Fig. 1

When cytochrome c is treated with sodium formaldehyde sulfoxylate ($CH_2OHOSONa$) the band at 3500 Å disappears and a new band appears at about 3100 Å, as depicted in Fig. 1b. At the same time the well characterized band of reduced cytochrome c becomes apparent in the visible at 5500 Å. Experiments are now in progress to determine the possible reversibility of this process and the complete significance of the above data is being further investigated.

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A Technique for the Perfusion of the Foetal Placental Circulation.*

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Investigation of the various factors which control the placental circulation has necessarily been limited owing to the experimental difficulties involved. It is suggested that the following technic may offer a line of approach to some of the problems involved.

Methods. The experimental animals used were cats or bitches which were in an advanced stage of pregnancy. Rabbits were found to be unsuitable owing to the friability of the placental vessels. Anesthesia was induced with open ether, and maintained with chloralose given intravenously in a dose of 100 mg/kilo body weight. Both vagi were cut, and the carotid blood pressure recorded by means of a mercury manometer. The abdomen was opened with as short an incision as was compatible with adequate access, and a part of the uterus containing one foetus brought up into the wound. A small cork platform approximately 5 cm square was approximated to the section of uterus exposed, and the uterine peritoneum loosely

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stitched to the two nearest corners of the platform with silk ligatures. An incision about 2 cm long was then made through a part of the uterine wall which was free of placental attachments, the membranes ruptured, and the hind-quarters of the foetus delivered until the umbilical cord came into view. If the foetus was lying in a favorable position, it was possible to expose the umbilicus with the umbilical vessels without delivering any part of the foetus. The umbilical cord was then ligatured in 2 places as close to the umbilicus as possible, divided, and the placental end delivered through the wound in the uterine wall. Thereafter the foetus was replaced within the uterus and the uterine wall stitched up again, leaving only the free end of the umbilical cord protruding. With practice it was possible to perform this operation without any appreciable loss of amniotic fluid, so that the intrauterine pressure was not materially altered.

The vessels of the cord were cleaned, a cannula was inserted into the umbilical artery and perfusion of the placental circulation immediately started by means of a small Dixon pump. The perfusion apparatus was the same as was used by Robson and Schild.[1] Another cannula was rapidly inserted into the umbilical vein to collect the perfusion fluid and thus prevent distention or clotting within the placental circulation.

The inflow perfusion pressure was recorded on the kymograph by a mercury manometer. The blood passing from the pump to the umbilical artery was kept at body temperature by passing the rubber tubing, which connected the two, through the heating apparatus of the operating table. The venous return from the umbilical artery was allowed to flow by gravity through the cannula and rubber tubing to the reservoir of the pump. The dead space of the perfusion apparatus (about 20 cc) was filled either with saline or with blood taken from the maternal circulation. Coagulation was prevented by means of repeated additions of heparin to the contents of the reservoir. Approximately 4 mg of heparin dissolved in 1 cc Ringer-Locke solution were required every half to one hour. The cannulae were maintained in position by skewering them to the cork platform, and this insured that there was no kinking of or traction upon the umbilical vessels.

The contractions of the part of the uterus containing the foetus were simultaneously recorded by means of a Cushny myograph. By the use of a small celluloid window and pads of cotton wool, the abdominal contents were maintained at a normal body temperature.

The minute volume of the circulation in the full-term foetus has been estimated to be of the order of 0.1 cc/g weight of the foetus in

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[1] Robson, J. M., and Schild, H. O., *J. Physiol.*, 1938, **92**, 9.

goats (Barcroft, *et al.*[2]). The weight of the foetus of the cat in the later stages of pregnancy is about 50 g. In order to insure an adequate blood flow through the placenta the Dixon pump was adjusted to deliver about 8 cc/min., and at this rate the perfusion pressure was usually approximately 80 mm Hg.

At the end of each experiment the adequacy of the perfusion was checked by injection of methylene blue into the venous cannula, and subsequent examination of the placenta. In all cases it was found that the perfusion had been satisfactory.

Results. When 1 μg of acetyl choline was injected intravenously into the maternal circulation it cause a small and transitory fall in the maternal blood pressure, but had no effect upon either the uterine contractions or the perfusion pressure. Ten μg caused a greater fall in the maternal blood pressure, but again did not affect either uteri contractions or perfusion pressure. When 1 μg of acetyl choline was injected into the arterial cannula of the perfusion system, a slight and transitory rise occurred in the perfusion pressure, and this effect was greater and more prolonged when the amount of acetyl choline injected was increased to 100 μg. In neither case was there any demonstrable effect upon either the uterine contractions or the maternal blood pressure.

Adrenalin was injected into the perfusion system in doses of 1 to 100 μg. In one experiment a sustained rise in perfusion pressure followed the injection of 10 μg of adrenalin, but in none of the other experiments did the administration of the drug produce any effect on the perfusion pressure, the maternal blood pressure, or the uterine contractions.

0.1-1.0 unit pituitary (posterior lobe) extract injected into the maternal circulation caused a prolonged rise in the maternal blood pressure, and an increase in both the rate and the amplitude of the uterine contractions, with a consequent increase in the rate and amplitude of the variations in the perfusion pressure. This is illustrated in Fig. 1. When 1 unit was injected into the perfusion system it caused a sustained rise in perfusion pressure, with, in one case, an increased rate of uterine contractions. In no case was any effect on the maternal blood pressure noted.

A constant observation in these experiments was that cyclical variations in perfusion pressure occurred synchronously with the uterine contractions. This is in contradistinction to the findings during artificial perfusion of the maternal-uterine circulation, where uterine tone and motility have no appreciable effect upon the perfusion pressure (Robson and Schild[1]).

[2] Barcroft, J., Kennedy, J. A., and Mason, M. F., *J. Physiol.*, 1939, **95**, 269.

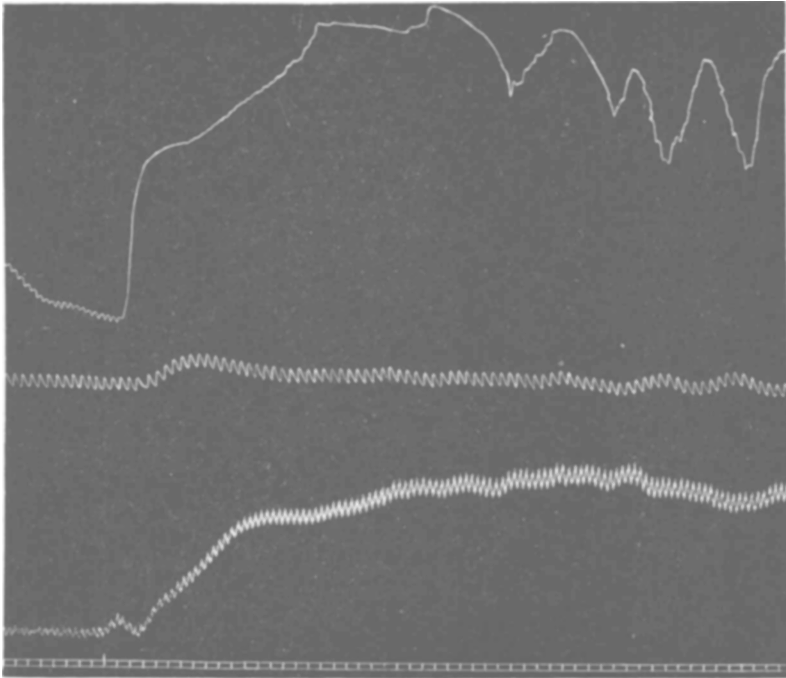

FIG. 1.

Cat Sb 38. Upper tracing: Uterine contractions. Middle tracing: Perfusion pressure. Lower tracing: Maternal blood pressure. Signal: 1 unit pituitary (posterior lobe) extract injected intravenously into maternal circulation. Time intervals: 1 min.

In addition to these variations in perfusion pressure it was also observed that the return of blood from the placenta into the reservoir of the perfusion pump was not a continuous flow, but was at a maximum during the period of uterine relaxation and during the early part of a contraction, and then sharply decreased as the contraction developed. These results suggest that uterine tone and motility may play a part in aiding the return of blood from the placenta during the later stages of pregnancy. The results also offer evidence that the blood flow through the foetal placenta is markedly decreased by the contractions of the uterus.

Clark[3] found that during uterine contractions there occurred a transient rise followed by a fall in the foetal blood pressure, and ascribed the fall to a reduced venous return from the placenta to the heart. This is in agreement with our own results on the return of blood from the placenta during uterine contractions.

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[3] Clark, G. A., *J. Physiol.*, 1932, **74**, 391.