent on degree of cardiac compensation as well as severity of the lesion. This may explain some of the difficulties encountered in using indicator-dilution curves to assess the extent of valvular stenosis.

To achieve a simple expression for the changes in the form of the indicator-dilution curve, an arbitrary time concentration index (TCI) was established by dividing the peak concentration by the product of appearance time, build-up time and decay time. The value of such an empirical expression is illustrated by the following procedure. The TCI index for each curve was expressed as per cent of the control value for that animal. The results were arranged in groups according to the amount of pulmonary artery constriction. The class interval for each group was a 10% reduction in the cross-sectional area of the pulmonary artery. The mean TCI for each of these groups, plotted against per cent of pulmonary artery stenosis is shown in Fig. 3. When this general relationship between TCI index and amount of stenosis present is known, the degree of constriction represented in any given curve can be identified within reasonable limits.

Summary and conclusions. Indicator-dilution curves were recorded from dogs with various degrees of acute pulmonary artery constriction. Time requirements for the various parts of the indicator-dilution curve decreased with mild pulmonary artery constriction and increased with more severe reduction in the lumen of the pulmonary artery. Peak concentration decreased with increasing constriction. These changes are consistent with the theoretical considerations of the genesis of indicator-dilution curves and the dynamics of pulmonary artery constriction. It is suggested that the form of the indicator-dilution curve is dependent upon degree of cardiac compensation as well as severity of the constriction. A time concentration index (TCI) was established for the curves. The per cent change in this index from control gives a sigmoid relationship when plotted against per cent reduction in cross-sectional area of the pulmonary artery.

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Received July 11, 1962. P.S.E.B.M., 1962, v111.