where p is the reciprocal of the osmotic pressure and v the reciprocal of the concentration of the proteins, that is, when the proteins decrease in arithmetical progression, the osmotic pressure decreases in geometric progression.

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Pupillary Reactions During Ether and Chloroform Anesthesia After Morphine.

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In the course of anesthesia by ether and chloroform in the dog, the pupil dilates at 2 stages, in the period of excitement and in the period of deep narcosis. If there is violent excitement the intermediary constriction is not observed. It is commonly held that the primary dilatation is a reflex phenomenon (inhibition of the oculomotor or stimulation of the sympathetic or both). There is no clear statement, however, whether the dilatation of the pupil in the stage of deep narcosis is the result of asphyxia or the direct effect of the anesthetic. While studying the response of the vagus nerve to morphine during ether and chloroform anesthesia, it was observed that in deep ether narcosis, the pupils of the dog under the influence of morphine were widely dilated, while in deep chloroform narcosis under the same conditions, the pupils were constricted. These observations seemed of interest in their bearing upon the mechanism of the pupillary changes produced by ether and chloroform. Twelve experiments were then performed to check and extend these observations and the results are the subject of the present report.

Ether and chloroform were administered by inhalation with the open cone method. The pupils were measured under constant conditions of light for any given experiment. Both eyes were examined; the pupils were found equal in all except one instance. Electrocardiographic records of the heart rate were taken at frequent intervals, making it possible in this way to correlate simultaneous effects upon the vagus and oculomotor nerves. The condensed protocols of the experiments with 2 dogs serve to illustrate the general results. The size of the pupils is expressed in percentage of the diameter of the iris. The stage of anesthesia is designated as "light" when voluntary movements as well as corneal conjunctival reflexes are present; as "deep" when these have disappeared; as "partial re-

covery" when the eye reflexes have reappeared; as "recovery" when voluntary movements begin.

PROTOCOL I. Dog, male, weight 11.2 kg.

Time	Size of pupil	Heart rate	Stage of anesthesia	Remarks.
3:18	40	—	—	Chloroform started.
3:20	90	—	Light	Violent struggling.
3:23	90	—	Deep	Resp. nearly ceased; chloroform withdrawn.
3:30	40	—	Part. Rec.	Ether started.
3:32	90	—	Light	Moderate struggling.
3:34	90	—	Deep	Ether withdrawn.
3:37	70	—	Part. Rec.	10 mg. morphine sulphate per kg., muscle.
3:45	5	64	—	Panting at 200 per min.; winks; enophthalmus; chloroform started.
3:48	5	60	Deep	No struggling; resp. nearly ceased, Cheyne-Stokes; tongue cyanotic; enophthalmus; chloroform withdrawn.
3:58	5	—	Part. Rec.	—
4:05	5	70	Recovery	Ether started.
4:07	20	—	Light	Slight struggling.
4:10	90	116	Deep	Exophthalmus.
4:14	90	142	Deeper	Resp. shallow; exophthalmus; ether withdrawn.
4:20	40	—	Part. Rec.	—
4:37	5	120	Recovery	—

In the dog, morphine does not ordinarily produce the degree of constriction seen in man. It does, however, increase oculomotor tone, particularly in evidence when inhibitory influences are removed, as by sleep. Thus, in this case, there was marked pupillary constriction after morphine, probably because the animal was still sufficiently depressed by the previous anesthetic.

Protocol I shows that, while in the normal dog deep ether and chloroform anesthesia both dilated the pupils, after a large dose of morphine, the pupils were dilated in deep ether and constricted in deep chloroform anesthesia. After a relatively small dose of morphine, Protocol II, insufficient to abolish struggling when the anesthetic was inhaled, chloroform in the stage of excitement caused dilatation of the pupils, but constriction in the period of deep narcosis. Ether, on the other hand, caused constriction of the pupils in the early stage of administration (there was no struggling, the animal having been depressed by the morphine and the previous anesthesia) and caused marked dilatation of the pupils in the period of deep narcosis.

Morphine slowed the heart rate. After the large dose of morphine, the heart rate remained slow in deep chloroform anesthesia, but became rapid in deep ether anesthesia. After a small dose of morphine, the same general relationship obtained; the heart accelerated moderately in chloroform anesthesia and markedly in ether anesthesia.

PROTOCOL II. Dog, male, weight 17.72 kg.

Time	Size of pupil	Heart rate	Stage of anesthesia	Remarks
3:28	40	75	—	1 mg. morphine sulphate per kg., muscle.
4:05	30	60	—	Chloroform started.
4:06	90	—	Light	Violent struggling.
4:20	20	95	Deep	—
4:21	40	—	Lighter	Corneal reflex just returned.
4:25	10	100	Very deep	Resp. very shallow; tongue cyanotic; eyes closed; enophthalmus; chloroform withdrawn.
4:33	50	85	Part. rec.	Ether started.
4:43	20	—	Light	Breathing so shallow that very little ether inhaled; no struggling.
4:45	20	115	Deep	Corneal reflex just disappeared; resp. deeper and faster.
4:50	50	130	Deeper	—
4:55	75	140	As above	Resp. good, 48 per minute.
4:56	90	160	As above	Exophthalmus; eyes open; ether withdrawn.
5:01	90	—	Part. rec.	—
5:07	80	160	Recovery	—

These experiments present evidence in support of the following statements: (1) The cause of dilatation of the pupils in the excitement period of chloroform anesthesia is different from that in deep anesthesia, since under given conditions one of these effects can be abolished and the other retained. (2) The dilatation of the pupils in the period of deep anesthesia is not the result of asphyxia but the direct effect of the anesthetic (probably direct depression of the oculomotor).

The parallel behavior of the cardio-inhibitor and the oculomotor is interesting. Morphine increases the tone of both nerves. After a large dose, chloroform, which did not depress the oculomotor, did not depress the cardio-inhibitor; while ether, which depressed the one, also depressed the other. After a small dose of morphine, however, the cardio-inhibitor was apparently more readily depressed than the oculomotor.

It seems probable that the difference shown between ether and chloroform in these experiments depends upon the fact recorded by Straub,[1] that morphine potentiates the toxicity of chloroform on the respiratory center. That the pupils dilate and the heart accelerates during deep chloroform anesthesia without morphine, but fail to do so after morphine, may be explained by the fact that in the latter case the animal dies of respiratory paralysis before a concentration of chloroform in the body is reached sufficient to depress the cardio-inhibitor and oculomotor nerves.

[1] Straub, W., *Munch. med. Wochenschrft.*, 1913, lx, 1823.