Those expiring within 10 minutes following intravenous paraldehyde had massive diffuse pulmonary hemorrhage and dilatation of the right heart. When death occurred 6 to 24 hours after anesthesia, acute pulmonary edema was evident. Animals recovered from anesthetic doses looked poorly. After one week autopsy revealed multiple pulmonary hemorrhages. Histo-pathological changes in other viscera were also observed. A further investigation of these is in progress.

Other observations during this study were directed toward respiratory and circulatory reactions.

In accord with clinical reports the respiratory rate was increased. Immediately after intravenous injection of paraldehyde there was often an apnea for several seconds. This was followed by rapid, shallow respirations; the rate increasing from 16-20 to as much as 120 per minute. Coughing was observed frequently and cyanosis was noted which became progressively more intense.

With doses producing anesthesia there was a prompt decrease in arterial blood pressure and an accelerated pulse rate. Even in animals which survived 12 to 24 hours, there was an immediate fall in the arterial blood pressure of more than 50%.

Conclusion. The intravenous administration of paraldehyde as recommended for clinical anesthesia is not without danger. In experimental animals there is a narrow margin of safety (Minimum Anesthetic Dose-Minimum Lethal Dose). Massive diffuse pulmonary hemorrhages and dilatation of the right heart occur when animals are killed with minimum lethal doses. Pulmonary hemorrhages are present in animals having recovered from anesthetic doses.

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Metabolism in Perfused Dog's Head During Sodium Pentobarbital Depression ann Metrazol* Stimulation.

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Previous studies on the effects of central nervous system depressants on brain metabolism have been largely confined to *in vitro* measurements of the oxygen consumption of minced brain tissue or

* Metrazol was supplied by the Bilhuber-Knoll Corporation.

slices (Quastel[1]). Determinations of the arterio-venous oxygen and glucose differences of cerebral blood in intact dogs after sodium pentobarbital administration indicated that the uptake of both were significantly reduced during depression. When pentamethylenetetrazol (metrazol) was then administered to the depressed dogs the oxygen and glucose uptakes by the brain were increased or restored to normal.[2] These measurements were possibly complicated by changes in blood flow and thus did not actually indicate the metabolism. Perfused dog head experiments suggested a method for making true metabolism studies.

The perfusions were made with a Dale-Schuster double pump.[3] One unit of the pump was used to perfuse isolated lungs for oxygenating the blood. The head was perfused with the other unit by cannulating the common carotid artery and external jugular on one side, starting the pump and then cannulating the vessels on the other side. By using this technic, the blood flow to the head was not interrupted at any time. Venous blood samples were obtained from the previously exposed superior sagittal sinus. Arterial samples were taken from a common carotid artery. Oxygen content of the samples was determined according to the method of Van Slyke and Neill,[4] glucose by the method of Hagedorn and Jensen.[5] After control blood samples had been taken, sodium pentobarbital was administered. Five minutes later samples were again taken. Metrazol was then administered and the third set of samples were taken after

TABLE I.
Glucose and Oxygen Uptake by the Brain in Perfusion Experiments.
Uptake in cc of oxygen and mg of glucose per minute.

Exp.		Control	Pentobarbital	Metrazol	Pentobarbital
1	Oxygen	24.7	16.9	19.3	14.8
	Glucose	16	9	15	11
2	Oxygen	15	9.5	13.2	—
	Glucose	18	11	20	—
3	Oxygen	17.3	12.3	27	16
	Glucose	21	6	30	7
4	Oxygen	24.7	18.4	20.4	—
	Glucose	39	22	36	—
5	Oxygen	13.5	7.3	19.2	14.5
	Glucose	9	6	16	2

[1] Quastel, J. H., *Physiol. Rev.*, 1939, **19**, 135.

[2] Handley, C. A., and Sweeney, H. Morrow, *Am. J. Physiol.*, 1941, **133**, 314.

[3] Brookman, Bruce T., and Sweeney, H. Morrow, *Am. J. Physiol.*, 1941, **133**, 226.

[4] Van Slyke and Neill, *J. Biol. Chem.*, 1924, **61**, 523.

[5] Hagedorn and Jensen, *Biol. Chem. Z.*, 1923, **135**, 46.

a similar interval. The amounts of the drugs added to the perfusion blood were of the order of 10^{-4} molal. The blood flow was determined at the time the samples were collected by measuring the return flow in a graduated cylinder.

Table I, representing 5 perfusion experiments, shows that following sodium pentobarbital both the glucose and oxygen uptake by the brain was reduced. Following metrazol administration these figures were again increased to about the control levels. It will be noted that the uptake values after metrazol were appreciably greater in 2 of the experiments (3 and 5) than the control values. The probable explanation is that the dogs were given sodium pentobarbital in preparing them for the perfusion and although blood from unnarcotized animals was used for the perfusion, enough narcotic was present in the perfused head to produce some depression at the beginning of the experiment. In some of the experiments, a second injection of the barbiturate was given after the metrazol. The uptake values were again reduced by this procedure. The results of these experiments indicate that barbiturate narcosis inhibits metabolism in the brain, while metrazol has a tendency to reverse this effect.

The corneal reflex served as a guide to the degree of depression in the perfused head. It was present at the beginning of the perfusion, depressed or absent after sodium pentobarbital administration and restored by metrazol.

Summary. The results of perfused head experiments show that during sodium pentobarbital depression there is a measurable reduction in both oxygen and glucose utilization. Metrazol administered during this depression returns the utilization of both to about the control levels or beyond.

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A Chemotherapeutic Agent with Osteotropic Properties.

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In a search for chemotherapeutic agents with specific osteotropic properties, a study was made of the general mechanism of drug fixation in bone. It has been shown in previous studies[1] that the fol-

[1] Ercoli, N., *Kongressberichte des XVI Internationalen Physiologenkongresses*, Zürich (Switzerland), 1938.