olfactory placode on the operated side. In series 3 large pieces of the fore-brain of stage 20 median to and almost on a level with the optic vesicle were used. Of the 8 embryos operated on 5 had definite olfactory invaginations appearing in the flank region. Two of the 5 showed well developed olfactory canals connecting with the invaginations. In all cases the olfactory placode on the operated side was missing or rudimentary.

In all of the cases the head ectoderm on one side was lifted up, the required portion of the brain (including the proximal end of the optic vesicle in most cases) was removed, and the head ectoderm was replaced. The piece of brain tissue was transplanted underneath the ectoderm of the flank region of the same embryo. The embryos were sectioned after 3 or 4 days of development.

Some evidence has been obtained which indicates that the olfactory placode is determined in the head ectoderm some time between the late neurula and early tail-bud stages. In series 4 the brain tissue was removed in stages 20, 22 and early tail-bud and the head ectoderm was replaced. No olfactory placode developed except in the case of the early tail-buds. In this stage the placode is already visible and so the removal of the brain does not interfere with its continued differentiation.

Removal of the presumptive olfactory placode in stages 17, 20 and 22 resulted in the formation of an olfactory placode from the ectoderm which healed over the wound. Even after the placode has formed in the early tail-bud stage a second one will form after extirpation. This may be due to a re-induction of an olfactory placode by the brain and not a regeneration as claimed by Bell and by Burr.[2]

7381 P

Measurement of Circulation Time from Antecubital Veins to Pulmonary Capillaries.

WILLIAM M. HITZIG.* (Introduced by B. S. Oppenheimer.)

From the Medical and Laboratory Services, The Mount Sinai Hospital, New York City.

Several methods are available for measuring the circulation time from the antecubital veins through the pulmonary bed to the capil-

2 Burr, H. S., *J. Exp. Zool.*, 1916, **20**, 27.

*Eugene Meyer, Jr., Fellow in Pathology.

laries of the systemic circuit. One method is the decholin method proposed by Winternitz, Deutsch, and Bruell,[1] and recently studied by Tarr, Oppenheimer and Sager.[2] Another is described by Fishberg, Hitzig, and King,[3] in which saccharin injected into an antecubital vein is detected in the tongue. No method has been devised clinically applicable for measuring circulation time from the peripheral veins to the capillaries of the lung. This may be obtained by introducing ether into an antecubital vein and determining the time that elapses before the patient perceives its odor. Ether is peculiarly adapted to this purpose because: 1. Its volatility at blood temperature is so great that when a small quantity is injected, a sufficient amount volatilizes in the pulmonary capillaries during the first circuit of the blood to be invariably perceptible by smell. 2. The small volume needed permits rapid intravenous introduction, the advantage of this being that it will flow in a small blood volume, resulting in a sharp definition of both the time of injection and the time of arrival in the pulmonary capillaries. 3. It is harmless in the quantities used. In over 200 injections, no untoward constitutional reactions were encountered. The subject is usually aware of a "creeping" feeling along the course of the vein. About 25% of the patients complain of transient pain in this location. In 28 cases in which the veins were carefully followed, thrombosis developed on 3 occasions. Paravenous infiltration causes no necrosis. In many instances, the measurement was carried out 2 and even 3 times within a few minutes without causing unpleasant reactions. 4. Because of its volatility, the measurement can be repeated as soon as desired.

The determination is performed in the following manner: The individual reclines comfortably with his arm at a level corresponding to the right auricle. He is familiarized at first with the odor of ether. He is then instructed to breathe normally, and to announce when he smells the ether. A mixture of 5 minims of ether and 3 minims of normal saline is rapidly injected into a large antecubital vein, only a fraction of a second being required. The end-point is sharp and unmistakable. Moreover, an observer, in a position close to the subject, can perceive the ether odor almost as rapidly as the patient. This objective confirmation, valuable as it is of itself, becomes of especial importance when studying unconscious patients. To obtain results which will check closely on repetition,

1 Winternitz, M., Deutsch, J., and Bruell, Z., *Med. Klin.*, 1931, **27**, 986.

2 Tarr, L., Oppenheimer, B. S., and Sager, R. V., *Am. Heart J.*, 1933, **8**, 766.

3 Fishberg, A. M., Hitzig, W. M., and King, F. H., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 651.

the subject must be told to relax and not to hold his breath during the procedure, for this retards the venous return to the heart. Similarly, hyperventilation will hasten the venous return and accelerate the circulation time.

The measurement was performed on 152 individuals, most of whom were hospital patients suffering from various conditions. The end-point was definite in practically every case, an occasional reading only requiring repetition. In 100 "normal" subjects, without evidence of circulatory disturbance, the circulation times showed the following distribution:

Circulation Time (sec.)	Number of Individuals
3½-3¾	7
4 -4¾	32
5 -5¾	27
6 -6¾	23
7 -7½	8
7¾-8	3

Repeated injections checked closely.

In view of the rapid rate of diffusion of a light gas in a gaseous mixture, it may be assumed that the time required for the ether to rise from the pulmonary alveoli to the nasopharynx is negligible in comparison to the actual circulation time.

The "ether time" is thus a measure of the circulation time from the antecubital vein to the capillaries of the lung. It is interesting to compare this circulation time with the "saccharin time", which is a measure of the speed of the circulation from the antecubital vein through the lungs to the capillaries of the tongue. The percentage relationship of "ether time" to "saccharin time" in 27 "normal" individuals showed the following variations:

Ether Time Expressed as % Saccharin Time	Number of Individuals
33-39	4
40-49	15
50-59	6
60-66	2

In a number of the cases studied, thrombosis developed following the consecutive injection of ether and saccharin into the same vein at the same sitting. Consequently, pending further study of the mechanism of such thrombosis, this procedure is not advocated.

The study has shown that in certain varieties of heart failure, the ether circulation time is considerably prolonged. The comparative study of the "ether" and "saccharin time", in various types of heart failure, is of value in localizing the portion of the circulation in

which blood flow is retarded. Thus there are instances of left heart failure, in which the "ether time" is within normal limits while the "saccharin time" is much prolonged. This shows that in these cases the retardation of the blood flow is downstream to the arterial capillaries of the lung.

7382 C

Intermediate Products of the Propionic Acid Fermentation.

H. G. WOOD AND C. H. WERKMAN.

Department of Bacteriology, Iowa State College, Ames, Iowa.

The dissimilations brought about by the propionic acid bacteria have received relatively little study. Phosphorylation appears to be a normal process with the intermediate formation of a hexose-monophosphate.[1] Methylglyoxal has been reported by Pett and Wynne[2] and Wood and Werkman have recently identified pyruvic acid[3] and a non-reducing carbohydrate[4] as intermediate products in the fermentation of glucose by *Propionibacterium arabinosum.* Virtanen[5] proposed the occurrence of lactic acid but was unable to detect its presence. Foote, Fred and Peterson[6] have reported the occurrence of lactic acid in the propionic acid fermentation. The intermediate mechanism leading to propionic acid is unknown. The fermentation of glycerol offers an opportunity of studying this phase. In this remarkable fermentation, glycerol is converted under anaerobic conditions practically quantitatively into propionic acid. No gas is produced (van Niel[10]).

To detect intermediate compounds the following medium was fermented: Yeast extract (Difco) 0.5%, glycerol 2.0%, and calcium carbonate 2.0%. Calcium sulfite (1.0%) was included in the medium as a fixing reagent. *P. arabinosum* was the species employed. The fermentation took place under anaerobic conditions at 30°C. After 5 or 6 days' incubation, the fermentations were tested for

1 Virtanen, A. I., and Karstrom, H., *Acta chem. Fennica,* 1931, series B, **7**, 17.

2 Pett, T. B., and Wynne, A. M., *Trans. Roy. Soc. Canada,* 1933, **27**, 119.

3 Wood, H. G., and Werkman, C. H., accepted for publication, *Biochem. J.*

4 Wood, H. G., and Werkman, C. H., *J. Biol. Chem.,* 1934, **105**, 63.

5 Virtanen, A. I., *Soc. Acta. Fennica, Comment. physico.-math.,* 1923, **1**, 36; 1925, **2**, 20.

6 Foote, Marion, Fred, E. B., and Peterson, W. H., *Centr. Bakt.,* 1930, 2 abt., **82**, 379.