which were quiescent before carbon dioxide administration was begun.

Hyperventilation of the mother with the aid of a respiratory pump resulted in slowing of respiration or complete apnea in the foetus. Upon suspension of artificial respiration the foetuses remained for several minutes in a state of respiratory quiescence but subsequently resumed their original rate.

On the basis of these studies we regard the onset of post-natal respiratory activity not as an event initiated abruptly at birth but rather as a transition from the type of respiratory movement discernible during intrauterine life. Our observations do not lend support to the view of Barcroft[6, 7] that the first breath of a new-born is caused by oxygen want. On the contrary, a diminished supply of oxygen depresses foetal respiration in the rabbit. In agreement with the results of Barcroft the foetus appears to be quite unresponsive to excess of carbon dioxide introduced through the mother. On the other hand a certain minimal carbon dioxide tension seems to be essential for the maintenance of foetal respiratory function.

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Ineffectiveness of Drugs upon Collateral Coronary Flow.*

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Valid experimental evidence as to whether a drug can improve collateral coronary blood flow to an ischemic area is difficult to obtain. Observation of color changes or comparison of size of infarcts without and with use of a drug are subject to too many contingencies to have a certain value. Observations as to the effects of drugs upon coronary inflow and outflow do not test the response of collateral vessels and ignore the hemodynamic alterations resulting from occlusion of the main branch.

We therefore studied the reliability of 4 other possible criteria of

[6] Barcroft, J., *Lancet*, 1935, **229**, 647.

[7] Barcroft, J., XV Internat. Physiol. Congress, Leningrad-Moscow, 1935, 21.

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changes in collateral flow, *viz.*, (1) changes in rate of blood flow from a peripheral coronary ramus; (2) alterations in mean peripheral coronary pressure; (3) changes in inflow rate at high perfusion pressures before and after use of drugs—the latter being administered during a period when the area was not perfused; and (4) the ability of drugs given by inhalation or intravenously to prevent contractile failure after ligating a ramus or of restoring such contractions in an ischemic area. The first and second of the methods cannot be used as criteria. The third method also proved to be no criterion of changes in collateral flow alone but is useful because the flow changes are a *resultant* of vascular and extravascular factors which modify resistance to flow.

The following results were obtained: 1. Drugs of the theobromine and theophylline group have a very insignificant effect on collateral flow to an ischemic region. 2. The nitrite group cause a slight decrease in coronary resistance within the ischemic area but it appears more probable that this is due to attendant reductions of intraventricular tension rather than to effects of drugs reaching the vessels of an ischemic area. At any event this slightly beneficial action is more than offset by the fact that the driving pressure in larger collateral vessels in the left ventricle is reduced. 3. Pressor drugs such as epinephrine and synephrine consistently increase resistance to flow in the ischemic area. If these drugs exert a dilating vascular action on collateral vessels it is overpowered by greater extravascular pressures in intact hearts.

The fourth method offers conclusive evidence as to whether collateral blood supply increases to a degree to be of functional use. This is ultimately the important question. Our results show that the abolition of contraction about one minute after occlusion of the ramus descendens anterior is not modified in the least by inhalation of oxygen, CO_2, amyl nitrite, nor by therapeutic intravenous doses of various theophylline preparations, nitrites, adenylic acid or epinephrine.

The conclusion is reached that an increase in collateral circulation sufficient to be of functional use cannot be attained by use of vasodilating drugs after complete coronary occlusion.